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Review

Transanal and Transvaginal Specimen Extraction in Laparoscopic Colorectal Surgery

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Keywords: Laparoscopic colorectal surgery; minimally invasive surgery; natural orifice specimen extraction; transanal specimen extraction; transvaginal specimen extraction.

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ABSTRACT

Due to its advantages, minimally invasive surgery has become a standard treatment approach in many surgical operations today. To address the complications associated with enlarged wounds for specimen extraction after minimally invasive surgery, the natural orifice specimen extraction (NOSE) method has been developed, allowing specimens to be extracted through natural openings. In addition to the existing advantages of laparoscopy, this method significantly reduces the rates of postoperative pain, infection, and hernia development.

Laparoscopic colectomy is frequently used in colorectal surgery. However, the specimen is typically extracted via mini-laparotomy. There are four potential approaches for extracting the specimen through natural openings after laparoscopic resection: transanal, transurethral, transoral, and transvaginal. In colorectal surgery, NOSE is generally categorized into two main approaches: the transanal and transvaginal routes, depending on the type of specimen extraction. Each of these methods has its own advantages and disadvantages.

This article aims to provide information on the transanal and transvaginal methods used for specimen extraction through natural openings in laparoscopic colorectal surgery and to compare these two approaches. Although specimen extraction via natural openings is a complex surgical procedure, it offers potential advantages. However, it requires advanced laparoscopic expertise. The transanal route can be used safely, particularly for early-stage and small-scale tumors, while the transvaginal route can be safely applied in female patients with larger lesions.

1. Introduction

Minimally invasive surgery has become a standard treatment approach in many surgical procedures today due to its well-known advantages such as shortening hospital stay, reducing wound complications, and improving cosmesis.[1,2] Although complex surgical procedures are performed in minimally invasive surgery, enlargement of the trocar entry site or additional incisions from a different area of the abdominal wall are often needed to extract the specimen. The increase in incision size contradicts the main aim of minimally invasive surgery.[3] This issue has led to the development of methods called natural orifices specimen extraction surgery (NOSES).[4]

Laparoscopy is frequently used because of its significant contributions to the treatment of colorectal diseases. Laparoscopic surgery has proven advantages.[5,6] The advantages of NOSES include an even shorter recovery time. Consequently, the incidence of abdominal wall hernia, surgical site infection, and postoperative pain is reduced.[7-9]

There are four potential approaches for extracting the specimen from natural openings after laparoscopic resection: transanal, transurethral, transoral, and transvaginal. In some studies in the literature, the term transanal is further subdivided into transanal, transrectal, and transcolonic. In colorectal surgery, NOSES is generally categorized into two types, transanal and transvaginal NOSES, based on the type of specimen extraction.[10]

2. History

Laparoscopic colon resection was first reported by Jacobs in 1991.[11] Franklin et al.[5] described the first transanal specimen extraction via flexible sigmoidoscopy in 1993. In 1996, Redwine et al.[6] first performed transvaginal extraction of the colon after laparoscopic segmental colectomy.

In the same year, Kim et al.[12] performed transvaginal extraction of the rectum after laparoscopic low anterior resection.

The only study in the literature comparing transanal and transvaginal specimen extraction in laparoscopic colon surgery was conducted by Franklin et al.[4]

3. Techniques

In general, the method used by the authors for NOSES is similar. Patients are operated on under general anesthesia in the modified Lloyd-Davies position. The transanal and transvaginal areas to be used for extraction are routinely lavaged with povidone-iodine solution. Pneumoperitoneum is created through the umbilicus using a Veress needle. Trocar sites are arranged according to the resection area. In most cases, four trocars (12 mm, 10 mm, and 2×0.5 mm) are used. The camera trocar is placed in the umbilical region, while the other trocars are positioned based on the disease's location.

Following radical surgical principles, the operation is performed laparoscopically. Subsequently, different procedures are applied for the laparoscopic-assisted approach and NOSES.

For specimen extraction after laparoscopic resection, the transanal route is chosen as the first option. If this fails or is deemed unsuitable, the transvaginal route is attempted in female patients. If both methods fail, the specimen is considered unsuitable for NOSES and is extracted through an abdominal wall incision.

3.1. Transanal Specimen Extraction Technique

The distal border is separated with staples. If the distal border is long enough, the stapled part of the rectal stump is resected, and the specimen is transanally extracted from the lumen. The upper limit of the anal region is determined and resected, and the anvil is placed into the abdomen through this site. The proximal end, closed with the stapler, is reopened, and the anvil is pushed into the proximal intestine. An end-to-side or end-to-end anastomosis is then performed.

3.2. Transvaginal Extraction Technique

After laparoscopic resection, the specimen is placed in a protective sheath. Using a grasper, the end of the bag is brought closer to the lower part of the abdomen, towards the Douglas pouch. The patient is positioned in the Trendelenburg and lithotomy positions. The uterus is tractioned. An orifice approximately 3 cm in size is opened and widened with a horizontal incision from the posterior superior vagina through the transvaginal route. A clamp is inserted through this opening, and the specimen bag with its contents is extracted. The posterior fornix is then closed with absorbable sutures.

Laparoscopic colon and rectal surgery requires experience with open methods as well as mastery of advanced laparoscopic techniques. Initially, port site metastases and technical difficulties hindered the rapid adoption of laparoscopic colon surgery compared to other laparoscopic procedures. Later, comparative multicenter studies demonstrated that laparoscopy is at least as safe as open methods, leading to its broader acceptance.[7]

Laparoscopic-assisted colectomy is the most frequently performed method in colorectal surgery worldwide. After the colon is released laparoscopically, the specimen is removed via minilaparotomy. In global literature, laparoscopic-assisted colectomy is generally referred to as laparoscopic colectomy or conventional laparoscopic colectomy. In real terms, total laparoscopic colectomy involves the extraction of the specimen through natural orifices and intracorporeal anastomosis. NOSES achieves this goal.

3.3. Extraction of the Specimen

The transanal route is primarily preferred for specimen extraction after resection. However, if the lesion is located close to the anal verge or the mass is too large to be extracted through the anal canal, transvaginal extraction is preferred in suitable female patients.

There is a risk of rectal injury with transvaginal extraction. Compared to transanal access, adjacent organs, especially the sigmoid colon and rectum, are more easily injured during transvaginal specimen extraction, which can result in longer recovery and hospital stays.[3] To minimize the risk of rectal injury during transvaginal extractions, it is beneficial to protect the rectum with a horizontal incision from the transvaginal posterior fornix and, if necessary, enlarge the incision horizontally. It is also crucial to make the incision as posterior-superior as possible so that it overlaps the peritoneal reflection.

Complications can be avoided by using the laparoscope's light to observe the transluminal view from the posterior cervix and by monitoring intra-abdominal localization during uterus traction while making the posterior fornix incision. If the patient has undergone a hysterectomy, performing a vaginotomy at the apex of the vagina instead of the posterior fornix is more practical. Additionally, since exposure is better in patients who have undergone hysterectomy, manipulations become easier.

In the study by Sanchez et al.,[13] the vagina was identified as the most practical and widely used area for specimen extraction. Since the bowel segment is resected in front of the rectum during transanal extraction, exposure can be more comfortable. This can be an advantage for transanal extractions.

3.4. Intracorporeal Anastomosis

In our opinion, the most reliable type of anastomosis in NOSE surgery involves the proximal and distal closure of the lesion with a stapler, resection, specimen extraction through the natural orifice, and performing an intracorporeal end-to-side or end-to-end anastomosis using an anvil inserted through the same route. However, since intracorporeal anastomosis requires advanced technical expertise, the learning curve is long.

4. Risk of Infection

One of the most debated issues in NOSES is the risk of abscess formation due to the leakage of intestinal contents into the peritoneum during perioperative opening of the intestine. However, studies have shown that findings after transanal specimen extraction do not significantly impact the inflammatory response or infectious morbidity.[14] Additionally, it is known that surgical site infections are less common in transvaginal extractions due to the rich blood circulation of the vagina.[15]

Costantino et al.[14] prospectively evaluated peritoneal contamination after NOSE surgery and found that 100% of sample fluid cultures were positive. However, they demonstrated that, despite contamination, it did not result in infectious morbidity, and there was no significant difference in clinical outcomes compared to those in the conventional laparoscopic approach.[14]

5. Anal Dilation

In transanal extractions, anal dilation is typically performed first. This procedure may be beneficial for both specimen extraction and the use of a circular stapler. However, it may lead to complications related to continence. For this reason, it is advisable to perform anal dilation selectively in patients where extraction can be performed through the anus but requires dilation or in cases where the passage of the stapler would be complicated.

It is also important to extract the specimen gently during this process. Sphincter dysfunction due to anal dilation or specimen extraction can be considered a disadvantage for transanal NOSES. In female patients with a high risk of sphincter dysfunction during transanal extraction, transvaginal extraction may be preferred, especially if the patient has completed her family and the specimen size is large.

6. Using a Protective Sheath

Studies have shown that a protective sheath is generally used in transanal incisions.[16,17] However, some authors have reported not using it.[16] Using a protective sheath prior to transanal extraction may be impractical, as the sheath's volume can make extraction more difficult. Nonetheless, it is beneficial to use a protective sheath in transvaginal extractions, particularly for malignant lesions, to avoid seeding.

Transvaginal extraction is often more feasible than transanal extraction due to the flexibility of the vagina. In the study by Zhou et al.,[18] it was observed that NOSES did not increase the risk of local recurrence, and that recurrence and long-term outcomes were comparable to conventional laparoscopic surgery, particularly at transanal extraction sites and port areas.[18]

Concerns regarding local recurrence and long-term oncological outcomes after colorectal NOSES have led to studies comparing it with conventional laparoscopic surgery.[3,19] These studies have demonstrated that NOSES alleviates such concerns completely.[3]

In two studies comparing abdominal and vaginal tract surgeries related to transvaginal extraction, no postoperative differences were observed in vaginal sensation, ability to achieve orgasm, pregnancy rates, or dyspareunia rates.[20,21]

7. Closing the Vaginal Opening

Although some publications state that the opening created in the posterior cervix does not need to be closed, it is typically closed routinely with absorbable suture material.[22] This closure is usually performed transvaginally; however, in cases where transvaginal closure is difficult, laparoscopic closure may be performed intracorporeally.

8. Rectovaginal Fistula

In cases of an anastomotic leak in the rectum following transvaginal extraction, the weakest point is often the area of the vagina where the incision was made. This can lead to the development of a rectovaginal fistula. Interestingly, this situation can sometimes be beneficial for controlling leakage and may even be considered advantageous in uncomplicated cases. In the study by Franklin et al.,[5] the rate of anastomotic leakage was reported as 1.1% in transanal extractions.

9. Disruption of the Integrity of the Specimen

One of the criticisms of colorectal NOSES is the division of the mesocolon or mesorectum. It may be necessary to divide the mesocolon or mesorectum to facilitate specimen extraction. However, this practice is not fully aligned with oncological principles and remains a topic of debate.

Although dividing the mesocolon or mesorectum is performed using vessel-sealing devices, there is a concern about the potential for tumor seeding. While this procedure is performed safely in benign diseases, it is subject to criticism in malignant cases. In my opinion, this is the weakest point of NOSES.

10. Limitations of the Procedure

Male gender, patient disapproval, inappropriate vaginal access, and large masses are limitations of the procedure. Additionally, inconsistency between the specimen size and the posterior fornix of the vagina, as well as a tumoral mass larger than 8-12 cm, can cause technical difficulties.

NOSES is not applied in locally advanced tumors, cases of acute intestinal obstruction, or tumor perforation. Transvaginal extraction is most suitable for T2 and T3 tumors, patients with a body mass index (BMI) of 30-35 kg/m², and specimens with a largest diameter of 3-5 cm. How-

ever, transvaginal extraction should not be recommended for young women who have not completed their families.

If the largest circumferential diameter of the specimen is less than 3 cm and the BMI is below 30 kg/m², transanal extraction is more appropriate. Transanal extraction is not suitable in the presence of anal stenosis or anal dysfunction.[3]

Conclusion

Despite its potential advantages, NOSES is a complicated surgical procedure that requires advanced technical expertise and is more time-consuming. Moreover, the surgeon must have significant experience in advanced laparoscopy.

In colorectal lesions, NOSES can be safely applied via the transanal route, particularly for benign lesions, early-stage tumors, or small lesions, and via the transvaginal route for larger lesions in female patients.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Conflict of Interest

None declared.

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Laparoskopik Kolorektal Cerrahide Transanal ve Transvajinal Spesmen Ekstraksiyonu

Minimal invaziv cerrahi, avantajları nedeniyle günümüzde birçok cerrahi operasyonda standart tedavi yaklaşımı haline gelmiştir. Minimal invaziv cerrahi sonrasında numunenin çıkarılması için genişlemiş yaraların komplikasyonları nedeniyle, numunenin doğal deliklerden çıkarılmasına olanak tanıyan doğal delikli numune çıkarma yöntemi geliştirilmiştir. Bu yöntemin mevcut laparoskopi avantajlarının yanı sıra ameliyat sonrası ağrı, enfeksiyon ve fıtık gelişme oranını da önemli ölçüde azalttığı gözlemlenmiştir.

Laparoskopik kolektomi kolorektal cerrahide sıklıkla kullanılmaktadır. Ancak spesmen mini lapartomi ile çıkarılmaktadır. Laparoskopik rezeksiyon sonrasında spesmenin doğal deliklerden çıkarılmasının dört olası yöntemi vardır: Transanal, transüretral, transoral ve transvajinal. Kolorektal cerrahide doğal orifislerden spesmen çıkarılma yöntemi, genel olarak transanal ve transvajinal yol olmak üzere iki kategoriye ayrılmaktadır. Bu iki ekstraksiyon yönteminin avantajları ve dezavantajları bulunmaktadır.

Bu makale, laparoskopik kolorektal cerrahide doğal deliklerden örnek çıkarmak için kullanılan transanal ve transvajinal yollar hakkında bilgi vermek ve bu iki yöntemi karşılaştırmak amacıyla yazıldı. Doğal deliklerden numune çıkarılması karmaşık bir cerrahi işlem olmasına rağmen potansiyel avantajlara sahiptir. Ancak ileri düzeyde laparoskopik deneyim gerektirir. Özellikle erken evre ve küçük çaplı tümörlerde transanal yol, lezyonları daha büyük olan kadın hastalarda ise transvajinal yol güvenle kullanılabilir.

Anahtar Sözcükler: Doğal deliklerden spesmen ekstraksiyonu; laparoskopik kolorektal cerrahi; minimal invazif cerrahi; transanal numune ekstraksiyonu; transvajinal numune ekstraksiyonu.

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Original Article

Evaluation of the Effect of Pelvic Organ Prolapse on Renal Function: Retrospective Cohort Study

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Keywords: Glomerular filtration rate; Hydronephrosis; Pelvic organ prolapse; Renal failure.

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ABSTRACT

Objective: Pelvic organ prolapse (POP) is a common condition; however, it is rarely observed to affect renal functions and cause hydronephrosis. In our study, we aimed to evaluate these effects of POP.

Methods: In this retrospective study, patients who underwent anti-prolapse surgery due to POP were included as the case group, and those who underwent hysterectomy for non-POP indications were included as the control group between January 1 and July 1, 2024. Renal function blood parameters (urea, creatinine, blood urea nitrogen [BUN], glomerular filtration rate [GFR], and uric acid values) were compared between the control and POP groups. Preoperative urinary system ultrasonography (US) data were also analyzed.

Results: Patients were included in the POP group and the control group (N1=N2=187). The groups were statistically similar and homogeneous in terms of age (p=0.678) and comorbidities (p=0.872). The number of patients with values outside laboratory cut-off values was 8, 17, 51, 16, and 15 patients in the POP group for creatinine, uric acid, GFR, urea, and BUN, respectively. GFR (p<0.001), urea (p=0.005), and BUN (p=0.008) values showed statistically significant differences between the two groups. When renal function tests were analyzed according to POP grades, no significant differences were detected for any parameter between grades 2, 3, and 4. Hydronephrosis was detected in 9 patients (16.4%) in the POP group evaluated with urinary US.

Conclusion: We determined that lower GFR, and higher BUN and urea values were present in the prolapse group. Although it is believed that this condition may regress after POP surgery, data supporting this could not be obtained due to the retrospective nature of the study.

INTRODUCTION

Pelvic organ prolapse (POP) is a condition that can present with vaginal bulging, urinary, defecation, and sexual problems and affects the quality of life.[1,2] Risk factors for POP include older age, higher gravidity and parity, obesity, smoking, chronic cough, and constipation.[2] The prevalence of surgery due to pelvic organ prolapse varies between 11% and 18% in the literature, and it is thought to increase further with the aging world population.[2-4] Many techniques have been described in the surgical treatment of pelvic organ prolapse, including anterior and posterior vaginal repair, sacrocolpopexy, sacrospinous fixation, uterosacral ligament suspension, and lateral suspension, which can be performed vaginally, abdominally, or laparoscopically.[2,5-7] The appropriate technique for treatment is selected individually for the patient, depending on the compartment and degree of prolapse.[2]

In current meta-analyses and studies, the prevalence of hydronephrosis (HN) and renal failure (RF) due to POP is 3.5-30.6% and 3.3%, respectively.[8,9] After surgical repair of prolapse, complete resolution or partial recovery may also ocur.[8,10] Although renal complications due to POP are rare, it may cause severe uretero-hydro-nephrosis, acute or chronic RF in patients, which may lead to dialysis and renal transplantation.[9] A positive correlation has been determined between the degree and duration of prolapse and the degree of HN and RF.[11] In this retrospective study, we aimed to evaluate POP-related renal function failure and the effect of hydronephrosis, if present.

MATERIALS AND METHODS

This study was designed retrospectively. An evaluation was made on patients at a tertiary health center between 01/01/2024 and 01/07/2024. Patients who underwent anti-prolapse surgery with hysterectomy indication for benign reasons within a 6-month period were determined as the case group. As the control group, patients who were not diagnosed with POP and underwent hysterectomy for benign gynecological indications were randomly selected in a 1:1 ratio. The study was approved by the Institutional Scientific Research Ethical Board (No: E-2024/010.99/6/26). Since it was a retrospective study, written and verbal consent was not obtained from the patients. In addition, the study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

The inclusion criteria were as follows: (1) age of 40–80 years; (2) patients who underwent only hysterectomy or concurrent anti-prolapse surgery for benign indications. The exclusion criteria were: (1) patients with malignancies; (2) patients with a history of renal disease or comorbidities that may cause renal failure, including uncontrolled diabetes mellitus or hypertension, etc.; (3) patients with previous POP surgery.

Patients' ages, parity, body mass index (BMI), comorbidity data, surgical procedure information, preoperative renal function blood parameters (urea, creatinine, BUN, GFR, and uric acid values), pelvic organ prolapse quantification (POP-Q) stages, presence of urinary system ultrasonography, and HN data were collected from the hospital database system. Cut-off ranges for blood parameters are <0.95 mg/dl, 2.6-6 mg/dl, ≥90 ml/min, 17-43 mg/dl, and 6-20 mg/dl for creatinine, uric acid, GFR, urea, and BUN, respectively (cut-off values have been validated by the hospital laboratory and biochemistry experts).

The primary outcomes involved assessing the effect of pelvic organ prolapse on renal function parameters. For this purpose, renal function blood parameters were compared between control and case groups. The secondary outcomes involved assessing the percentage of hydronephrosis in the POP group.

Statistics Analysis

Normality assumptions were assessed using the Shapiro–Wilk test and skewness/kurtosis values. Descriptive statistics included mean, standard deviation (SD), median, number, and frequency. The Chi-square test and Fisher's Exact Test were used to compare categorical variables. Normally and non-normally distributed paired groups for preoperative blood parameters were compared using paired samples t-test and ANOVA test. The data were analyzed with IBM SPSS Statistics version 22.0 (IBM Corporation, Armonk, NY, USA). All tests were two-sided, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

In the study, 374 patients were evaluated between January 1, 2024, and July 1, 2024. To compare 187 patients who underwent surgery due to pelvic organ prolapse, 187 patients were randomly selected as the control group. The groups were statistically similar and homogeneous in

Table 1. Group characteristics and comparison of renal function tests between pelvic organ prolapse and control groups

	Pelvic organ prolapse group (n=187)	Control Group (n=187)	p
Age (year)	60.19±7.11	58.86±6.52	0.678
Surgery type (n,%)			
VH + McCall culdoplasty	45 (24)		
VH + Sacrospinous fixation	23 (12.4)		
VH + vaginal sacrouterine plication	67 (35.8)		
TAH + Abdominal sacrocolpopexy	21 (11.2)		
TLH + Laparoscopic sacrouterine plication	18 (9.6)		
Laparoscopic lateral suspension	13 (7)		
TAH (+/- BSO)		44 (23.5)	
TLH (+/- BSO)		125 (76.9)	
Ovarian cystectomy		18 (9.6)	
Creatinin (mg/dl)	0.67±0.16	0.66±-0.24	0.558
Uric acid (mg/dl)	4.48±1.08	4.29±1.13	0.116
GFR (ml/min)	93±14.06	103.9±13.59	<0.001
Urea (mg/dl)	32.02±9.71	25.98±7.93	<0.001
BUN (mg/dl)	14.93±4.49	12.14±3.77	<0.001
Hb (g/dl)	13.01±0.96	11.49±1.48	<0.001

VH: Vaginal hysterectomy; TAH: total abdominal hysterectomy; TLH: total laparoscopic hysterectomy; BSO: bilateral salpingo-oophorectomy; GFR: Glomerular filtration rate; CK: creatinine kinase; BUN: blood urea nitrogen.

terms of age (p=0.678) and comorbidities (p=0.872).

In the control group, 123 patients (65.8%), 41 patients (21.9%), and 23 patients (12.3%) underwent surgery due to abnormal uterine bleeding, myoma uteri, and adnexal cyst, respectively. The types of surgeries performed in the two groups are given in Table 1. Preoperative renal function test values are provided in Table 1. The number of patients with values outside laboratory cut-off ranges was 8, 17, 51, 16, and 15 for creatinine, uric acid, GFR, urea, and BUN, respectively, in the POP group. GFR, urea, and BUN values showed statistically significant differences between the two groups (Table 1 and Table 2). Lower GFR and higher BUN and urea values were observed in the prolapse group. When renal function tests were analyzed according to POP grades, no significant difference was detected for any parameter between grades 2, 3, and 4 (Table 3).

The preoperative hemoglobin value in the control group was found to be 11.49±1.48, significantly lower than in the POP group.

It was determined that 1 patient (1.7%) with POP grade 2 and 54 patients (42.2%) with grades 3 and 4 had urinary system ultrasonography (US) in the retrospective screening. Hydronephrosis was detected in 9 patients (16.4%) in the POP group evaluated with urinary US. Of these patients, 6 had grade 1 HN and 3 had grade 2 HN. In the postoperative period, 2 of the 3 patients with grade 2 HN underwent control US, and it was found that the HN had decreased to grade 0.

DISCUSSION

Pelvic organ prolapse (POP) may be associated with mi-

Table 2. Comparison of renal function parameters between pelvic organ prolapse and control groups according to laboratory reference values

	Pelvic organ prolapse group (n=187)	Control Group (n=187)	p
Creatinin			
<0.95 mg/dl	179 (95.7)	183 (97.9)	
≥0.95 mg/dl	8 (4.3)	4 (2.1)	0.284
Uric acid			
2.6-6 mg/dl	170 (90.9)	172 (92)	
≥6 mg/dl	17 (9.1)	15 (8)	0.427
GFR			
≥90 ml/min	136 (72.7)	168 (89.8)	
<90 ml/min	51 (27.3)	19 (10.2)	<0.001
Urea			
17-43 mg/dl	171 (91.4)	183 (97.9)	
≥43 mg/dl	16 (8.6)	4 (2.1)	0.005
BUN			
6-20 mg/dl	172 (92)	183 (97.9)	
≥20 mg/dl	15 (8)	4 (2.1)	0.008

GFR: Glomerular filtration rate; BUN: blood urea nitrogen; Variables are reported n (percentage,%) format.

Table 3. Comparison of renal function parameters of patients in the pelvic organ prolapse group according to prolapse grades

	Grade 2 POP (n=59)	Grade 3 POP (n=56)	Grade 4 POP (n=72)	p
Creatinin (mg/dl)	0.66±0.15	0.68±0.20	0.67±0.13	0.661
Uric acid (mg/dl)	4.47±1.08	4.06±1.14	4.38±1.05	0.349
GFR (ml/min)	93.7±13.57	92.73±15.41	92.61±13.51	0.789
Urea (mg/dl)	31.71±7.37	31.26±13.20	32.86±8.14	0.788
BUN (mg/dl)	14.79±3.45	14.62±6.16	15.29±3.66	0.491
Hb (g/dl)	13.04±0.94	12.98±0.93	13.01±1.02	0.855

POP: Pelvic organ prolapse; GFR: Glomerular filtration rate; BUN: blood urea nitrogen; Hb: hemoglobin.

nor or major urological problems, including urinary tract infection, hydronephrosis (HN), and renal dysfunction.[9,12] The main reason for the pathophysiology of this condition is thought to be that the bladder or uterus pushes downward, increasing ureteral pressure, causing mucosal edema, and leading to partial/total obstruction.[9] It has been suggested that there is a relationship between hydronephrosis/renal failure and the severity and duration of prolapse.[8,11]

In this study, we determined that lower GFR and higher BUN and urea values were present in the prolapse group. However, it was found that this change in renal function parameters was not associated with the degree of prolapse, contrary to expectations. It was thought that this situation might be caused by the different cohort and the small number of patients. The hemoglobin value in the control group was found to be lower due to the fact that the indication for most surgeries was abnormal uterine bleeding. However, since the average hemoglobin value of the control group was above the anemia threshold, we think that this difference did not affect renal perfusion and can be considered negligible.

In a systematic review investigating hydronephrosis associated with POP, the prevalence of hydronephrosis was found to be between 3.5% and 30.6%, and it was stated that hydronephrosis had complete resolution in 56% to 83% of cases after surgical treatment of prolapse.[8] Additionally, current literature suggests that urinary system ultrasonography (US) should be performed routinely in severe POP cases.[11] Urinary system US was performed in 42.2% of patients with stage 3 and 4 POP, and the hydronephrosis rate was found to be 16.4%, similar to the literature. Complete recovery was detected by control US in 2 of 3 patients with grade 2 HN postoperatively. Control urinary US was not performed in patients with grade 1 HN. This retrospective study showed that the evaluation of hydronephrosis in patients with POP is lacking and awareness should be raised among clinicians on this issue.

Although HN and renal failure (RF) due to POP are rare complications, POP repair usually resolves prolapse-associated hydronephrosis and prevents serious long-term complications.[10,13] However, some studies have found that renal functions did not significantly improve (GFR value) after POP repair or were limited to partial recovery (creatinine value).[14,15] As the authors, we think that the degree and duration of prolapse may affect the return of renal functions and HN in the postoperative period. Early surgical repair of POP may preserve renal function in patients with symptomatic prolapse.

To the best of our knowledge, this study is the first to compare renal functions with a control group in the literature, but it also has some limitations. The main limitation is that, since it was a retrospective study, postoperative renal functions and hydronephrosis were not clearly evaluated. This study can be expanded prospectively with a larger patient population in future research.

Conclusion

Renal function parameters, including GFR, urea, and BUN, are negatively affected by the presence of POP. Although it is thought that there may be improvement in HN and renal function parameters after POP surgery, data supporting this could not be obtained since it was a retrospective study. It should be kept in mind that there may be HN and RF associated with POP, and evaluation should be performed using both blood tests and renal US in the preoperative and postoperative periods.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 26.07.2024, Decision No: E-2024/010.99/6/26).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: P.B.İ., M.M.K., B.C., A.İ.; Design: P.B.İ., M.M.K., B.C., A.İ.; Supervision: P.B.İ., M.M.K.; Materials: P.B.İ., M.M.K., B.C., A.İ.; Data collection &/or processing: P.B.İ., M.M.K., B.C., A.İ.; Analysis and/or interpretation: P.B.İ., M.M.K.; Literature search: P.B.İ., M.M.K., B.C., A.İ.; Writing: P.B.İ., M.M.K., B.C., A.İ.; Critical review: P.B.İ., M.M.K.

Conflict of Interest

None declared.

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Pelvik Organ Prolapsusunun Böbrek Fonksiyonu Üzerine Etkisinin Değerlendirilmesi; Retrospektif Kohort Çalışması

Amaç: Pelvik organ prolapsusu (POP) yaygın bir durumdur; ancak böbrek fonksiyonlarını etkilediği ve hidronefroza neden olduğu nadiren görülür. Çalışmamızda, POP'un bu etkilerini değerlendirmeyi amaçlıyoruz.

Gereç ve Yöntem: Bu retrospektif çalışmada, POP nedeniyle anti-prolapsus cerrahisi uygulanan hastalar vaka grubu olarak, POP dışı endikasyonlarla histerektomi uygulanan hastalar ise kontrol grubu olarak dahil edildi. Böbrek fonksiyonu kan parametreleri (üre, kreatinin, kan üre azotu [BUN], glomerüler filtrasyon hızı [GFR] ve ürik asit değerleri) kontrol ve POP grupları arasında karşılaştırıldı. Ameliyat öncesi üriner sistem ultrasonografisi (US) verileri de analiz edildi.

Bulgular: Hastalar POP grubu ve kontrol grubuna (N1=N2=187) dahil edildi. Gruplar yaş (p=0.678) ve komorbiditeler (p=0.872) açısından istatistiksel olarak benzer ve homojendi. Laboratuvar eşik değerleri dışında değerlere sahip hasta sayısı kreatinin, ürik asit, GFR, üre ve BUN için POP grubunda sırasıyla 8, 17, 51, 16 ve 15 hastaydı. İki grupta GFR (p<0.001), üre (p=0,005) ve BUN (p=0.008) değerleri arasında istatistiksel olarak anlamlı fark vardı. Böbrek fonksiyon testleri POP derecelerine göre incelendiğinde, derece 2, 3 ve 4 arasında hiçbir parametrede anlamlı fark saptanmadı. Renal US ile değerlendirilen POP grubunda 9 hastada (%16.4) hidronefroz tespit edildi.

Sonuç: Prolapsus grubunda daha düşük GFR, yüksek BUN ve üre değerleri olduğunu saptadık. Bu durumun POP ameliyatından sonra geri leyebileceği düşünülse de, retrospektif bir çalışma olduğu için bunu destekleyen veri elde edilemedi.

Anahtar Sözcükler: Böbrek yetmezliği; glomerüler filtrasyon hızı; hidronefroz; pelvik organ prolapsusu.

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Original Article

Factors Affecting Recurrence in Transverse Colon Tumors: A Single-Center Study

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Keywords: ECOG; histopathological subtype; lymphovascular invasion; MSI status; pathological T stage; perineural invasion; prognosis; recurrence factors; transverse colon cancer.

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ABSTRACT

Objective: The localization of colon tumors has prognostic significance. Based on the origin of the primary mass, tumors are classified as right or left colon tumors. During embryological development, right colon tumors (RCC) originate from the mid-gut, while left colon tumors (LCC) originate from the hind-gut. Transverse colon tumors (TCC) account for 10% of all colon tumors. Due to their heterogeneous embryological development, these tumors can behave similarly to either right or left colon tumors. Our knowledge of prognosis is limited due to their inclusion in studies as right colon tumors or exclusion from studies. Our study aims to investigate whether TCC differs from right or left colon tumors by utilizing clinical, pathological, and molecular prognostic factors known to be important in colon cancer, as well as their anatomical localization.

Methods: Non-metastatic patients who underwent surgery for transverse colon cancer at our hospital were retrospectively included. Demographic data, pathological features, and treatment status were analyzed.

Results: Seventy-six patients with transverse colon tumors who underwent surgery were included in our study. No significant difference was found between recurrence and gender, comorbidity, type of surgery, stage at diagnosis, grade, pathological nodal stage, MSI status, and adjuvant treatment status ($p>0.05$). However, a significant difference was observed in the relationship between recurrence and histopathological subtype, ECOG, perineural invasion, lymphovascular invasion, and pathological T stage. Multivariable analysis of parameters associated with recurrence revealed that the presence of perineural invasion alone increased recurrence by 25 times and was found to be an independent poor prognostic factor.

Conclusion: Perineural invasion was found to be an independent prognostic indicator that predicts recurrence by 25 times in non-metastatic patients with transverse colon tumors. This result can be effectively used in predicting prognosis and making treatment decisions in patients.

INTRODUCTION

The primary tumor localization in colorectal cancers holds prognostic significance in both the local and metastatic stages.[1] Tumors are classified as right or left colon cancers based on the origin of the primary mass. Masses located proximal to the splenic flexure are considered right colon tumors, while those distal to it are classified as left colon tumors. During embryonic development, right colon tumors (RCC) originate from the mid-gut, and left colon tumors (LCC) from the hindgut, resulting in distinct anatomical, developmental, and carcinogenic differences.[2] Due to these fundamental differences, right and left colon tumors not only exhibit variations in prognosis but also demonstrate distinct surgical approaches in the local stage and predictive differences in response to therapeutic agents in the metastatic stage. In metastatic disease, anti-EGFR agents are preferred in left-sided, RAS/BRAF wild-type tumors in addition to chemotherapy, whereas Bevacizumab is used alongside chemotherapy in right-sided tumors.[3-6] However, the adjuvant treatment of surgically resected localized transverse colon tumors is similar to that of tumors originating from other parts of the colon.

The proximal two-thirds of the transverse colon, including the hepatic flexure, is considered to be of midgut origin, while the distal one-third, including the splenic flexure, is derived from the hindgut. Transverse colon cancers (TCC) account for only 10% of all colon cancers.[7] Due to their heterogeneous embryologic development, these tumors may exhibit behavior akin to either right or left colon cancers. Like right-sided tumors, TCCs are often diagnosed with bulky masses at an advanced stage (T4), as they do not present with specific symptoms until late

in their course.[8] Additionally, microsatellite instability is frequently observed in these tumors.[9]

Conversely, like LCCs, RAS/BRAF wild-type tumors in TCCs have shown good responses to anti-EGFR therapy.[10] Due to their inclusion in studies alongside right-sided tumors or their exclusion from studies altogether, there needs to be more information on the treatment responses and prognosis of these tumors.[11,12] A retrospective analysis demonstrated that tumors originating from the transverse colon have a distinct mutational profile and consensus molecular subtype (CMS) frequencies compared to left- and right-sided colorectal cancers.[9] This study highlighted that transverse colon tumors exhibit unique mutational characteristics that differentiate them from both right and left colon tumors, suggesting that they should be regarded as separate entities.

Given these considerations, our study aims to investigate whether TCC differs from right or left colon cancers by examining clinical, pathological, and molecular prognostic factors and assessing the impact of anatomical localization, which is known to be significant in colon cancer.

MATERIALS AND METHODS

Study Design and Patients

We evaluated patients diagnosed with transverse colon cancer who underwent surgery and received follow-up care at our center, between 2005 and 2024. Our study was designed as a retrospective, cross-sectional, and descriptive analysis. Transverse colon tumors were defined to include those located at the hepatic flexure and those distal to the splenic flexure. All patients included in our study were non-metastatic and aged 18 years or older. The localization of all tumors was verified through both colonoscopy and radiological imaging methods. A total of 76 patients with surgically resected transverse colon cancer who met the study's inclusion criteria were analyzed.

This study complied with the Declaration of Helsinki, and local ethics committee approval was obtained from our hospital (Approval number: 2024/010.99/6/10, approval date: 26.07.2024).

Clinical Data Collection

We collected demographic data from the study population, including sex, age, and Eastern Cooperative Oncology Group (ECOG) performance status at diagnosis. Additionally, we assessed the type of surgery performed, whether the operation was conducted as an emergency, whether patients received adjuvant therapy, and, if so, the specific drugs included in the adjuvant treatment. Histopathological data were also collected, including pT, pN, tumor grade, presence of a mucinous component, lymphovascular invasion (LVI)/perineural invasion (PNI), and tumor localization (hepatic flexure, mid-transverse colon, splenic flexure). Furthermore, metastasectomies and systemic treatments administered to patients who experienced recurrence were evaluated.

Statistical Analysis

The primary outcome variables were disease-free survival (DFS), defined as the time from diagnosis to disease recurrence or the development of distant metastasis, and overall survival (OS), defined as the time from diagnosis to death from any cause. Chi-square and Fisher's exact tests were employed to compare categorical variables such as age, gender, and ECOG performance score. The relationships between clinicopathologic parameters were initially analyzed using univariate logistic regression. The Cox regression model was applied to identify the most significant predictor variables through univariate and multivariate analyses. A p-value of <0.05 was considered statistically significant for all analyses. Statistical analyses were conducted using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, New York, USA).

RESULTS

A total of 76 patients diagnosed with localized or locally advanced transverse colon cancer who underwent surgery were included in our study. The median age of the patients was 60.76 years (range: 29-86 years). Forty-seven patients (61.8%) were male, and 29 (38.2%) were female. The clinicopathologic characteristics of the patients are summarized in Table 1. Ninety percent of the patients had an ECOG score of 0 or 1. Emergency surgery due to obstruction or perforation was performed in 7 patients (9.6%). The most common pathological stages observed were pT3 (72.4%) and N0 (64.5%). The most frequently diagnosed stage at presentation was stage 2 (59.2%), followed by stage 3 (35.5%). Adenocarcinoma was the most common histological type (78.9%), with mucinous adenocarcinoma observed in 15 patients (19.7%).

Among stage 2 patients, key factors influencing the decision to administer adjuvant therapy included high microsatellite instability (MSI) rate of 26.8%, grade 3 disease in 15.5% of patients, inadequate lymph node dissection (<12 lymph nodes) in 14.7%, presence of lymphovascular invasion in 70.6%, perineural invasion in 68.2%, and pT4 tumor stage in 19.7%. Adjuvant therapy was administered to 46 patients (60.5%), with XELOX being the most commonly used regimen (65.9%). The most frequent duration of treatment was six months (68.2%).

During the follow-up period, 11 patients experienced recurrence or metastasis. Systemic treatment was administered to six of these patients. No statistically significant differences were found between recurrence and factors such as gender, comorbidity, type of surgery, stage at diagnosis, tumor grade, pathological nodal stage, MSI status, and receipt of adjuvant therapy ($p>0.05$). However, significant associations were observed between recurrence and histopathological subtype, ECOG performance score, perineural invasion, lymphovascular invasion, and pathological T stage (Table 2). In the multivariable analysis of recurrence-related parameters, the presence of perineural invasion emerged as an independent poor prognostic factor,

Table 1. Demographic and Clinical Characteristics of Patients

Varaible	n=76 (%)
Age (mean±SD)	60.76±13.3
Gender	
Female	29 (38.2)
Male	47 (61.8)
Comorbidity (n=73)	
Present	32 (43.8)
Absent	41 (56.2)
Type of surgery (n=73)	
Emergency	7 (9.6)
Elective	66 (90.4)
Histopathology	
Adenocarcinoma	60 (78.9)
Mucinous adenocarcinoma	15 (19.7)
Medullary carcinoma	1 (1.3)
Grade (n=71)	
Grade 1	11 (15.5)
Grade 2	49 (69.0)
Grade 3	11 (15.5)
Lymphovascular Invasion (n=68)	
Present	48 (70.6)
Absent	20 29.4)
Perineural Invasion (n=66)	
Present	45 (68.2)
Absent	21 (31.8)
Pathological T Stage	
T1	1 (1.3)
T2	5 (6.6)
T3	55 (72.4)
T4	15 (19.7)
Pathological N Stage	
N0	49 (64.5)
N1	20 (26.3)
N2	7 (9.2)
Lymph Node Dissection (n=75)	
<12 lymph nodes	11 (14.7)
≥12 lymph nodes	64 (85.3)
Microsatellite Instability (n=56)	
MSI-Low	13 (23.2)
MSI-Stabil	28 (50.0)
MSI-High	15 (26.8)
Stage at Diagnosis	
I	4 (5.3)
II	45 (59.2)
III	27(35.5)
Age	
>60 years	38 (50.0)
≤60 years	38 (50.0)
ECOG (n= 65)	
0	33 (50.8)
1	26 (40.0)
2	5 (7.7)
3	1 (1.5)
Adjuvant Therapy	
Received	46 (60.5)
Not received	30 (39.5)
Adjuvant Chemotherapy Regimen (n=44)	
XELOX	29 (65.9)
FOLFOX	3 (6.8)
Capecitabine	12 (27.3)
Duration of Adjuvant Therapy (n= 44)	
3 months	12 (27.3)
4 months	2 (4.5)
6 months	30 (68.2)
Recurrence	
Present	11 (14.5)
Absent	65 (85.5)

ECOG: Eastern Cooperative Oncology Group; n: number of patients; T stage: tumor stage; N stage: node stage; MSI: Microsatellite Instability; MSI-Low: Microsatellite Instability-Low MSI-Stabil: Microsatellite Stable; MSI-High: Microsatellite Instability-High; XELOX: Capecitabine + Oxaliplatin; FOLFOX: 5-Fluorouracil + Leucovorin + Oxaliplatin; SD: Standard Deviation.

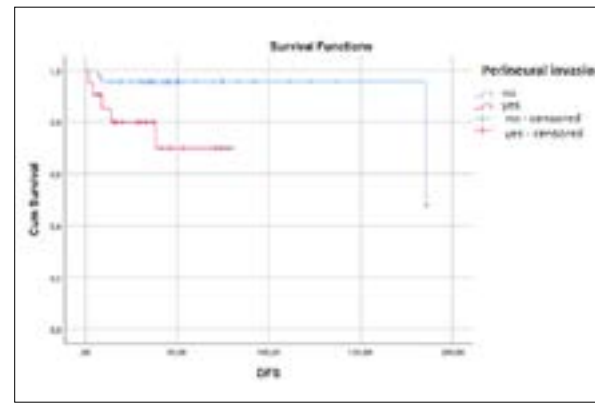

Figure 1. Kaplan_Meier curve of disease-free survival analysis according to perineural invasion.

increasing the risk of recurrence by 25-fold (HR 25.7, 95% CI: 1.23-534.8, p=0.03) (Fig. 1). The mean DFS for patients without perineural invasion was 177.7 months, compared to 60.8 months for those with perineural invasion.

DISCUSSION

The localization of the primary tumor has become increasingly important in the management of metastatic colorectal cancer. Whether the tumor is localized in the right or left colon significantly influences the approach to the disease and treatment options. However, considering the embryonic development, vascularization, and lymphatic drainage of the colon, more than a simple right-left classification may be required to capture the complexity of the disease entirely, necessitating more detailed subtyping of the colon. Research in this area is ongoing.[7,9,13]

Table 2. Analysis of Factors Influencing Disease-Free Survival (DFS) in Patients

All Patients (n=76)	Recurrence n=11	p	Multivariate analysis HR (95%CI)	p
Gender				
Female	5	0.34		
Male	6			
Comorbidity (n=73)				
Present	6	0.35		
Absent	4			
Type of Surgery (n=73)				
Emergency	1	0.72		
Elective	9			
Histopathology				
Adenocarcinoma	7			
Mucinous adenokarsinom	3	0.00*	9.57 (0.88-103.3)	0.06
Medullary Carcinoma	1			
Grade n=71				
Grade 1	2			
Grade 2	6	0.84		
Grade 3	2			
Lymphovascular Invasion n=68				
Present	6	0.03*	0.9 (0.13-6.70)	0.95
Absent	4			
Perineural Invasion n=66				
Present	5	0.01*	25.7 (1.23-534.8)	0.03*
Absent	3			
Pathological T Stage				
T1	0			
T2	1	0.02*	3.77 (0.44-32.03)	0.22
T3	5			
T4	5			
Pathological N Stage				
N0	4			
N1	5	0.08		
N2	2			
Lymph Node Dissection n=75				
<12 lymph nodes	2	0.58		
≥12 lymph nodes	8			
Microsatellite Instability n=56				
MSI-Low	2			
MSI-Stabil	4	0.89		
MSI-High	3			
Stage at Diagnosis				
I	0			
II	4	0.07		
III	7			
Age				
>60 yaş	6	0.48		
≤60 yaş	5			
ECOG n=65				
0	3			
1	5	0.00*	3.92 (0.60-25.50)	0.15
2	0			
3	1			
Adjuvant Therapy				
Received	6	0.81		
Not Received	5			
Adjuvant Chemotherapy Regimen n=44				
XELOX	3			
FOLFOX	1	0.36		
Capecitabine	1			
Duration of Adjuvant Therapy n=44				
3 months	1			
4 months	0	0.73		
6 months	4			

ECOG: Eastern Cooperative Oncology Group; n: number of patients; T stage: tumor stage; N stage: node stage; MSI: Microsatellite Instability; MSI-Low: Microsatellite Instability-Low MSI-Stabil: Microsatellite Stable; MSI-High: Microsatellite Instability-High; XELOX: Capecitabine + Oxaliplatin; FOLFOX: 5-Fluorouracil + Leucovorin + Oxaliplatin; SD: Standard Deviation.

In our study, we evaluated the impact of clinicopathological and molecular data on recurrence and survival in patients with surgically treated transverse colon cancer. Despite the retrospective nature of our study, the relatively small sample size, and the challenges in accessing detailed patient data, our patient sample was consistent with literature data.[8,9,11,14] Previous analyses have often categorized transverse colon tumors with right-sided colon tumors, yet these tumors can exhibit behaviors similar to both right- and left-sided colon cancers.[15-17] As a result, making definitive statements regarding the treatment approach and prognosis of these tumors is challenging.

Given these considerations, we included 76 patients in our study, focusing on transverse colon cancer as a separate group. Most of our patients were male (61.8%), and the mean age was 60.76 years. The most common stage at diagnosis was stage 2 (59.2%). While literature suggests that left-sided colon tumors are more prevalent in males compared to right-sided tumors, there is limited detailed data on transverse colon tumors by gender.[18,19] In our study, 15 patients (19.7%) had mucinous histology. Large studies have shown that mucinous histology is observed in 19% of right-sided colon tumors, compared to 4% of all colon tumors.[20] This finding aligns the mucinous histology rate in our study more closely with right-sided colon tumors.

There is conflicting literature on the prognosis of tumors with mucinous histology. Some studies report a negative impact on survival, while others do not find a significant effect.[21,22] In our study, the overall survival of patients with mucinous histology was similar to that of the general patient population. The small sample size in our study may explain the lack of a significant difference in survival. It is known that the MSI-H status can reach up to 30% in tumors originating from the right colon, whereas it is observed in only 2% of left-sided colon tumors.[23] The MSI-H rate in our study was 26.8%, similar to right-sided colon tumors. During the follow-up, 11 patients experienced recurrence, with factors such as ECOG performance score, pathological T stage, lymphovascular invasion, and, most notably, perineural invasion being highlighted as significant.

Two studies in the literature are particularly noteworthy in comparison to our study. A study by Küçükarda et al.[24] investigated prognostic factors in patients with surgically treated transverse colon cancer. The study excluded stage 4 patients, similar to our patient population. It was reported that transverse colon tumors showed a molecular and prognostic course more similar to right-sided colon tumors, and BRAF mutation was identified as a poor prognostic factor even in early-stage disease. However, we did not analyze BRAF mutation in early-stage patients in our study, so we cannot comment on this finding.

Another study by Roberto et al.[12] presented data on 97 patients with stage 1-4 transverse colon tumors. Unlike our study, stage 4 patients were included. Similar to our findings, most patients were male (61%), and 68% had an ECOG score of 0. The study reported an MSI-H rate of 26%, a KRAS mutation rate of 37%, and a BRAF mutation rate of 24%. High tumor grade and BRAF mutation positivity were identified as factors negatively affecting overall survival.

Our study has some limitations. First, it was a retrospective study conducted at a single oncology center. Second, we could not analyze all patients' molecular data due to the lack of comprehensive data in patient files. A large-scale, multi-center prospective study is needed to validate the prognostic factors for TCC.

Conclusion

This study provides more comprehensive insights into the clinicopathological characteristics of TCC patients. It emphasizes the role of PNI as a potential predictive factor of response to targeted treatment in patients with a worse prognosis, even from the early stages of the disease. We encourage further clinical trials, including TCC patients, to establish new treatment algorithms specific to this subgroup of colon cancer.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 26.07.2024, Decision No: 2024/010.99/6/10).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: D.I.; Design: D.I.; Supervision: D.I., H.S.; Fundings: D.I., H.S.; Materials: D.I., O.K.; Data collection &/or processing: D.I., O.K.; Analysis and/or interpretation: D.I., H.S.; Literature search: D.I.; Writing: D.I., O.K.; Critical review: D.I., H.S.

Conflict of Interest

None declared.

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Transvers Kolon Tümörlerinde Nükse Etki Eden Faktörler: Tek Merkez Deneyimi

Amaç: Kolon tümörlerinde primer kitlenin lokalizasyonu prognostik önem göstermektedir. Primer kitlenin orijin aldığı bölgeye göre sağ veya sol kolon tümörü tanımı kullanılmaktadır. Embriyolojik gelişim esnasında sağ kolon tümörleri (RCC) mid-gut; sol kolon tümörleri (LCC) ise hind-gut'tan köken alırlar ve lokal evrede cerrahi yaklaşımlar, metastatik evrede ise kullanılan tedavi ajanlarına karşı prediktif farklar izlenmektedir. Transvers kolon tümörleri (TCC) tüm kolon tümörlerinin yüzde 10'luk kısmını oluşturmaktadır. Bu tümörler, heterojen embriyolojik gelişimleri nedeniyle sağ veya sol kolon gibi davranış gösterebilirler. Klinik çalışmalarda çoğunlukla sağ kolon tümörlerine dahil edilmeleri ya da çalışmadan dışlanmaları nedeniyle prognoz hakkında net bilgimiz bulunmamaktadır. Çalışmamızda kolon kanserinde önemini bildiğimiz klinik, patolojik ve moleküler prognostik faktörleri ve anatomik lokalizasyonunun fark gösterip göstermediğini kullanarak TCC'nin sağ veya sol kolon tümörlerinden farklı olup olmadığını araştırmayı amaçladık.

Gereç ve Yöntem: Hastanemizde transvers kolon kanseri nedeniyle ameliyat olmuş nonmetastatik hastalar retrospektif olarak dahil edildi. Demografik veriler ve patolojik özellikleri ile tedavi durumları incelendi.

Bulgular: Çalışmamıza transvers kolon yerleşimli ameliyat edilmiş 76 hasta alındı. Nüks ile cinsiyet, komorbidite, operasyon şekli, tanı anı evresi, grade, patolojik nod evresi, MSI durumu ve adjuvan tedavi durumunun ilişkisi incelendiğinde anlamlı fark bulunmadı ($p>0.05$). Histopatolojik alt tip, ECOG, perinöral invazyon, lenfovasküler invazyon ve patolojik T evresi ile nüks ilişkisi incelediğinde anlamlı fark olduğu görüldü. Nüks ile ilişkisi olan parametrelerin multivariable analizinde ise perinöral invazyon varlığının tek başına nüksü 25 kat artırıp bağımsız kötü prognostik faktör olduğu bulundu.

Sonuç: Çalışmamızda nonmetastatik opere transvers kolon yerleşimli kolon kanserli hastalarda perinöral invazyonun nüksü 25 kat öngören bağımsız prognostik bir belirteç olduğu bulundu. Bu sonuç, hastalarda prognozu öngörmek ve tedavi kararı verme sürecinde etkili kullanılabilir.

Anahtar Sözcükler: ECOG; histopatolojik alt tip; lenfovasküler invazyon; MSI durumu; nüks faktörleri; patolojik T evresi; perinöral invazyon; prognoz; transvers kolon kanseri.

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Original Article

Laminectomy Infections

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Keywords: Laminectomy; spondylolisthesis; surgical site infections.

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ABSTRACT

Objective: Hematoma, infections, and wound dehiscence are the most common causes of readmission following laminectomy operations. The aim of this study was to identify and prevent infectious agents to reduce additional costs and mortality.

Methods: A retrospective analysis was conducted on 4295 laminectomies performed over a 7-year period. The study included 30 infected adult patients and 40 isolated microorganisms. The analysis determined demographic data, risk factors, isolated microorganisms, and resistance patterns.

Results: Out of 4295 laminectomy operations, only 30 patients (0.7%) developed surgical site infections (SSIs). The median age of the patients was 55.18 years, and the median duration of hospitalization was 35.54 days. Of the patients, 56.7% were female and 43.3% were male. The risk factors for SSI were the use of peripheral venous catheters (93.3%), urinary catheters (26.7%), and central venous catheters (16.7%). The isolated agents were *A.baumannii*, *K.pneumoniae*, and *E.coli*, which accounted for only 50% of the total cases.

Conclusion: The main goal should be to prevent surgical site infections (SSIs) after laminectomy surgery, rather than treating.

INTRODUCTION

The most frequent causes of hospital readmission following spine surgery are hematoma, infections, and wound dehiscence, respectively. Surgical site infection (SSI) after laminectomy is a severe complication. It is classified as primary superficial SSI if it involves the skin and subcutaneous tissues, and primary deep SSI if it involves the muscle and fascia. If it spreads to organs and cavities, it can result in meningitis and ventriculitis. Re-hospitalization can result in new surgical interventions, physical and psychological disorders, additional costs, increased morbidity, and mortality. We aimed to reduce these risks in our hospital.

MATERIALS AND METHODS

A retrospective analysis was conducted on 4295 laminectomy operations performed at our Neurosurgery Clinic between November 2016 and October 2023, using the hospital automation system. The study included 30 patients with surgical site infections (0.7%) and 40 isolated microorganisms. Patients under 18 years of age were excluded. Wound cultures were obtained from patients with superficial and subcutaneous surgical site infections (SSI), while aerobic and anaerobic blood cultures and cerebrospinal fluid (CSF) cultures were obtained from patients with organ cavity infections. The study analyzed demographic data, reasons for surgery, comorbidities, SSI classifications, risk factors, isolated microorganisms, and antibiotic resistance. Categorical variables were presented as frequency and percentage, while continuous variables that did not show normal distribution were presented as median values.

Our study was approved by the Health Sciences University Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee on 29.11.2023 with decision number 2023/514/262/19.

RESULTS

During a 7-year period, 4295 laminectomy operations were performed, resulting in 30 infected patients (0.7%) with positive cultures for a total of 40 microorganisms.

Of these patients, 17 (56.7%) were female and 13 (43.3%) were male, with a median age of 55.18 (range 20-85) years and a median hospitalization duration of 35.54 (range 12-96) days for surgical site infections (SSIs). Two patients (6.6%) were diagnosed with meningitis-ventriculitis, 20 (66.7%) with primary deep SSI, and 8 (26.7%) with primary superficial SSI. The causative agent was isolated from the wound site in blood and cerebrospinal fluid (CSF) cultures obtained simultaneously from two patients with ventriculitis and meningitis. One of these patients (3.3%) died, while the others (96.7%) were successfully treated.

Ten (33.3%) patients underwent surgery for lumbar spondylolisthesis, nine (30%) for lumbar disc herniation, three for fractures due to falls, three for cervical disc herniation, two for malignant tumor metastasis, and one each for lumbar schwannoma, thoracic disc herniation, and thoraco-lumbar disc herniation. A total of 24 laminectomies were performed in the lumbar region, with three laminectomies each in the thoracic and cervical regions.

Out of the total number of patients, 21 (70%) had diabetes mellitus (DM), 14 (46.7%) had hypertension, and the remaining patients had various other conditions, including arrhythmia, cerebrovascular disease, anemia, pulmonary embolism, hyperthyroidism, asthma bronchiale, atrial fibrillation, chronic renal failure, congestive heart failure, rheumatoid arthritis (RA), chronic obstructive pulmonary disease (COPD), and benign prostatic hypertrophy.

Peripheral venous catheter was present in 28 (93.3%) patients, urinary catheter in 8 (26.7%), and central venous catheter in 5 (16.7%). Total parenteral nutrition was used in 3 patients, and endotracheal intubation in 2 patients. These were identified as the most important risk factors facilitating the occurrence of SSI. H2 receptor antagonists were used by 15 (50%) patients.

Table 1. Isolated Microorganisms and Their Rates

Microorganisms	%	n
Acinetobacter baumannii	22.5	9
Klebsiella pneumoniae	15.0	6
Escherichia coli	12.5	5
CNS	10.0	4
Pseudomonas aeruginosa	7.5	3
Staphylococcus aureus	7.5	3
Serratia marcescens	7.5	3
Enterobacter cloacae	7.5	3
Enterococcus faecalis	5.0	2
Enterococcus faecium	2.5	1
Enterobacter hormaechei	2.5	1

CNS; Coagulase-negative Staphylococci.

The mean duration of infection after laminectomy surgery was 12.08 (range 3-39) days. There was growth in 33 (82.5%) wound cultures, 1 abscess culture, 4 blood cultures, and 2 CSF cultures. One patient diagnosed with meningitis and ventriculitis had *A.baumannii* isolated in all cultures, while the other had *K.pneumoniae* isolated.

Standard isolation methods were used to isolate microorganisms. Of the microorganisms, 75% were Gram-negative and 25% were Gram-positive. *A.baumannii*, *K.pneumoniae*, and *E.coli*, the first three, constituted half of all causative microorganisms. Coagulase-negative staphylococci (CNS) was the most frequently isolated Gram-positive microorganism (Table 1).

Carbapenem resistance was observed in all *A.baumannii* strains, while it was present to a lesser extent in other Gram-negative agents. *K.pneumoniae* showed a 20% resis-

Table 2. Resistance Patterns of Isolated Microorganisms

	AMP	CZ	AN	CN	FEP	CAZ	CRO	TZP	CIP	TGC	MER	IMP	COL	SXT	VAN	LZD
A.baumannii			11.1	50				100	100	11.1	100	100	0	100		
K.pneumoniae			16.7	40	33.3	40	50	33.3	33.3	20	16.7	16.7	20	16.7		
E.coli			0	20	60	60	60	0	20	0	0	0	0			
CNS	100	100		75					50	33.3				0	0	0
P.aeruginosa			0	33.3	33.3	33.3	33.3	33.3	33.3		33.3	33.3	0			
S.aureus	33.3	33.3		0					33.3	0				0	0	0
S.marcescens			0	100	100	100		66.7	100	33.3	0	0	100	0		
E.cloacae			0	33.3	33.3	66.7			66.7	0	0	0	0	33.3		
E.faecalis	0	0							0	0				0	0	0
E.faecium	0	0							0	0				0	0	0
E.hormaechei			0	0	0	0	0	0	0	0	0	0	0	0		

AMP; Ampicillin, CZ; Cefazolin, AN; Amikacin, CN; Gentamicin, FEP; Sefepim, CAZ; Seftazidim, CRO; Ceftriaxone, TZP; Piperacillin-tazobactam, CIP; Ciprofloxacin, TGC; Tigecycline, MER; Meropenem, IMP; İmipenem, COL; Polymyxin-E (Colistin), SXT; Trimethoprim-sulfamethoxazole, VAN; Vancomycin, LZD Linezolid, *A.baumannii; Acinetobacter baumannii, K.pneumoniae; Klebsiella pneumoniae, E.coli; Escherichia coli, CNS; Coagulase-negative Staphylococci, P.aeruginosa; Pseudomonas aeruginosa, S.aureus; Staphylococcus aureus, S.marcescens; Serratia marcescens, E.cloacae; Enterobacter cloacae, E.faecalis; Enterococcus faecalis, E.faecium; Enterococcus faecium, E.hormaechei; Enterobacter hormaecei.*

tance to both colistin and tigecycline. Tigecycline resistance was also observed in other Gram-negative agents.

Enterococci did not show any resistance to ampicillin. All Gram-positive agents were susceptible to vancomycin, linezolid, tigecycline, and trimethoprim-sulfamethoxazole (Table 2).

DISCUSSION

The presence of surgical site infections (SSI) can result in hospital readmission, new surgical interventions, physical and psychological impairment, additional costs, and increased morbidity and mortality.[1] The most frequent reasons for reoperations following spine surgery are hematoma, infections, and wound dehiscence.[2] Foraminotomy, rheumatoid arthritis (RA), advanced age, and occipito-cervical surgery are risk factors for surgical site infections (SSI). Other risk factors include dural tear and leakage, a higher number of operated levels, steroid use, male gender, diabetes mellitus (DM), increased subcutaneous adipose tissue thickness, obesity, hypoalbuminemia, and smoking.[3-7] In our patient sample, laminectomy was performed at two levels in 60% (n=24) and at more than two levels in 20% (n=6). The presence of DM was identified as a significant risk factor, with a rate of 70%. A multicenter retrospective study found that smoking did not increase the incidence of SSIs in posterior cervical decompression surgery.[8] The occurrence of surgical site infections (SSIs) is more frequent in posterior approaches compared to anterior approaches, in open surgeries compared to minimally invasive surgeries, and in instrumented surgeries compared to non-instrumented surgeries. Additionally, SSIs are more common in thoracic operations and less common in lumbar operations.[9]

Computerized tomography and magnetic resonance imaging are the most valuable imaging modalities for diagnosing SSI, particularly in cases of abscesses, soft tissue infections, and bone infections.[10]

Preoperative cefazolin prophylaxis significantly reduces the development of surgical site infections (SSI). The appropriate dose should be adjusted according to the patient's weight, with 1 g of cefazolin used for every 60 kilograms. The dose should be repeated every four hours during surgery.[11] Intraoperatively, suprafascial powdered vancomycin has been used to prevent SSI in spine surgery and has been found to be as effective as subfascial use.[12]

The incidence of SSI after laminoplasty ranges from 1.4% to 13%.[1] In our study, this rate was 0.7%. The study included patients with a mean age of 55.18 years (range 20–85 years), with 56.7% being female and 43.3% being male. The mean age of female patients was 59.27 years, while that of male patients was 50.45 years.

The Turkish National Surveillance Guidelines for Healthcare Associated Infections recommend a follow-up period of 30 days for primary superficial and primary deep SSI, and 90 days for meningitis and ventriculitis.[13] The average time for patients to become infected after laminectomy surgery was 12.08 days (range 3–39 days). The infection rate was 10.27 days for men and 13.53 days for women. On average, patients were hospitalized for SSI for 35.54 days (range 12–96 days), with males staying for 30.27 days and females for 39.2 days.

Primary deep surgical site infections (SSIs) were diagnosed in 66.7% of patients, and primary superficial SSIs were diagnosed in 26.7%. Organ and cavity SSIs were considered in two patients. Simultaneous wound, blood, and cerebrospinal fluid (CSF) cultures were obtained. A. baumannii was found in all cultures of one patient, and K. pneumoniae was found in the other. Although the patients were successfully treated, one female patient died in the intensive care unit due to additional complications, including meningitis and ventriculitis.

In our study, indications for laminectomy were disc herniation (46.7%), spondylolisthesis (33.3%), malignancies (10%), and fractures due to falls (10%). Specifically, hepatocellular carcinoma metastasized at L3, malignant breast cancer metastasized at L4-5, and schwannoma involved the L3-4 level. Fractures related to falls occurred between T10 and L2. Laminectomies were performed in the lumbar region in 80% of cases, in the thoracic region in 10% of cases, and in the cervical region in 10% of cases.

The study found that the most common comorbidities were diabetes mellitus (DM) in 70% of cases and hypertension in 46.7% of cases. Another study identified DM and obesity as independent risk factors.[14] No literature was found indicating hypertension as a risk factor. Additionally, one patient each had arrhythmia, cerebrovascular disease, anemia, pulmonary embolism, hyperthyroidism, asthma bronchiale, atrial fibrillation, chronic renal failure, congestive heart failure, rheumatoid arthritis (RA), chronic obstructive pulmonary disease (COPD), and benign prostatic hypertrophy. In a prospective surveillance study conducted across multiple centers, it was found that endoscopic tubular surgery served as an independent protective factor, while operations lasting more than two hours were identified as an independent risk factor.[15]

In our study, the risk factors for SSI were peripheral venous catheter (93.3%), urinary catheter (26.7%), central venous catheter (16.7%), total parenteral nutrition (in 3 patients), and endotracheal intubation (in 2 patients). Additionally, 50% of patients were found to have used H2 receptor antagonists.

Of these, 33 (82.5%) were from wound culture, one was from abscess culture, four were from blood culture, and two were from CSF culture (refer to Table 1). A total of 40 microorganisms were isolated in this study. In contrast to many other studies, Gram-negative microorganisms were the most commonly isolated agents in our study, rather than Gram-positive ones.[14]

A.baumannii (22.5%), the most frequently isolated agent, was not resistant to colistin, while amikacin and tigecycline resistance was the least (11.1%). They were resistant to all

other antibiotics. In K. pneumoniae strains (15%), the least resistance was to carbapenems, amikacin, and trimethoprim-sulfamethoxazole (16.7%), while the highest resistance was to ceftriaxone (50%). *E.coli* strains (12.5%) had no resistance to colistin, tigecycline, piperacillin-tazobactam, and carbapenem, while cefepime, ceftazidime, and ceftriaxone had 60% resistance. Carbapenem resistance was 33.3% in *P.aeruginosa* strains but not in other Gram-negative strains (*S.marcescens*, *E.cloacae*, and *E.hormaechei*) (Table 2).

No resistance to vancomycin or linezolid was observed in coagulase-negative staphylococci (KNS), which accounted for 10% of the microorganisms. Enterococci were sensitive to all antibiotics tested, but methicillin resistance was observed in 33.3% of *S.aureus* strains (Table 2). Studies have shown that treating methicillin-resistant S.*aureus* nasal colonization preoperatively and performing cervical laminectomy did not significantly affect treatment outcomes.[15,16] Our hospital does not perform routine nasal cultures.

Conclusion

Postoperative surgical site infections (SSIs) following laminectomy surgery have been shown to increase readmissions, length of stay, treatment costs, and mortality rates. Therefore, it is crucial to prioritize preventing SSIs rather than treating them. To achieve this, it is recommended that catheter maintenance be performed under appropriate conditions and terminated in a timely manner.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 29.11.2023, Decision No: 2023/514/262/19).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: B.K., S.Ş., S.D.T., E.A.; Design: B.K., S.Ş., S.D.T., E.A.; Supervision: B.K., S.Ş., S.D.T., E.A.; Fundings: B.K., S.Ş., S.D.T., E.A.; Materials: B.K., S.Ş., S.D.T., E.A.; Data collection &/or processing: B.K., S.Ş., S.D.T., E.A.; Analysis and/or interpretation: B.K., S.Ş., S.D.T., E.A.; Literature search: B.K., S.Ş., S.D.T., E.A.; Writing: B.K., S.Ş., S.D.T., E.A.; Critical review: B.K., S.Ş., S.D.T., E.A.

Conflict of Interest

None declared.

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Laminektomi Enfeksiyonları

Amaç: Laminektomi ameliyatlarına bağlı yeniden yatışların en sık nedenleri hematom, enfeksiyonlar ve yara açılmasıdır. Ek maliyetleri ve mortaliteyi engellemek için enfeksiyon etkenlerinin belirlenip önlenmesi amaçlandı.

Gereç ve Yöntem: Yedi yıllık süreçte yapılan 4295 laminektomi ameliyatı retrospektif olarak irdelendi. Enfekte olan 30 erişkin hasta ve bunlardan izole edilen 40 mikroorganizma çalışmaya dahil edildi. Hastaların demografik verileri, risk faktörleri, izole edilen mikroorganizmalar ve direnç paternleri belirlendi

Bulgular: 4295 laminektomi ameliyatının 30'unda (%0.7) cerrahi alan enfeksiyonu (CAE) gelişti. Hastaların %56.7'si kadın, %43.3'ü erkek olup ortanca yaşları 55.18 yıl, ortanca hastane yatışı 35.54 gündü. CAE için risk faktörleri periferik venöz kateter (%93.3), üriner kateter (%26.7) ve santral venöz kateter (%16.7) kullanımıydı. İzole edilen etkenlerin sadece %50'si *A.baumannii*, *K.pneumoniae* ve *E.coli*'den ibaretti.

Sonuç: Laminektomi ameliyatlarından sonra gelişen CAE'yı tedavi etmek yerine, oluşmasını engellemek primer amaç olmalıdır.

Anahtar Sözcükler: Cerrahi alan enfeksiyonları; laminektomi; spondilolistezis.

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Original Article

Evaluation of Corneal Endothelial Cell Morphology Using Specular Microscopy and Corneal Topographic Parameters in Children with Hyperopic Anisometropic Amblyopia

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Keywords: Axial length; corneal topography; high-order aberration; hyperopic anisometropic amblyopia; specular microscopy.

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ABSTRACT

Objective: To evaluate anterior segment parameters in pediatric patients with hyperopic anisometropic amblyopia (HAA).

Methods: The study included 35 amblyopic and 35 healthy eyes of 35 HAA patients examined in the Pediatric Ophthalmology Department between January and April 2021 and 40 eyes of 40 healthy emmetropic children. The axial length (AL) was measured using a Lenstar LS-900 biometer, and the anterior segment and corneal endothelial layer parameters were evaluated using Scheimpflug imaging and non-contact specular microscopy, respectively.

Results: The mean age of the children was 8.5±3.1 years in the HAA group and 8.9±2.2 years in the healthy control group (p=0.252). A statistically significant difference was found in the three groups regarding best-corrected visual acuity and AL (p<0.001 for all). Of the anterior segment parameters, a statistically significant difference was determined between the groups in terms of anterior corneal curvature, corneal volume, anterior chamber depth, total high-order aberrations, and spherical aberration (p=0.019, p=0.034, p=0.015, p=0.037, and p<0.001, respectively). No statistically significant difference was determined between the groups concerning the endothelial parameters (p>0.05 for all).

Conclusion: The results of this study demonstrated that there could be statistically significant differences in anterior segment parameters between amblyopic eyes, fellow eyes, and emmetropic healthy eyes. A thorough assessment of anterior segment parameters in patients can significantly inform both diagnostic and therapeutic approaches.

INTRODUCTION

Amblyopia is a decrease in unilateral or bilateral best-corrected visual acuity (BCVA) that occurs due to vision loss or abnormal binocular interaction during the critical period of vision development.[1] It is among the most frequent reasons for loss of visual acuity in pediatric patients.[1] Amblyopia may develop associated with strabismus, anisometropia, bilateral high refractive error, or visual deprivation. In cases where the etiology cannot be identified, it is called idiopathic amblyopia.[2]

Anisometropia develops due to a significant refractive error between the two eyes, with the amblyogenic effect being more significant in hyperopic anisometropia than in myopic and astigmatic anisometropia.[3] Spheric and astigmatic changes occur due to some anatomic differences in the axial length and corneal and lenticular curvature between the two eyes. Treatment includes optic correction, eye patching, and medications such as atropine and levodopa.[4] However, even with the correct diagnosis, treatment success has been reported in only 60-75% of cases.[5]

Several studies addressed the relationship of amblyopia with the axial length (AL), topographic parameters of the cornea, and corneal high-order aberrations (HOA), with the latter having an adverse effect on treatment results.[6-8] However, no study has evaluated the relationship between amblyopia and changes in endothelial parameters as measured by non-contact specular microscopy.

Specular microscopy, a noninvasive imaging technique, is used to assess the morphology of the corneal endothelium, the innermost layer of the cornea that is responsible for corneal transparency.[9] Changes in the corneal

endothelium may occur due to ocular diseases as well as systemic diseases.[9] These changes in corneal endothelial cells affect not only the corneal parameters but also visual quality and acuity.[10] Corneal endothelial changes may not always be apparent during routine ophthalmic examination. Fung et al.[11] reported no lesions in 13% of the patients with posterior polymorphous corneal dystrophy and lower endothelial cell density (ECD) in these children compared to healthy controls. Specular microscopy, in this respect, may play an essential role in the assessment of corneal endothelial changes.

This study aimed to evaluate the anterior segment parameters, especially the corneal endothelial parameters, of the amblyopic eyes of pediatric patients with hyperopic anisometropic amblyopia (HAA) compared to fellow healthy eyes and emmetropic healthy eyes.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Pediatric Ophthalmology between January and April 2021 and included patients with HAA aged 5-15 years. The study's approval was obtained from the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (Protocol No: 2021/514/205/2), and our study was performed according to the principles of the Declaration of Helsinki. It was not possible to obtain written consent for study participation because it was a retrospective design.

The diagnosis of HAA was based on a discrepancy of >1.00 diopter (D) (spherical equivalent) between the two eyes and a disparity of >two rows in BCVA based on Snellen visual acuity charts, with a BCVA of ≥0.63 in the fellow eye in patients younger than six years, and ≥0.8 in patients aged ≥six years. The spherical equivalents were calculated following cycloplegic refraction (spherical power + ½ cylinder power). The refraction measurements were made 45 minutes after administering 1% cyclopentolate hydrochloride twice at 5-minute intervals. The control groups consisted of one randomly selected emmetropic eye of age- and sex-matched children with normal ocular findings on routine ophthalmologic examinations. Emmetropia was defined as an uncorrected visual acuity (UCVA) of >0.8 on a Snellen chart.

Exclusion criteria included a history of any ocular disease (strabismus, nystagmus, uveitis, retinal and corneal diseases, cataract, optic disc anomalies, and diseases, or glaucoma), any history of ocular or head trauma, intraocular surgery, the presence of astigmatism >1D, the presence of any neurologic disease or developmental retardation, or inability to cooperate during eye examinations.

All participants underwent a detailed eye examination, including UCVA and BCVA on the Snellen chart (the Snellen equivalent was converted to logMAR), an alternating cover test, intraocular pressure (IOP) measured using an air-puff tonometer, a slit-lamp biomicroscopic examination, and dilated fundus evaluations. Laterality (eye with anisometric hyperopic amblyopia) was identified in patients with HAA.

The AL, defined as the distance between the retinal pigment epithelium and the corneal vertex, was measured three times by the same experienced technician using a Lenstar LS-900 biometer (LS 900 Haagstreit AG; Koeniz, Switzerland) and was averaged. Before each measurement, the participant was instructed to blink the eye to obtain an integrated tear film layer.

The same skilled technician measured the anterior segment parameters, including anterior and posterior corneal curvatures (ACC and PCC, respectively), central corneal thickness (CCT), corneal volume (CV), and anterior chamber depth (ACD) and volume (ACV) using Scheimpflug imaging technology (Sirius Topography, CSO, Florence, Italy). The root mean squares of the total HOAs within 6 mm of the central cornea were evaluated while the pupil was at the physiologic size in the mesopic condition.

The same technician used a non-contact specular microscope (Tomey EM-4000; Tomey Corp.) to measure the corneal endothelial cells. The center approach was used to repeat each measurement at least three times, with a minimum of 110 cells in each measurement. The values recorded for all patients were the endothelial cell density (ECD), average cell area (ACA), minimum cell area (CAmin), maximum cell area (CAmax), standard deviation of cell area (SD), coefficient of variation in cell area (CV), and hexagonal cell ratio (HEX).

Statistical Analysis

The study's data were examined using the statistical program Jamovi 2.2.5. Depending on the distribution, continuous data were presented as standard deviation or median (interquartile range) values. The independent samples t-test was used to compare groups based on age, and the Chi-square test was used to compare genders. The homogeneity and normalcy of the distribution were evaluated using the Shapiro-Wilk and Kolmogorov-Smirnov tests. In the comparisons between groups, continuous data with a normal distribution were subjected to a one-way analysis of variance (ANOVA), while non-normal data were subjected to the Kruskal-Wallis test. After a significant result from a one-way ANOVA, a multiple comparison test called the post-hoc Games-Howell test was employed. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

This study included 70 eyes of 35 patients with HAA and 40 eyes of 40 emmetropic healthy control subjects. The HAA group consisted of 19 males and 16 females, and the healthy control group included 18 males and 22 females. The mean ages of the two groups were 8.51±3.08 and 8.92±2.16 years, respectively. Regarding gender and age, there was no significant difference between the HAA and healthy control groups ($p=0.252$ and $p=0.951$, respectively). Most (68%) of the eyes with HAA were on the left side. The control group eyes were 55% right-side and 45% left-side (Table 1).

Table 1. Clinical and demographic characteristics of participants.

	All participants (n=75)	Participants With Amblyopia (n=35)	Participants With no Amblyopia (n=40)	P
Age, (years)				
mean±sd	8.73±2.62	8.51±3.08	8.92±2.16	0.252
M (min-max)	(4-16)	(4-16)	(4-14)	
Gender, n (%)				
Female	34 (45.3%)	19 (54.3 %)	22 (55%)	0.951
Male	41 (54.7%)	16 (45.7%)	18 (45%)	
Laterality of amblyopia (Right/Left)	11/64	11/24	22/18	

No pathology was detected in the slit-lamp biomicroscopic and dilated fundus examinations of any study participants. In the study, there were three groups of eyes included: amblyopic eyes of patients with HAA, non-amblyopic fellow eyes of patients with HAA, and emmetropic eyes of healthy controls. There was a statistically significant difference in the refractive errors following cycloplegic refraction, BCVA, and AL when comparing amblyopic eyes with both fellow eyes and healthy eyes ($p<0.001$ for all).

Among the anterior segment measurements, statistically significant differences were found between the groups for ACC, CV, and ACD ($p=0.019$, $p=0.034$, and $p=0.015$, respectively). The ACC and CV values showed a statistically significant difference ($p=0.035$, $p=0.046$) between the amblyopic eyes and the control group, and the ACD values showed a statistically significant difference between the amblyopic eyes and both the non-amblyopic fellow eyes as well as the control group eyes ($p=0.045$, $p=0.045$).

The CCT values were found to be higher in the amblyopic eyes than in the control group, but the difference was not

Table 2. Comparison of refractive and corneal parameters of participants.

	Participants With Amblyopia (n=35)		Participants With no Amblyopia (n=40)	P	Post-hoc
	Amblyopic Eye	Non Amblyopic Fellow Eye	Non Amblyopic Control Eye		
Refraction, D, SE, mean±sd	+5.31±1.92	+3.35±2.23	+0.05±1.17	<0.001	1&3 p<0.001 2&3 p<0.001 1&3 p<0.001
BCVA (logMAR)	0.30±0.32	0.00	0.00	<0.01	1&3 p<0.001 1&2 p<0.001
IOP, mmHg	14.7±2.17	14.8±2.89	15.7±1.95	0.071	
CCT, (µm), mean±sd	581±43.3	585±48.4	563±37.8	0.059	
AL (mm)	22.2±1.39	23.2±0.94	23.3±0.94	<0.001	1&3 p<0.001 1&2 p=0.004
ACC, D	59.5±3.81	59.7±3.53	57.7±3.55	0.019	1&3 p=0.035
PCC, D	-5.53±2.82	-5.97±0.34	-5.81±1.92	0.053	
CV, mm^3	43.6±1.29	42.8±1.51	42.7±1.59	0.034	1&3 p=0.046
ACD, mm	3.50±0.34	3.50±0.34	3.68±0.25	0.015	1&3 p=0.045 2&3 p=0.045
Total HOA	0.15±0.16	0.09±0.07	0.07±0.02	0.037	1&3 p=0.024
Coma	0.08±014	0.03±0.03	0.04±0.06	0.295	
Spherical Aberation	0.09±0.34	0.05±0.03	0.01±0.008	<0.001	1&3 p<0.001
Trefoil	0.06±0.06	0.04±0.04	0.05±0.03	0.155	
Pupil Diameter, mm	3.53±0.72	3.62±0.71	3.45±0.51	0.066	

D: Diopters; SE: Spherical equivalent; BCVA: Best corrected visual acuity; IOP: Intraocular pressure; CCT: Central corneal thickness; AL: Axial lenght, ACD: Anterior corneal depth; CV: Corneal volüme; HOA: High order aberration; ACC: Anterior corneal curvature; PCC: Posterior corneal curvature; 1: ambliyopic eye; 2: Non ambliyopik fellow eye; 3: Non ambliyopic control eye.

Table 3. Comparison of specular microscopy parameters of participants

	Participants With Amblyopia (n=35)		Participants With no Amblyopia (n=40)	P
	Amblyopic Eye	Non Amblyopic Fellow Eye	Non Amblyopic Control Eye	
ECD (cells/mm)	3126±332.0	3122±326.0	3039±240.0	0.312
ACA	324.0±36.9	324.0±36.7	331.0±26.1	0.498
SD	111.0±30.2	111.0±25.5	114.0±23.7	0.822
CV	33.9±6.42	34.1±5.51	34.3±5.51	0.970
HEX	55.4±9.64	55.4±10.1	56.4±11.0	0.904

ECD: Endothelial cell density; ACA: Average cell area; SD: Standard deviation of cell area; CV: Coefficient of variation in cell area; HEX: Hexagonal cell ratio.

statistically significant (p=0.059). Of the HOAs, the total HOA and spherical aberration values were statistically significantly different between the three groups (p=0.037 and p<0.001, respectively). Particularly between the amblyopic eyes and the healthy control group, there was a difference (p=0.024, p<0.001) (Table 2).

The endothelial parameters measured using specular microscopy are shown in Table 3. There was no statistically significant difference among the groups (p>0.05 for all).

DISCUSSION

The results of this study demonstrated differences in the anterior segment parameters of the amblyopic eyes of patients with HAA compared with the fellow non-amblyopic eyes and the healthy control group. To the best of our knowledge, this is the first study to evaluate the endothelial parameters of patients with HAA in addition to AL and corneal topographic parameters. HAA is seen at an equal frequency in males and females.[7,12] Although some studies reported that it was more common in males, the frequency was similar in both genders in the current study.[7] Some studies reported that amblyopia was seen more often in the left eye in HAA, and even rates two-fold higher compared with the right eye have been reported.[8] This has been associated with the fact that ocular dominance is seen more often in the right eye in the general population. It is thought that to prevent diplopia arising from image disparity, ocular dominance leads to interocular suppression, albeit at a low level.[13] Romboust et al.[14] showed that the dominant eye in a healthy individual activated a broader visual cortex, which was thought to be linked to a more effective emmetropisation process in the eye with ocular dominance.

The optical and anatomical developmental stages and mechanisms of the eye are not entirely known, but there are various opinions on emmetropisation.[15] The hyperopic eye in newborn infants progresses towards emmetropisation over time. This change is rapid in the first three years and tends to decrease over time, with AL reaching the adult level at the age of 15 years.[16] During this period, the refractive power of the cornea and lens decreases, and a decrease in hyperopia is observed. Consequently, while the sagittal axis of the eye lengthens in the emmetropisation process, the ACD and vitreous chamber depth deepen, and flattening of the cornea and lens occurs due to equatorial stretching.[16] Emmetropisation cannot be completed when there is a delay in development in this sensitive period, which triggers the development of amblyopia. Previous studies have shown that AL is significantly shorter in eyes with HAA.[15,17] Cass and Tromans reported a disproportionate increase in lens and corneal thickness and shortening of the AL, attributing this to the developmental delay in emmetropisation.[17] Some studies suggested this condition was due to insufficient visual quality in the anisometropic amblyopic eye, affecting AL through a negative feedback mechanism.[18] Therefore, it can be postulated that a bidirectional interaction exists between ocular structures and the emmetropisation process. In this study, AL was observed to be statistically significantly shorter in amblyopic eyes, and the ACD in HAA eyes and the fellow eyes was found to be significantly shallower than in the healthy emmetropic eyes of the control group, which we attributed to the inability to complete the emmetropisation process correctly in the amblyopic eye.

Wang et al.[19] found no statistically significant difference among the anterior segment parameters of amblyopic eyes and fellow eyes. They stated that this situation may develop because the fellow eye may not be normal in patients with HAA. Unlike this study, Yuksel et al.[6] included a third group of healthy emmetropic children and observed no statistically significant difference among the groups in their study. In contrast to these studies, Cankurtaran et al.[7] reported thicker CCT in anisometropic hyperopic eyes than in fellow eyes. They attributed this to the abnormal emmetropisation process and the absence of flattening and thinning of the cornea due to equatorial stretching that would be expected to occur during ocular sagittal expansion. In this study, both the CCT of the amblyopic eye and the fellow eye were thicker than the control group, but they were not found to be statistically higher. These

results also revealed that the evaluation of the fellow eye as normal may not be completely accurate and that the delay in the emmetropisation process may have an effect on CCT differences. At the same time, the ACC and CV parameters were significantly higher in the HAA eyes than in the control group. CV shows a tendency to decrease with aging and has been reported to be associated with parameters such as ACD, CCT, anterior corneal asphericity, and PCC, especially in inverse proportion to AL and the white-to-white distance.[20] The significantly shorter AL and proportionately thicker CV in HAA eyes in the current study were thought to be related to each other.

HOAs are corneal aberrations that affect visual quality, and their increase can lead to symptoms such as halo, glare, and distortion.[10] The correction of HOAs increases visual acuity and contrast sensitivity.[8,21] Whereas low-order aberrations show a 90% effect on retinal image quality, there is a 10% effect on HOAs such as coma, spherical aberrations, and trefoil.[22] Prakash et al.[23] compared amblyopic eyes with healthy eyes and reported a significant difference in HOA patterns. Some studies have attributed this to the amblyogenic effect of the change in HOAs.[22,24] In contrast, it has also been claimed that there is no relationship between amblyopia and HOAs.[25,26] However, one of these studies, Levy et al.'s [25] study, included adult patients with amblyopia, and it is known that HOAs may change with aging. Brunette et al.[27] reported that ocular aberrations reduced slowly in early adulthood, reaching the lowest level in the fourth decade of life, and then at advanced ages, showed an increase associated with changes in the lens.

In a study by Dominguez-Vicent et al.,[26] no relationship was reported between idiopathic amblyopia and HOAs, but remarkably few patients were included in that study. In contrast, it has been claimed that HOAs are more effective than the amblyogenic effect on the relationship between amblyopia and the treatment success of amblyopia in some studies.[21,22] Kwan et al.[28] showed that coma and spherical aberration were particularly common in healthy eyes. Zhao et al.[22] reported that coma affected amblyopia. Previous studies have shown a significant relationship between coma and astigmatism.[21,27] Choi et al.[21] reported a statistically significant difference in spherical aberration in eyes with hyperopic amblyopia. The current study found a statistically significant difference in total HOA and spherical aberration in eyes with HAA. This difference was especially seen between the amblyopic and healthy control group eyes. It is known that corneal aberrations are twice as common in infants than in adults, and together with aging, progress towards emmetropisation is similar to low-order aberrations.[29] In this study, it was thought that the differences in total HOA and spherical aberration were related to abnormalities in the emmetropisation process in amblyopic eyes, and there was no statistically significant difference in coma because the patients in the current study were patients with <1D astigmatism.

In humans, corneal endothelial cells are stopped in the G1 phase of the cell cycle.[30] Due to this limited proliferative capacity, visual function and quality may be significantly compromised following disease or injury related to corneal endothelial loss. In addition to the reduction in the quantity of corneal endothelial cells, changes in endothelial cell morphology also affect visual quality. Patients with Fuchs' endothelial corneal dystrophy (FECD) have been reported to experience visual impairment even in the absence of corneal stromal or epithelial edema. Corneal endothelial morphological changes can adversely affect visual quality by inducing light scattering. Furthermore, in individuals with FECD, there is a proportional relationship between the corneal endothelial morphological changes and measures such as corrected distance visual acuity, letter contrast sensitivity, and visual quality related to light scattering.[29]

Therefore, changes in the corneal endothelial layer that occur during the sensitive period when emmetropization develops in childhood may cause amblyopia. It has been reported that astigmatic anisometropic amblyopia developed due to endothelial changes in patients with posterior polymorphous corneal dystrophy, which causes changes in the corneal endothelial layer.[12] There was no discernible difference observed in the current study between the groups when endothelial morphology was examined using non-contact specular microscopy. This study includes only the hyperopic anisometropic patient group; however, examining the endothelial parameters in all amblyopia cases (hyperopic, myopic, and astigmatic anisometropic amblyopia cases) may provide insights into idiopathic amblyopia cases whose causes remain unexplained.

The limited sample size, retrospective design, absence of long-term follow-up, and lack of comparisons between amblyopia treatment and outcomes constitute several of the study's limitations. Additionally, patients with amblyopia due to refractive errors other than hypermetropia were not included.

Conclusion

In conclusion, amblyopia is one of the most common causes of vision loss; however, it is preventable and treatable in childhood. Understanding the pathophysiology of HAA, which is seen more often in children, is extremely important for preventing and treating the disease. The results of this study demonstrated that there could be statistically significant differences between amblyopic eyes, fellow eyes, and healthy eyes in terms of anterior segment parameters. As a result, a comprehensive evaluation of the anterior segment parameters of patients could provide valuable guidance for both diagnosis and treatment.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 12.07.2021, Decision No: 2021/514/205/2).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: U.K., B.T., A.T.K.; Design: U.K., S.Ö.Y., B.T., A.T.K.; Supervision: U.K., B.T., A.T.K.; Materials: U.K., S.Ö.Y., A.T.K., E.S.; Data collection &/or processing: U.K., E.S., S.Ö.Y., A.T.K., B.T.; Analysis and/or interpretation: U.K., B.T., A.T.K.; Literature search: U.K., E.S., S.Ö.Y., B.T., A.T.K.; Writing: U.K., A.T.K.; Critical review: U.K., S.Ö.Y., A.T.K., E.S., B.T.

Conflict of Interest

None declared.

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Hipermetrop Anizometropik Ambliyopili Çocuklarda Kornea Endotel Hücre Morfolojisinin ve Korneal Topografik Parametrelerin Değerlendirilmesi

Amaç: Hipermetrop anizometropik ambliyopili (HAA) pediatrik hastalarda ön segment parametreleri değerlendirildi.

Gereç ve Yöntem: Çalışmaya Ocak-Nisan 2023 tarihleri arasında pediatrik göz hastalıkları kliniği'nde muayene edilen 35 HAA hastasının 35 ambliyopik ve 35 sağlıklı gözü ile 40 sağlıklı emetrop çocuğun 40 gözü dahil edildi. Aksiyal uzunluk (AL), Lenstar LS-900 biyometresi kullanılarak ölçüldü. Korneal anterior segment ve endotel tabakası parametreleri sırasıyla Scheimpflug görüntüleme ve temassız speküler mikroskopi kullanılarak değerlendirildi.

Bulgular: Çocukların ortalama yaşı HAA grubunda 8.5±3.1 yıl, sağlıklı kontrol grubunda ise 8.9±2.2 yıl idi (p=0.252). En iyi düzeltilmiş görme keskinliği ve AL açısından üç grup arasında istatistiksel olarak anlamlı fark bulundu (p<0.001). Anterior segment parametrelerinde gruplar arasında ön kornea eğriliği, kornea hacmi, ön kamara derinliği, toplam yüksek dereceli aberasyonlar ve sferik aberasyonlar açısından istatistiksel olarak anlamlı farklılık olduğu saptandı (sırasıyla, p=0.019, p=0.034, p=0.015, p=0.037 ve p<0.001). Endotel parametreleri açısından gruplar arasında istatistiksel olarak anlamlı bir fark saptanmadı (tümü için p>0.05).

Sonuç: Bu çalışma, ambliyopik hastalarda ambliyopik gözler ve diğer sağlıklı gözler ile emetropik sağlıklı gözler arasında ön segment parametrelerinde istatistiksel olarak anlamlı farklılıklar olabileceğini göstermiştir. Hastalarda ön segment parametrelerinin ayrıntılı değerlendirilmesi hem tanı hem de tedavi yaklaşımlarını önemli ölçüde etkileyebilir.

Anahtar Sözcükler: Aksiyal uzunluk; hipermetrop anizometropik ambliyopi; kornea topografisi; speküler mikroskopi; yüksek dereceli sapma.

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Original Article

Assessing Dyspnea Measurement Methods and Functional Parameters in COPD

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ABSTRACT

Objective: Dyspnea, a major symptom of COPD, reflects both physiological and psychological factors influencing a patient's health status. This study aimed to evaluate the correlation between clinical methods used to measure dyspnea and physiological measures in stable COPD patients.

Methods: A total of 25 stable COPD patients participated in this cross-sectional study, undergoing detailed pulmonary function tests (PFTs), a six-minute walking test, and dyspnea assessments using both indirect and direct methods. Indirect methods included the Turkish versions of the Oxygen Cost Diagram (OCD), Medical Research Council (MRC) Dyspnea Scale, and Baseline Dyspnea Index (BDI), while the direct method employed was the Turkish version of the Borg Dyspnea Scale. Statistical evaluation was made using Spearman's and Pearson correlation ranks, and r and p values were calculated. $p<0.05$ was considered statistically significant. All results were presented separately and as median±standard deviation (SD) for every patient.

Results: The median age of patients was 65 years. The mean values of PFT were FVC 74%±21, FEV1 53%±22, and FEV1/FVC 56%±11. The mean six-minute walking distance was 398±140 meters. Significant correlations were found between most dyspnea measurement methods and the six-minute walking distance, particularly with OCD ($r=0.659$, $p<0.01$), MRC ($r=-0.538$, $p<0.05$), and various BDI components. FVC also correlated significantly with several dyspnea measures.

Conclusion: We showed that different dyspnea measurement methods in COPD patients correlated well with spirometry and six-minute walking test results. OCD was strongly correlated with 6MWT, whereas mMRC and BDI were moderately correlated. There were moderate/weak correlations between OCD, BDI, Borg2, mMRC, and spirometric measures. Our results indicate that dyspnea measurements are components of COPD severity assessment, along with functional exercise capacity and spirometry, and are in alignment with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) system.

INTRODUCTION

COPD is defined as chronic, slowly progressive airway obstruction, with spirometry being the accepted gold standard for diagnosing the disease. FEV1 measurement from spirometry is generally considered the best single predictor of mortality and is used for staging disease severity. However, the use of FEV1 as the primary evaluation parameter is often questioned. Due to the multidimensional nature of COPD and FEV1's low correlation with symptoms, there has long been a recognized need for better categorization and systematic evaluation of patients with COPD.[1]

On the other hand, dyspnea is the subjective perception of breathing discomfort arising from complex and multidimensional mechanisms. These include abnormalities in the respiratory control system, neurochemical receptors, ventilation, respiratory muscles, gas exchange, and more.[2]

When COPD patients become symptomatic, the major complaints are dyspnea, cough, fatigue, sleep disturbances, and exercise intolerance. Inactivity follows dyspnea, which results in physical deconditioning and worsening quality of life. Although a relationship between dyspnea and measurements of lung function does exist, no single physiological measurement (e.g., FEV1) can efficiently explain the various pathologies that cause dyspnea in patients with COPD.[3] Patients with the most severe airflow obstruction might be expected to experience the worst dyspnea, but patients with comparable levels of FEV1 can exhibit very different levels of dyspnea.[4]

This discrepancy between dyspnea amplitude and disease

severity has led to a growing interest in clinical assessment methods. There are globally three ways to clinically evaluate dyspnea:

1. Measurement of dyspnea during activities of daily living (indirect method).

2. Measurement of dyspnea during exercise testing (direct method).

3. The assessment of the effect of dyspnea on "health-related quality of life" using a disease-specific questionnaire.[5]

The aim of this cross-sectional study was to assess the correlation between clinical methods used to measure dyspnea and functional parameters and exercise testing in stable COPD patients, and to determine which methods better reflect the severity of COPD.

MATERIALS AND METHODS

This prospective cross-sectional investigation, carried out between January 2000 and May 2001, was in alignment with the Helsinki Declaration and Good Clinical Practice Guidelines.

Study Population

Twenty-five patients with known, stable COPD defined by the American Thoracic Society[6] were recruited for the study at the outpatient clinic.

Inclusion Criteria:

1. Smoking history of more than 10 pack-years.

2. No exacerbation history in the last 6 weeks.

3. FEV1/FVC ratio of less than 0.7.

4. No history suggestive of asthma.

5. <200 mL and <12% increase in FEV1 after bronchodilator.

6. Being literate.

7. No known cardiac failure.

Exclusion Criteria:

1. History of any other significant respiratory disease.

2. Recent myocardial infarction or unstable angina.

3. Severe musculoskeletal disorders limiting exercise.

4. Cognitive impairment.

5. Severe comorbidities that could affect study participation.

Measurements

After the diagnostic and differential diagnostic steps were completed, spirometry, lung volume measurements, diffusing capacity, and maximal inspiratory and expiratory pressures were measured with Vmax 22 Sensormedics. Six-minute walking test and evaluation of dyspnea using Turkish versions of indirect and direct methods were also performed. All eligible patients underwent these dyspnea assessment tests on the day of recruitment.

Dyspnea Evaluation Methods

1. Indirect Methods:

a. Oxygen Cost Diagram (OCD): This is a visual analog scale that correlates with oxygen requirements at various activity levels (e.g., sleeping, sitting, rapid walking, shopping). It is reported as a value ranging from zero to 100, with a score of 100 indicating no impairment.[7]

b. Modified Medical Research Council (mMRC) Dyspnea Scale: This is a five-point scale based on degrees of different physical activities that precipitate dyspnea. 0 indicates the best and 4 the worst state according to dyspnea sensation.[8]

c. Baseline Dyspnea Index (BDI): It was created to assess dyspnea at a specific moment. This assessment is conducted through a brief interview and includes evaluations of functional impairment (the extent to which daily activities are hindered), magnitude of effort (the total effort required to carry out activities), and magnitude of task. The BDI quantifies the patient's dyspnea in each dimension on a scale from 0 (no impairment) to 4 (severe).[9]

2. Direct Method:

Modified Borg Dyspnea Scale: This method evaluates dyspnea on a 10-point scale. 0 means no dyspnea, whereas 10 indicates the maximum degree of dyspnea. By applying this scale before (Borg 1) and after (Borg 2) the six-minute walking test, a direct measurement of dyspnea is made.[10]

All functional measurements were performed according to the standards defined by the ATS in 1994.[11] The detailed functional assessment included measurements of static lung volumes, diffusion capacity, and inspiratory and expiratory pressures.

Exercise capacity was evaluated using the six-minute walking test (6MWT) as described by ATS Statement 2002.[12] This test measures the distance that a patient can quickly walk on a flat, hard surface in 6 minutes (6MWD). The self-paced 6MWT evaluates the submaximal level of functional capacity. Most patients do not reach their maximum exercise capacity during the 6MWT. They determine their own exercise intensity and are allowed to stop and rest as needed during the test. Since most daily activities are carried out at submaximal exertion levels, the 6MWD may more accurately represent the functional exercise level required for everyday physical activities.[12]

The patients were asked to walk as much as they could in a 20 m hospital corridor. The test was terminated when severe symptoms such as intolerable dyspnea, chest pain, palpitation, or leg cramps appeared. Dyspnea was measured before and after the test using a modified Borg dyspnea scale. Walking distance was recorded in meters.[10,12] The same physician accompanied all the patients.

The GOLD guideline published in 2001[13] made a classification of COPD by severity depending on lung function test results. Patients were categorized as:

• Stage 0: Normal spirometry.

• Stage I (Mild): FEV1/FVC<70% and FEV1≥80%.

• Stage II (Moderate): FEV1<80% but ≥30%.

o Stage IIA: FEV1≥50% but <80%.

o Stage IIB: FEV1≥30% but <50%.

• Stage III (Severe): FEV1<30%.

Statistical Analysis:

Statistical evaluation was made with the NCSS 2000/PASS 2000 program using Spearman's and Pearson correlation ranks, and r and p values were calculated. p<0.05 was considered statistically significant. All results were presented separately and as median±standard deviation (SD) for every patient.

RESULTS

The median age of patients was 65±9 years, duration of disease was 9±6.6 years, the amount of cigarette smoking was 47.5±28.2 pack-years, and the duration of quitting smoking was 7±5 years. 7 (28%) of COPD patients were still smoking when they were recruited. 21 (84%) of the patients were men and 4 (16%) were women.

The detailed functional measurement results were for FVC 2491±741ml (74±21%), FEV1 1403±548 ml (53±22%), FEV1/FVC ratio 56±11%, DLco (ml/min/mmHg) 13.3±5.3 (55±20%), DLCO/VA (ml/mmHg/l/min) 3.4±0.9 (63±15%), FRC 4235±1162ml (129±30%), RV 3552±1154ml (156±46%), RV/TLC (%) 57±9, TLC 6176±1518ml (104±22%), MIP (cmH2O) 74±17 (78±27%), and MEP (cmH2O) 92±34 (49±15%), respectively.

The maximum and minimum values for FVC were 129% and 43%; for FEV1 108% and 21%; for FEV1/FVC 70% and 31%, respectively.

The patients were evaluated according to GOLD guideline 2001.[13] Three patients had mild (Stage I), 4 patients had severe (Stage III) COPD. The remaining 18 patients were in Stage II. 11 of them were fit for Stage IIA, 7 of them for Stage IIB.

The results of dyspnea measurement methods and exercise capacity are shown in Table 1.

FVC showed significant correlation with OCD (r=0.420, p<0.05), BDI functional impairment part (r=0.428, p<0.05), BDI magnitude of effort part (r=0.492, p<0.05), BDI magnitude of task part (r=0.473, p<0.05), BDI focal score (r=0.458, p<0.05) and Borg 2 (r=-0.544, p<0.01). It seems that while FVC decreases, the patients get more dyspneic according to both indirect and direct dyspnea measurement methods. Only the BDI magnitude of effort part has a positive correlation with FEV1 (r=0.460, p<0.05). As FEV1 declines, the patients get dyspneic in situations where less effort is demanded.

No correlation was detected between direct dyspnea measurement method (modified Borg dyspnea scale) and static lung volumes. The part of BDI that questions the magnitude of effort that causes dyspnea shows negative correlation with RV/TLC (r=-0.694) values. This means that increasing intrathoracic gas volume leads to dyspnea in smaller efforts.

6 minute walking test results have significant correlation with all the dyspnea measurement methods except BDI magnitude of task part and Borg dyspnea scale. OCD, BDI magnitude of effort part and BDI focal score had the most significant correlations. Table 2 shows the functional parameters that have significant correlation with dyspnea measurement methods and walking distance.

DISCUSSION

The most important result from the provided data is that Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 second (FEV1) show significant correlations with measures of dyspnea and functional impairment in patients. There is a significant correlation with OCD and

Table 1. Results of indirect and direct dyspnea measurement methods and exercise capacity

Parameter	Maximum	Minimum	Median±SD
Indirect Methods			
OCD (0-100 mm)	100	10	49±23
mMRC (0-4)	4	0	2±1
BDI Function (0-4)	4	0	3±1
BDI Task (0-4)	4	0	3±1
BDI Effort (0-4)	4	1	2±1
BDI Focal (0-12)	12	1	8±2
Direct Methods			
Walking Distance (m)	682.5	78	398±140
Borg 1	6	0	1±2
Borg 2	7	0	3±2

Abbreviations: SD: Standard deviation; OCD: Oxygen cost diagram; mMRC: Modified Medical Researc Council; BDI: Baseline Dyspnea Index.

Table 2. Correlation Between Dyspnea Measurement Methods, Functional Parameters, and Walking Distance (r values of correlation; *p<0.05, **p<0.01)

Parameter	FVC	FVC %	FEV1	RV/TLC	Walking Distance (m)
OCD	0.420*	0.408*	0.355	-0.140	0.659**
mMRC	-0.354	-0.188	-0.129	-0.073	-0.538*
BDI Function	0.428*	0.342	0.303	-0.157	0.532*
BDI Task	0.473*	0.309	0.401	-0.473	0.366
BDI Effort	0.492*	0.462*	0.460*	-0.694**	0.615**
BDI Focal	0.458*	0.378	0.407	-0.512*	0.543**
Borg 1	-0.291	-0.188	-0.233	0.289	0.024
Borg 2	-0.544**	-0.411	-0.405	0.136	-0.009

Abbreviations: SD: Standard deviation; OCD: Oxygen cost diagram; mMRC: Modified Medical Researc Council; BDI: Baseline Dyspnea Index.

walking distance and FVC, FVC%. Hajiro et al.[5] compared different dyspnea measurement methods and found the best correlation between OCD result and FEV1. On the other hand, Robinson et al.[14] investigated the relationship of respiratory drives to dyspnea and exercise performance in COPD patients. They used OCD as the only dyspnea measurement method and found no correlation between FEV1% or FVC% and OCD results.

In our study, OCD results failed in providing a clue about flow limitation. The correlation of OCD results and walking distance shows the value of this dyspnea measurement method in predicting exercise performance.

In our study, the Medical Research Council dyspnea scale (mMRC) shows correlation only with the walking distance. Walking distance reflects an aspect of exercise tolerance which plays a significant role in the quality of life. Hajiro et al.[15] compared the level of dyspnea versus disease severity in indicating the health-related quality of life of patients with COPD. They categorized the patients according to the level of dyspnea using the mMRC scale. They concluded that staging the disease based on FEV1 measurements fails in describing the quality of life when compared with staging according to dyspnea level.

This result, achieved in a large group of patients, suggests that breathlessness measured with mMRC and exercise capacity measured with a 6-minute walking test can reflect a better vision about the patients' general condition than FEV1 measurement only. Although we have not performed health-related quality of life measurement, our results are consistent with this view in the literature.

We found significant correlation between all components and focal score of BDI and FVC. BDI magnitude of effort component had correlation with FVC%, FEV1 and RV/TLC. Walking distance has significant correlation with BDI functional impairment, magnitude of effort components and BDI focal score.

Mahler et al.[9] presented BDI and TDI as new clinical indexes in measurement of dyspnea and compared them with older methods. The older methods examine mainly the magnitude of task that incites dyspnea and do not take the accompanying effort into consideration. Additionally, these methods do not evaluate functional impairment.

The visual analog scale as used in OCD measures the degree of dyspnea but is not enough to disclose all the factors that lead to breathlessness. In the study of Mahler et al.,[9] correlation was sought between dyspnea scores, spirometric measurements, and 12-minute walking test results. BDI focal score showed the best correlation with the 12-minute walking test results. It is weakly correlated with FVC and FEV1.

Foglio et al.[16] recruited COPD and asthma patients with chronic airway obstruction in their study. They reported age, hyperinflation expressed as RV/TLC ratio, and dyspnea measured with BDI scale to be three factors that affect exercise performance. They concluded that FEV1 was insufficient in predicting physiologic deterioration.

BDI, questioning the sensation of dyspnea on a larger scale than the other dyspnea measurement methods, has strong correlation with walking distance. It is also the only dyspnea measurement method that shows a correlation with RV/TLC, which reflects hyperinflation.

In our study, the BDI scale seems to be the most detailed method. It minimizes the subjectivity of the patient, as it is applied by the physician, which—in our opinion—strengthens its reliability.

Modified Borg dyspnea scale[10] principally does not differ from the OCD, which also relies on a visual analog scale. When the modified Borg dyspnea scale is used in combination with an exercise test like the 6-minute walking test, it can disclose the dyspnea generated during this exercise. As it measures dyspnea under observation during a particular exercise, it is categorized as a direct dyspnea measurement method.

In our study, no correlation is found between Borg 1, which reflects the dyspnea degree before the walking test, and lung function results as well as blood gas values. There is no correlation between Borg 1 and walking distance. Borg 2, which reflects the dyspnea degree after the walk-

ing test, has the only correlation with FVC. No correlation exists between blood gas values, walking distance, and Borg 2 results.

We would expect Borg 2 to have significant correlations with airway obstruction, inspiratory and expiratory muscle strength, and walking distance, as it is measured directly after completion of the walking test. Similarly, Hajiro et al.[5] found no correlation between the end-of-exercise Borg and all the functional parameters. It is possible that Borg applied after the exercise could reflect a different aspect of breathlessness.

We would expect but did not detect significant correlation between walking distance and modified Borg dyspnea scale results. As previously mentioned, walking distance shows significant correlation with all the indirect dyspnea measurement methods. OCD, BDI magnitude of effort, and BDI focal score have the most significant correlations.

Borg scale applied before the exercise evaluates the patient's breathlessness in a steady state independent from their functional capacity or muscle strength. Therefore, it is reasonable that this measurement has no correlation with the walking distance.

As many studies have shown inconsistent degrees of correlation between lung function parameters (e.g., FEV1) and measures of dyspnea, clinicians look for new relationships that could reflect the overall condition of the patients. As studies assessing dyspnea and quality of life in patients with chronic, stable COPD grow in number, measurement of short-term changes of these parameters following acute exacerbations is also gaining interest.[17]

A study that compares the effects of the degree of dyspnea and disease severity as evaluated by airway obstruction on the 5-year survival rate of patients with COPD ended in favor of dyspnea measurement. The categorization of patients with COPD based on the level of dyspnea was more discerning than staging of disease severity using the ATS guideline with respect to 5-year survival. It is advisable to include dyspnea as one of the parameters, in addition to airway obstruction, for evaluating patients with COPD in terms of mortality.[18]

Chhabra et al.[19] investigated the inter-relationships among commonly used scales to measure dyspnea—the mMRC grading, BDI, and OCD—in COPD patients. They found it to be moderately strong. In their study, the BDI and OCD scales were significantly associated with some of the measures of physiological impairment, while the mMRC grade was not.

This is also in accordance with our results, as mMRC shows the least correlation with lung function parameters. However, the mMRC grade found its place in the current GOLD staging of COPD as it is simple, easy to administer, and validated as a useful marker in COPD.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was initiated in 1998 with the aim of producing recommendations for the management of COPD based on the best scientific findings. The first report, Global Strategy for the Diagnosis, Management and Prevention of COPD, was released in 2001.[13]

Growing evidence showed that the global evaluation of COPD patients considering functional status, quality of life, and dyspnea is crucial for the optimal management of disease. So, in the last version of the GOLD report—GOLD 2024,[20] we see the disease as a preventable and treatable lung condition which has many aspects.

Our study showed symptomatology reflected by dyspnea measurement scales in COPD patients correlated well with spirometry results.

Nowadays pulmonary rehabilitation programs are improved for achieving better quality of life for patients with chronic respiratory diseases. The aim of these programs is to improve the lung functions of the patients and to relieve the patient-reported outcomes (PROs). One of the most relevant of these outcomes is dyspnea.

New perspectives divide dyspnea into three dimensions: the impact dimension (ID), perception dimension (PD), and emotional dimension (ED). In the study of Molinier et al.,[21] the impact dimension of dyspnea was evaluated with the mMRC scale and was significantly and negatively correlated with FEV1 and baseline 6MWD. Though it was not associated with the two other dimensions (PD and ED) either at baseline or in terms of evolution of the rehabilitation program.

They concluded that the three dimensions of dyspnea should be taken into consideration when treating and rehabilitating COPD patients. This suggestion further supports our findings, which show the need for detailing and encompassing all the dimensions of symptoms and functional measurements in these patients.

As COPD continues to have progressive morbidity and high mortality, patient-reported outcomes are taken widely into consideration. A recent review by Afroz et al.[22] summarized COPD-specific PROs from randomized controlled trials of approved and widely used COPD drugs. They concluded that incorporating dyspnea measurement methods and quality of life measurement methods should be standardized when designing clinical trials. So the relevant PROs are also becoming more helpful in yielding the best benefits patients can achieve.

The present study has several limitations. First, with only 25 patients, the statistical analysis may not have detected some significant results. Second, the cross-sectional analysis does not consider the responsiveness of each measure over time. Third, the absence of a control group prevents extrapolation of the results to other disease groups.

Conclusion

In conclusion, in patients with lower vital capacity and higher intrathoracic gas volume, dyspnea sensation seems to be more pronounced generally. Exercise capacity of

these patients is also limited. The majority of the functional parameters show no correlation with direct and indirect dyspnea measurement methods. So they fail in giving an idea on how dyspneic a patient gets in daily life.

We saw that exercise tolerance, as evaluated using a 6-minute walking test, has significant correlation with almost all dyspnea measurement methods. This points out that dyspnea measurement methods can give useful information about exercise tolerance of COPD patients and serve as complementary tools in both the assessment as well as management of the disease.

The methods used for measuring dyspnea are promising and valuable tools for staging and monitoring COPD patients, as well as assessing their therapy modalities in relation to exercise tolerance. Although somewhat subjective, these dyspnea measurement methods are easy to perform and can serve as a complementary examination in the evaluation of COPD patients.

This study showed that dyspnea—the major symptom of COPD—and lung function tests, which guide the therapeutic decisions, have no significant correlation with each other. In an era where improving the health-related quality of life is a major target of medicine, there is a need for more prospective studies that focus on symptom relief.

Clinical Implications

The findings suggest that routine use of dyspnea scales can be valuable in the clinical management of COPD patients. These tools are easy to administer and can provide insights into the functional status beyond what is captured by spirometry alone.

Patients with a low vital capacity and a high intrathoracic gas volume experienced more breathlessness and had lower exercise tolerance. Although somewhat subjective, dyspnea measurements are easy to perform and can be used as complementary examinations in the follow-up of COPD patients.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: F.I.U., B.U.; Design: F.I.U., B.U.; Supervision: B.U., F.I.U.; Fundings: F.I.U.; Materials: F.I.U.; Data collection &/or processing: F.I.U., B.U.; Analysis and/or interpretation: F.I.U., B.U.; Literature search: F.I.U., B.U.; Writing: F.I.U., B.U.; Critical review: F.I.U., B.U.

Conflict of Interest

None declared.

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KOAH'ta Dispneyi Değerlendiren Yöntemlerin ve Fonksiyonel Parametrelerin Analizi

Amaç: Dispne, KOAH hastalarının en önemli yakınmalarından birisidir. Bu semptom, hastanın fonksiyonel sağlık durumunu gösteren fizyolojik ve psikolojik faktörlerin toplamıdır. Bu çalışmanın amacı, stabil KOAH hastalarında dispneyi ölçmek için kullanılan yöntemler ile fizyolojik ölçümler arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Bu kesitsel, prospektif çalışmaya toplam 25 stabil KOAH hastası alındı. Detaylı solunum fonksiyon testleri, altı dakika yürüme testi ve dolaylı ile doğrudan yöntemlerle dispne ölçümleri değerlendirildi. Dolaylı yöntemler, Türkçe versiyonları olan Oksijen Maliyet Diyagramı (OCD), Medical Research Council (mMRC) Dispne Ölçeği ve Başlangıç Dispne İndeksi (BDI) kullanılarak ölçüldü. Doğrudan yöntem olarak Borg Dispne Ölçeği Türkçe versiyonu kullanıldı. İstatistiksel değerlendirme için Spearman ve Pearson korelasyon testleri yapıldı. P<0.05 değeri istatistiksel olarak anlamlı kabul edildi. Tüm sonuçlar ayrı ayrı ve her hasta için medyan±standart sapma (SD) olarak sunuldu.

Bulgular: Hastaların medyan yaşı 65 idi. Ortalama FVC %74±21, FEV1 %53±22, FEV1/FVC %56±11 saptandı. Altı dakikalık yürüme mesafesi ortalama 398±140 metre olarak belirlendi. Çoğu dispne ölçüm yöntemi ile altı dakikalık yürüme mesafesi arasında, özellikle OCD (r=0.659, p<0.01), MRC (r=-0.538, p<0.05) ve çeşitli BDI bileşenleri ile anlamlı korelasyonlar bulundu. FVC çoğu dispne skalası ile anlamlı korelasyon gösterdi.

Sonuç: KOAH hastalarında farklı dispne ölçüm yöntemlerinin spirometri ve 6 dakikalık yürüme testi sonuçları ile iyi korelasyon gösterdiğini belirledik. OCD, 6MWT ile güçlü bir korelasyon gösterirken, mMRC ve BDI orta derecede korelasyon gösterdi. OCD, BDI, Borg2 ve mMRC ile spirometrik ölçümler arasında orta/zayıf korelasyonlar bulundu. Sonuçlarımız, dispne ölçümlerinin fonksiyonel egzersiz kapasitesi ve spirometri açısından KOAH'ın bileşenleri olduğunu ve bunun da Küresel Kronik Obstrüktif Akciğer Hastalığı Girişimi (GOLD) sistemi ile uyumlu olduğunu göstermektedir.

Anahtar Sözcükler: Dispne ölçüm yöntemleri; fonksiyonel değerlendirme; KOAH.

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Original Article

Comparison of Clinical Characteristics and Outcomes in Pediatric Patients with Ruptured and Unruptured Pulmonary Hydatid Cysts

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Keywords: Pediatric surgery; pulmonary hydatid cyst; ruptured cyst.

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ABSTRACT

Objective: Pulmonary hydatid cyst is a significant health concern, particularly in pediatric patients in endemic regions. Ruptured cysts can lead to severe complications such as bronchopleural fistula and pleural effusion. Surgical management remains the gold standard, with varying approaches based on the rupture status of the cyst. This study aims to compare the clinical characteristics and surgical outcomes of pediatric patients with ruptured and non-ruptured pulmonary hydatid cysts.

Methods: This retrospective observational study included pediatric patients who underwent surgery for pulmonary hydatid cysts at a tertiary care hospital between January 1, 2014, and January 1, 2024. Patients were categorized into two groups: those with ruptured cysts and those with non-ruptured cysts. Demographic data, cyst size, Indirect Hemagglutination Assay (IHA) results, and postoperative complications were compared.

Results: A total of 17 pediatric patients (14 males, 3 females) with a mean age of 11.18 years were included. There were no significant differences between ruptured and non-ruptured cysts in terms of age (p=0.793), gender (p=0.757), cyst size (p=0.962), or IHA positivity (p=0.683). Complications occurred in 50% of patients with ruptured cysts and 46.15% of those with non-ruptured cysts, with no significant difference (p=0.958). One patient with a ruptured cyst developed a bronchopleural fistula requiring lobectomy, while another in the non-ruptured group experienced postoperative pleural effusion managed by Video-Assisted Thoracoscopic Surgery (VATS).

Conclusion: Although no significant differences were found in demographic or clinical variables, ruptured cysts were associated with more severe complications. Careful surgical management and postoperative monitoring are essential in both ruptured and non-ruptured pulmonary hydatid cysts to prevent and manage complications.

INTRODUCTION

Cystic echinococcosis (CE) is a zoonotic infection resulting from the Echinococcus granulosus parasite and is a significant public health concern worldwide. This disease is commonly transmitted in a cyclical pattern between definitive hosts, like dogs, and intermediate hosts, such as sheep. Humans inadvertently become intermediate hosts within this cycle, contributing to the disease's progression. CE leads to the formation of cystic lesions in organs such as the liver and lungs, with the lungs being the most commonly affected site in children.[1-4]

Pulmonary hydatid cysts, especially in children, can lead to significant clinical outcomes. The elastic nature of lung tissue allows cysts to grow rapidly, increasing the likelihood of serious complications. Rupture of the cysts can result in the spread to the bronchial pathways or pleural cavity, leading to complications such as hemoptysis, pneumothorax, and empyema.[5-8] Surgical intervention is regarded as the gold standard for treating pulmonary hydatid cysts, with a preference for lung-preserving surgical techniques. However, whether the cyst is ruptured or not can significantly affect surgical outcomes and the likelihood of developing complications.[9-11]

This research seeks to evaluate the clinical features and surgical outcomes of pediatric patients with both ruptured and non-ruptured pulmonary hydatid cysts.

MATERIALS AND METHODS

This retrospective observational study included pediatric patients who underwent surgery for hydatid cysts at the thoracic surgery department of Kartal Dr. Lütfi Kırdar City Hospital between January 1, 2014, and January 1, 2024. Ethical approval was secured from the local ethics committee (Ethics Committee Number: 2024/010.99/4/13, Date: 27/05/2024). All procedures were carried out in accordance with ethical rules and the principles of the Declaration of Helsinki.

The study included pediatric patients diagnosed with hydatid cysts who underwent surgical treatment. Patient data were collected retrospectively from hospital records. The inclusion criteria were defined as children aged 0-18 years who had surgical intervention for pulmonary hydatid cysts. Based on preoperative radiological assessments (chest X-ray and thoracic computed tomography) and clinical findings, patients were categorized into two groups: those with ruptured cysts and those with non-ruptured cysts. Information was gathered on patient demographics (age, gender), clinical symptoms, laboratory results, cyst size and location, type of surgical procedure, postoperative complications, and length of hospital stay. The results of the Indirect Hemagglutination Assay (IHA) were analyzed alongside the rupture status of the cysts. Additionally, pre- and postoperative albendazole use was recorded for each patient.

All patients underwent standard posterolateral thoracotomy for surgical intervention. The surgical management differed between ruptured and non-ruptured cysts. For non-ruptured cysts, enucleation and capitonnage techniques were preferred, while for ruptured cysts, bronchial fistula closure and cleaning of the cyst cavity were performed. Additionally, in suitable cases, Video-Assisted Thoracoscopic Surgery (VATS) was utilized. This technique is minimally invasive and was preferred in cases with smaller cysts and a lower risk of complications. Capitonnage was performed to close the cyst cavity. In patients with ruptured and/or infected cysts, the germinative membrane was meticulously removed after making an incision in the pericyst, and the cyst cavity was suctioned and irrigated with 5% hypertonic saline. Bronchial openings were identified and closed during this process. Capitonnage was avoided in cases of infected cysts. Postoperatively, albendazole was administered at a dosage of 20 mg/kg/day in patients with multiple cysts, ruptured cysts, or abdominal cysts.

Statistical Analysis

Statistical analyses were conducted to compare the characteristics and outcomes of patients with ruptured and non-ruptured pulmonary hydatid cysts. Continuous variables, such as age and cyst size, were evaluated using the independent samples t-test, with the results reported as mean±standard deviation. Categorical variables, including gender, IHA results, complications, and albendazole use, were analyzed using the chi-square test or Fisher's exact test, where appropriate. A significance threshold of $p<0.05$ was set for all tests. The statistical analyses were carried out using SPSS version 25 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 17 pediatric patients with pulmonary hydatid cysts were included in this study, consisting of 14 males (82.35%) and 3 females (17.65%), with a mean age of 11.18 years (range: 3–16 years) (Table 1). The patients were classified into two groups: those with ruptured cysts (n=4) and those with non-ruptured cysts (n=13) (Fig. 1).

The mean age of patients in the ruptured cyst group was 11.5±5.45 years, compared to 11.08±4.94 years in the non-ruptured group, with no statistically significant age difference between the groups (p=0.793). In the ruptured cyst group, 75% (n=3) were male, while 84.62% (n=11) were male in the non-ruptured group. The gender distribution difference was not statistically significant (p=0.757).

The mean cyst size was 6.75±1.50 cm in the ruptured group and 6.69±2.59 cm in the non-ruptured group. There was no significant difference in cyst size between the two groups (p=0.962) (Table 2). In the ruptured group, 50% (n=2) had positive IHA results, compared to 61.54% (n=8) in the non-ruptured group, with no statistically significant difference (p=0.683).

Complications were observed in 50% (n=2) of patients with ruptured cysts and in 46.15% (n=6) of those with non-ruptured cysts, with no significant difference in the incidence of complications between the groups (p=0.958). In the ruptured cyst group, one patient developed a bronchopleural fistula, which required a left lower lobectomy. In the non-ruptured cyst group, one patient experienced postoperative pleural effusion on the third day, which necessitated debridement and drainage via VATS. No other significant complications were observed in the remaining patients.

Table 1. Patiens Characteristics

Characteristic	Value
Total Patients	17
Mean Age (years)	11.18±4.77
Male (%)	14 (82.35%)
Female (%)	3 (17.65%)
Mean Cyst Size (cm)	6.71±2.02
IHA Positive (%)	15.0 (93.75%)
Complications (%)	2 (11.76%)
Albendazole Usage (%)	17 (100.00%)

IHA: Indirect Hemagglutination Assay.

Table 2. Comparison of age, gender, and cyst characteristics between ruptured and unruptured Cysts

Variable	Ruptured (n=4)	Unruptured (n=13)	p-value
Age (years)	11.75±4.79	11.00±4.95	0.793
Gender (Male)	4 (4)	10 (13)	0.757
Cyst Size (cm)	6.75±2.75	6.69±1.89	0.962
IHA Positive	5.0 (4)	10.0 (13)	0.683

IHA: Indirect Hemagglutination Assay.

Table 3. Comparison of complications and albendazole usage between ruptured and unruptured cysts

Variable	Ruptured (n=4)	Non-Ruptured (n=13)	p-value
Complications	1 (4)	1 (13)	0.958
Albendazole Usage	4 (4)	13 (13)	1.000

All patients in both groups were treated with albendazole, and there was no significant difference in its use between the groups (p=1.0) (Table 3).

DISCUSSION

This study compared the clinical characteristics and surgical outcomes of pediatric patients with ruptured and non-ruptured pulmonary hydatid cysts. Our findings indicate no significant effect of rupture on age, gender, cyst size, IHA results, or overall complications. However, ruptured cysts were associated with a higher risk of severe complications.

Pulmonary hydatid cysts represent a significant health concern in pediatric patients, particularly in endemic regions. Due to the elastic nature of lung tissue, cysts tend to grow rapidly in children, increasing the risk of rupture. The rupture of these cysts can lead to severe complications, necessitating surgical intervention. In the surgical treatment of pulmonary hydatid cysts, parenchyma-preserving techniques such as enucleation and capitonnage are generally preferred. However, in cases of ruptured cysts, bronchial fistula closure and careful cleaning of the cyst cavity are required.[12,13]

In this study, various complications were observed following the surgical treatment of both ruptured and non-ruptured pulmonary hydatid cysts. In the ruptured cyst group, one patient developed a bronchopleural fistula requiring a left lower lobectomy. In the non-ruptured cyst group, one patient experienced postoperative pleural effusion, which was managed with debridement and drainage via VATS. The most common complications in the surgical management of pulmonary hydatid cysts include bronchopleural fistula, pleural effusion, pneumothorax, hemoptysis, and infections. These complications can be effectively managed with careful postoperative monitoring and appropriate interventions.[14,15]

There are numerous studies in the literature regarding pulmonary hydatid cysts. In the study conducted by Kocaman and colleagues, a total of 120 pulmonary hydatid cysts were identified in 94 pediatric patients, with cyst rupture observed in 52.5% of cases. Similar to our study, this research compared ruptured and non-ruptured cysts and found that cyst size significantly impacted the likelihood of rupture. The study reported that cysts larger than 10 cm had a higher risk of rupture, which aligns with the findings of our study. Additionally, their study reported prolonged air leakage as the most common postoperative complication (7.4%). In our study, while we observed more severe complications in ruptured cysts, none of the patients experienced prolonged air leakage.[16]

In the study by Ngcobo and colleagues, 38 pediatric patients were examined, and male predominance was reported in 60.5% of the cases. The majority of the cysts (84.2%) were classified as large (5-9 cm) or giant cysts (>10 cm). In our study, the average cyst size was 6.7 cm, and no significant relationship between cyst size and rupture was found (p=0.962). In Ngcobo's study, 33.3% of ruptured cysts were associated with postoperative complications, with bronchopleural fistula and prolonged air leakage being the most common complications.[17] Similarly, in our study, severe complications such as bronchopleural fistula and the need for lobectomy were observed in the ruptured cyst group.

This study has several limitations. First, its retrospective design may have resulted in incomplete data collection, potentially leading to missing or incomplete information. Second, the small sample size limits the generalizability of the findings. Lastly, the absence of long-term follow-up data restricts a comprehensive assessment of postoperative complications and recurrence rates. Future studies with larger sample sizes and prospective designs are needed to validate these results.

Conclusion

In this study, no significant differences were found in age, gender, cyst size, IHA results, or complication rates between pediatric patients with ruptured and non-ruptured

pulmonary hydatid cysts. However, ruptured cysts were associated with more severe complications, such as bronchopleural fistula requiring lobectomy. These findings underscore the importance of meticulous surgical management for both ruptured and non-ruptured cysts, as well as the necessity of close postoperative monitoring to prevent and manage potential complications.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospita Hospital Ethics Committee (Date: 27.05.2024, Decision No: 2024/010.99/4/13).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.B., R.D.; Design: M.B., A.O., M.T.D., R.B.Ç.; Supervision: M.B., R.D.; Fundings: M.B., R.D.; Materials: M.İ.S., Y.E.Ö.; Data collection &/or processing: M.İ.S., Y.E.Ö.; Analysis and/or interpretation: M.İ.S., Y.E.Ö., M.B.; Literature search: M.B., A.O., M.T.D., R.B.Ç.; Writing: M.B., R.D. Critical review: M.B., R.D.

Conflict of Interest

None declared.

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Rüptüre Olmuş ve Olmamış Pulmoner Hidatik Kistleri Olan Pediatrik Hastalarda Klinik Özellikler ve Sonuçların Karşılaştırılması

Amaç: Pulmoner hidatik kist, özellikle endemik bölgelerdeki pediatrik hastalarda önemli bir sağlık sorunudur. Rüptüre olmuş kistler, bronkopulmoner fistül ve plevral efüzyon gibi ciddi komplikasyonlara yol açabilir. Cerrahi tedavi, kistin rüptür durumuna bağlı olarak değişen yaklaşımlar ile altın standart olarak kabul edilmektedir. Bu çalışma, rüptüre ve rüptüre olmamış pulmoner hidatik kistlere sahip pediatrik hastaların klinik özelliklerini ve cerrahi sonuçlarını karşılaştırmayı amaçlamaktadır.

Gereç ve Yöntem: Bu retrospektif gözlemsel çalışma, 1 Ocak 2014 ile 1 Ocak 2024 tarihleri arasında üçüncü basamak bir hastanede pulmoner hidatik kist nedeniyle cerrahi müdahale geçiren pediatrik hastaları içermektedir. Hastalar, rüptüre ve rüptüre olmamış kistler olmak üzere iki gruba ayrıldı. Demografik veriler, kist boyutu, indirekt hemaglutinasyon testi (IHA) sonuçları ve postoperatif komplikasyonlar karşılaştırıldı.

Bulgular: Toplamda, ortalama yaşı 11,18 olan 17 pediatrik hasta (14 erkek, 3 kız) çalışmaya dahil edildi. Rüptüre ve rüptüre olmamış kistler arasında yaş (p=0.793), cinsiyet (p=0.757), kist boyutu (p=0.962) veya IHA pozitifliği (p=0.683) açısından anlamlı bir fark bulunmadı. Komplikasyonlar, rüptüre kistli hastaların %50'sinde ve rüptüre olmamış kistli hastaların %46,15'inde meydana geldi; bu oranlar arasında anlamlı bir fark yoktu (p=0.958). Rüptüre kistli bir hastada lobektomi gerektiren bronkopulmoner fistül gelişirken, rüptüre olmamış grupta bir hastada postoperatif plevral efüzyon oluştu ve bu durum video yardımlı torakoskopik cerrahi (VATS) ile tedavi edildi.

Sonuç: Demografik veya klinik değişkenler açısından anlamlı bir fark bulunmamasına rağmen, rüptüre kistlerin daha ciddi komplikasyonlarla ilişkili olduğu görülmüştür. Hem rüptüre hem de rüptüre olmamış pulmoner hidatik kistlerde komplikasyonları önlemek ve yönetmek için dikkatli cerrahi müdahale ve postoperatif izlem büyük önem taşımaktadır.

Anahtar Sözcükler: Pediatrik cerrahi; pulmoner hidatik kist; rüptüre kist.

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Original Article

The Purpose of Lung Wedge Resections in Thoracic Surgery Practice

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ABSTRACT

Objective: Lung wedge resection, frequently used in thoracic surgery practice, is the only non-anatomic resection. This study aims to determine the instances in which wedge resection was performed in our center and their frequency.

Methods: In this study, we included patients over the age of 18 who underwent wedge resection in our clinic between 01.01.2020 and 01.06.2023. In addition to the demographic information of all patients, we retrospectively analyzed medical records such as diagnosis, applied surgical method, number of resections, duration of drainage, duration of hospitalization, and complications. The obtained data were evaluated statistically.

Results: Our team included a total of 166 patients in the study, of whom 109 (65.7%) were male and 57 (34.3%) were female. The mean age of the study population was 49.89±19.35 years, 49.40±20.33 years for males, and 50.82±17.43 years for females. Our team performed diagnostic wedge resections in 81 (48.8%) and curative wedge resections in 85 (51.2%) of the patients included in the study. The mean age of the patients who underwent diagnostic resection was significantly higher than the patients who underwent curative resection. While in diagnostic resection cases, the most common diagnoses were nodule and interstitial lung disease, in curative resection cases, the most common diagnoses were bullae-bleb and CAI (cyst-abscess-infection). We performed video-assisted surgery in 90 cases, thoracotomy in 75 cases, and sternotomy in one case. The rate of multiple wedges was significantly higher in the thoracotomy group than in the video-assisted thoracoscopic surgery (VATS) group. In other comparative analyses, no significant difference was found between the two groups using different surgical techniques.

Conclusion: Wedge resections are the most commonly used resection technique by thoracic surgeons in clinical practice. While it is frequently used for diagnostic purposes in metastatic lung diseases and less frequently in interstitial lung diseases, it is particularly used for curative purposes in bullous lung diseases.

INTRODUCTION

Lung wedge resection, frequently used in thoracic surgery clinical practice, is the only non-anatomic resection. Lung resections are applied in a wide variety of diseases, ranging from lung cancer and metastatic diseases to diagnosis and treatment of lungs' non-malignant parenchymal diseases and infections.

Until the middle of the twentieth century, pneumonectomies were the most accepted type of resection, particularly in lung cancer.[1,2] Today, lobectomy is the most commonly used resection method in lung cancer, but recent studies have shown that sub-lobar resections are also successful.[3] For this reason, wedge resections, one of the sub-lobar resection methods, are being used in malignant lung diseases as well as in non-malignant parenchymal diseases.

In our study, we aimed to determine the cases in which wedge resection was performed in our center and their frequencies.

MATERIALS AND METHODS

In this study, we included patients over the age of 18 who underwent wedge resection in our clinic between 01.01.2020 and 01.06.2023. In addition to the demographic information of all patients, we recorded medical

information such as diagnosis, performed surgery, surgical method, number of wedge resections, duration of drainage, hospitalization, and complications. Patients with insufficient data and patients who required anatomical resection during the procedure or according to the frozen section results were excluded from the study.

The data obtained were statistically analyzed using SPSS (Statistical Package for the Social Sciences Version 22.0; SPSS Inc. Chicago, IL, USA) software. For continuous variables, values with kurtosis and skewness levels between ±2 were assumed to show normal distribution.[4] Categorical data were presented as number (n) and percentage (%), continuous data not showing normal distribution were presented as median (25th–75th percentiles), and continuous data showing normal distribution were presented as mean±standard deviation. The relationship between categorical data was analyzed by Chi-Square analysis and Fisher's exact test. The relationship between continuous and categorical variables was analyzed by the Independent Groups T-test and Mann Whitney-U test. In the analyses, results with a p-value below 0.05 were considered statistically significant.

Our study was conducted following the decision and approval of the Non-Interventional Clinical Research Ethics Committee of İzmir Katip Çelebi University, with the approval number 0303, dated June 15, 2023.

RESULTS

We included 166 patients in the study, of whom 109 (65.7%) were male and 57 (34.3%) were female. The mean age of the study population was 49.89±19.35, 49.40±20.33 in males, and 50.82±17.43 in females. According to the surgical purpose, the population was divided into two groups: diagnostic resection group and curative resection group. In the patients included in the study, wedge resection was performed for diagnostic purposes in 81 patients (48.8%) and for curative purposes in 85 patients (51.2%). The distribution of the parameters in the whole population and both groups and the results of comparative analysis between the two groups are presented in Table 1.

The mean age of the patients who underwent diagnostic resection was significantly higher than the patients who underwent curative resection. The most common diagnoses were nodule and interstitial lung disease in cases with diagnostic resection, while the most common diagnoses were bullae-bleb and infectious causes in cases with curative resection. The need for additional surgical intervention was most frequently observed in the curative resection group, and the most common additional surgery was decortication. On the other hand, mediastinal lymph node sampling was the most common surgical intervention in the diagnostic resection group. The need for additional treatment, the most common additional treatment being oncological treatment, was mostly observed in the diagnostic resection group.

Recurrence was observed in 26 (15.6%) of the patients who underwent wedge resection, while 2 of the patients with recurrence underwent surgery for hydatid cyst and 7 for pneumothorax. In 17 patients who underwent wedge resection for metastasectomy, new metastatic nodules were observed to develop during their follow-up. There was no significant difference between the two groups in terms of gender, surgical method, wedge count, drainage duration, follow-up time, hospitalization duration, and recurrence. One case in which sternotomy was preferred as a surgical intervention was excluded from the analyses.

Fourteen (8.4%) of the patients underwent resection due to primary lung carcinoma. Three of these patients underwent curative resection. One of the patients who underwent curative resection underwent wedge resection due to limitations in the pulmonary function test. In the other patient, bulla resection was performed due to secondary pneumothorax, and minimally invasive adenocarcinoma with negative surgical margins was detected incidentally, so no additional surgical intervention was considered, and the patient was followed up. In the third patient, the procedure was terminated because the pathological diagnosis was not clear as a result of the frozen examination studied during the surgery. Upon the pathology result of a typical carcinoid tumor and the surgical margins were negative, additional surgical intervention was not considered. In 11 patients with advanced stages, the diagnosis was made by wedge resection of the mass itself or its metastases, as the diagnosis could not be made with minimally invasive procedures.

Various complications were observed in 42 (25.3%) cases during follow-up, and their distribution in all cases and the groups according to the purpose of surgery is presented in Figure 1. The most common complication was found to be prolonged air leak (PAL)-expansion defect in all populations and groups.

Considering the number of wedge resections performed, 121 (72.8%) of 166 patients underwent single wedge resection, and 45 (27.3%) underwent multiple wedge resection. No complications were observed in 71.9% of the patients

Figure 1. The distribution of complications according surgical purpose groups.

Table 1. The distribution of parameters between groups according to surgical purpose

		Surgical Purpose Groups		
	Total population	**Diagnostic Resection**	**Curative Resection**	**p**
Age (/year)	49.89±19.35[a]	62.75±11.20[a]	37.63±17.44[a]	0.001
Gender				
Male	109(%65.7)	49(60.5)	60 (%70.6)	0.171
Female	57 (%34.3)	32 (%39.5)	25 (%29.4)	
Diagnostic Groups				
Nodule	70 (%42.2)	62 (%76.5)	8 (%9.4)	0.001
Bullae-bleb	68 (%41.0)	1 (%1.2)	67 (%78.8)	
ILD	18 (%10.8)	17 (%21.0)	1 (%1.2)	
C-A-I	10 (%6.0)	1 (%1.2)	9 (%10.6)	
Surgical method				
VATS	90 (%54.2)	39 (%48.1)	51 (%60.7)	0.105
Thoracotomy	75 (%45.2)	42 (%51.9)	33 (%39.3)	
Sternotomy	1 (%0.6)	-	-	-
Wedge count				
Singular	121 (%72.9)	55 (%67.9)	66 (%77.6)	0.158
Multiple	45 (%27.1)	26 (%32.1)	19 (%22.4)	
Additional surgical intervention				
None	26 (%15.7)	17 (%21.0)	9 (%10.6)	0.001
Decortication	67 (%40.4)	6 (%7.4)	61 (%71.8)	
Cyst treatment	2 (%1.2)	-	2 (%2.4)	
Mediastinal LN sampling	57 (%34.3)	46 (%56.8)	11 (%12.9)	
Decortication+LN sampling	13 (%7.8)	12 (%14.8)	1 (%1.2)	
Mediastinal mass excision	1 (%0.6)	-	1 (%1.2)	
Duration of drainage (/day)	4.0(2.0-5.0)[b]	4.0 (2.0-5.0)[b]	4.0 (3.0-7.0)[b]	0.119
Duration of hospitalisation (/day)	6.0 (4.0-9.0)[b]	6.0 (4.0-8.0)[b]	7.0 (4.0-9.0)[b]	0.151
Additional treatment requirement				
None	138 (%83.1)	57 (%70.4)	81 (%95.3)	0.001
Oncological treatment	21 (%12.7)	20 (%24.7)	1 (%1.2)	
PM treatment	7 (%4.2)	4 (%4.9)	3 (%3.5)	
Recurrence				
Yes	140 (%84.3)	64 (%79.0)	76 (%89.4)	0.065
No	26 (%15.7)	17 (%21.0)	9 (%10.6)	

ILD: Interstitial Lung Disease; C-A-I: Cyst-Abcess Infection; VATS: Video-Assisted Thoracoscopic Surgery; LN: Lymph Node; PM: Pulmonary Medicine a: Mean±Standard deviation; b: median (25.-75th percentile).

who underwent single wedge resection and 82.2% of the patients who underwent multiple wedge resection. Of the patients who underwent curative wedge resection, 66 had single wedge resection and 19 had multiple wedge resections. The mean postoperative drain follow-up was 5.18 days, 5.52 days in patients with single wedge resection, and 4.82 days in patients with multiple wedge resection. There was no significant difference between drain follow-up or hospital stay in patients who underwent single or multiple wedge resection.

We divided the study population according to the surgical method into two groups as video-assisted thoracoscopic surgery (VATS) group (n:90) and the thoracotomy group (n:75) and presented the distribution and comparative analyses of various parameters between the groups in Table 2. In the comparative analyses, the sternotomy case (n:1) was excluded from the analysis. The rate of multiple wedges was significantly higher in the thoracotomy group compared with the VATS group. The mean age of the cases in which the VATS method was used was significantly lower than in the cases in which the thoracotomy method was used. The most common diagnosis was bullae-bleb in the VATS group, while the most common diagnosis was nodule in the thoracotomy group. In cases in which thoracotomy was used, the rate of multiple wedges was significantly higher than in the VATS group. In other comparative analyses, no significant difference was found between the two groups using different surgical techniques.

The distribution of postoperative complications in all cases and cases with different surgical methods is presented in

Table 2. The distribution of parameters between groups according to surgical method

	Total population	Surgical method groups		p
		VATS	Thoracotomy	
Age (/year)	49.87±19.40[a]	46.20±21.74[a]	54.29±15.16[a]	0.007
Gender				
Male	108 (%65.5)	57 (%63.3)	51 (%68.0)	0.530
Female	57 (%34.5)	33 (%36.7)	24 (%32.0)	
Diagnostic Groups				
Nodule	69 (%41.8)	36 (%40.0)	33 (%44.0)	0.011
Bullae-bleb	68 (%41.2)	44 (%48.9)	24 (%32.0)	
ILD	18 (%10.9)	9 (%10.0)	9 (%12.0)	
C-A-I	10 (%6.1)	1 (%1.1)	9 (%12.0)	
Surgical purpose				
Diagnostic	81 (%49.1)	39 (%43.3)	42 (%56.0)	0.105
Curative	84 (%50.9)	51 (%56.7)	33 (%44.0)	
Wedge count				
Singular	120 (%72.7)	72 (%80.0)	48 (%64.0)	0.022
Multiple	45 (%27.3)	18 (%20.0)	27 (%36.0)	
Additional surgical intervention				
None	26 (%15.8)	10 (%11.1)	16 (%21.3)	0.094
Decortication	67 (%40.6)	42 (%46.7)	25 (%33.3)	
Cyst treatment	2 (%1.2)	-	2 (%2.7)	
Mediastinal LN sampling	56 (%33.9)	29 (%32.2)	27 (%36.0)	
Decortication+LN sampling	13 (%7.9)	9 (%10.0)	4 (%5.3)	
Mediastinal mass excision	1 (%0.6)	-	1 (%1.3)	
Duration of drainage (/day)	4.0 (2.0-5.0)[b]	4.0 (2.0-6.0)[b]	4.0 (2.5-5.0)[b]	0.861
Duration of hospitalisation (/day)	6.0 (4.0-9.0)[b]	6.0 (4.0-9.0)[b]	7.0 (5.0-9.5)[b]	0.094
Additional treatment requirement				
None	137 (%83.0)	79 (%87.8)	58 (%77.3)	0.200
Oncological treatment	21 (%12.7)	8 (%8.9)	13 (%17.3)	
PM treatment	7 (%4.2)	3 (%3.3)	4 (%5.3)	
Recurrence				
Yes	139 (%84.2)	76 (%84.4)	63 (%84.0)	0.938
No	26 (%15.6)	14 (%15.6)	12 (%16.0)	

ILD: Interstitial Lung Disease; C-A-I: Cyst-Abcess Infection; VATS: Video-Assisted Thoracoscopic Surgery; LN: Lymph Node; PM: Pulmonary Medicine a: Mean±Standard deviation; b: median (25.-75th percentile).

Figure 2. The number of complications in VATS cases was 24 (26.7%), while the number of complications in thoracotomy cases was 17 (22.7%), and there was no difference between the groups in terms of complication occurrence. The most common complication in both groups was found to be prolonged air leak-expansion defect.

When our patients with complications were evaluated according to the Clavien-Dindo surgical complication classification, the complications of the patients were grade 1 in 26, grade 2 in eight, grade 3A in one, grade 3B in three, and grade 4A in three. None of the patients who underwent surgery developed grade 5 complications.

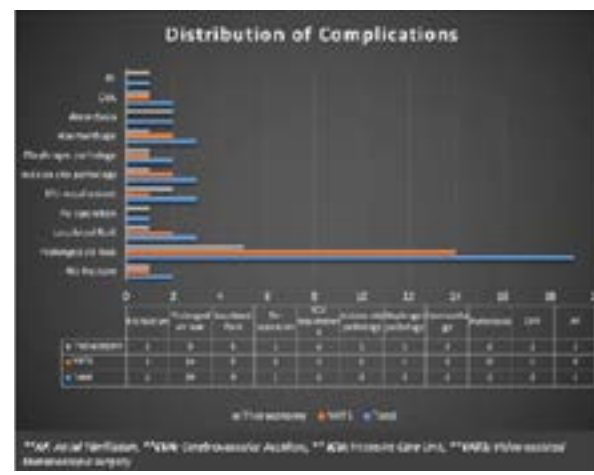

Figure 2. The distribution of observed complications according to surgical method groups.

DISCUSSION

After dividing the cases into two groups (diagnostic re-

section group and curative resection group), we reached a similar number of patients, but we discovered that the mean age was significantly lower in patients who underwent resection for curative purposes. The reason for this may be that the surgical indications differ significantly in the curative and diagnostic groups. We believe that the cause of this difference was the fact that pneumothorax cases, which we observed more frequently in the young patient group, were more common in the curative group and that the nodules that underwent surgical procedures due to suspicion of malignancy were more common in the diagnostic group. However, in the surgical treatment of early-stage non-small cell lung carcinoma (NSCLC), the trend on resection type has recently been towards sub-lobar resections, with wedge resection being among the alternatives.[5-6] In the future, wedge resections may be more common in the early-stage curative surgical treatment of NSCLC and should be considered as a factor that may affect the mean age.

Significant differences were observed between the two groups in the variety of additional surgical interventions. While decortication was the most common additional procedure in curative procedures, mediastinal lymph node sampling was the most common in diagnostic wedge resections performed for suspected malignancy. The main factor in this difference was considered to be the widespread use of apical pleurectomy in pneumothorax surgery[7] and the need to reveal the lymph node metastasis status in operations performed for suspected malignancy.[8] When malignancy is proven after wedge resections performed due to suspicion of malignancy, oncological methods step in the treatment process in appropriate patients.[9] Therefore, oncological treatment has come into prominence as the most common additional treatment after the operation.

While evaluating our complications, we observed that, in accordance with the literature, the most common complication in both groups was prolonged air leak-expansion defect.[10-12] Although not only air leaks exceeding 5 days but also minimal expansion defects observed after drainage termination were included in this complication group, complications were observed within the rates stated in the literature.[11]

While evaluating the wedge resections according to the surgical method used, we observed that VATS was used more frequently in our clinic, and the mean age of patients who underwent VATS was significantly lower than thoracotomy (p=0.007). Currently, in the surgical treatment of pneumothorax, which is observed more frequently in young patients, thoracotomy is rarely used.[13] In other indications as well, VATS, which offers more patient comfort and has been shown to shorten the duration of hospitalization, is more prominent as stated in the literature.[14] However, thoracotomy is still an actively used method due to the need for diagnosis by detecting increasingly small nodules, technical difficulties in detecting deeply located nodules, and the need for digital examination in the presence of multiple nodules.[15] In our study, it was shown that thoracotomy was used more frequently in patients who needed multiple wedge resection.

Although there are studies in the literature showing that VATS can be performed with lower complication rates, there are also studies indicating more air leak complications.[16,17] In our study, no significant difference was observed in both groups in terms of complication occurrence.

Conclusion

Wedge resections are the most common type of resection used by thoracic surgeons in clinical practice. They can be performed for diagnostic or curative purposes in different patient groups. Nowadays, with the inclination towards less invasive methods, VATS has become a more frequently used method in wedge resections in our clinic too. However, it should be kept in mind that thoracotomy, which has similar complication rates, can also be used in necessary cases.

Ethics Committee Approval

The study was approved by the Izmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee (Date: 15.06.2023, Decision No: 2023/303).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.K., A.C.Y.; Design: M.K., M.Ü., A.C.Y.; Supervision: M.K., M.Ü., A.C.Y.; Fundings: M.K., N.A., N.B.S., M.Ü., S.Ş., K.İ.T., A.C.Y., E.B.; Materials: N.A., N.B.S., S.Ş., K.İ.T.; Data collection &/or processing: N.A., N.B.S., S.Ş., K.İ.T.; Analysis and/or interpretation: A.C.Y.; Literature search: M.K., M.Ü., A.C.Y.; Writing: M.K., M.Ü., A.C.Y., E.B.; Critical review: M.K., E.B.

Conflict of Interest

None declared.

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Göğüs Cerrahisi Pratiğinde Akciğer Kama Rezeksiyonlarının Kullanım Amacı

Amaç: Akciğer kama rezeksiyonu, göğüs cerrahisi pratiğinde kullanılan tek anatomik olmayan rezeksiyondur ve sıklıkla uygulanmaktadır. Bu çalışmada, kama rezeksiyon uygulanan durumları ve sıklıklarını belirlemeyi amaçladık.

Gereç ve Yöntem: Çalışmamıza 01.01.2020–01.06.2023 tarihleri arasında kliniğimizde kama rezeksiyon uygulanan 18 yaş üzeri olgular dahil edildi. Tüm olguların demografik bilgileri yanında tanı, uygulanan cerrahi yöntemi, rezeksiyon sayıları, dren kalış süreleri, hastane yatış süreleri ve komplikasyonları gibi tıbbi kayıtları retrospektif olarak incelendi. Elde edilen veriler istatistiksel olarak değerlendirildi.

Bulgular: Çalışmaya toplam 166 hasta dahil edilmiş olup bunların 109'u (%65.7) erkek; 57'si (%34.3) kadındı. Çalışma popülasyonunun yaş ortalaması 49.89±19.35 olup erkeklerde 49.40±20.33; kadınlarda ise 50,82±17.43 olarak izlendi. Çalışmaya dahil edilen hastalara wedge rezeksiyon işlemi 81'inde (%48.8) tanısal amaçlı, 85'inde (%51.2) küratif amaçlı yapıldığı görüldü. Tanısal amaçlı rezeksiyon yapılan vakaların yaş ortalamaları, küratif amaçlı rezeksiyon yapılan vakalara göre anlamlı olarak yüksek saptanmıştır. Tanısal amaçlı rezeksiyon yapılan vakalarda en sık izlenen tanılar nodül ve interstisyel akciğer hastalığı iken, küratif amaçlı rezeksiyon yapılan vakalarda en sık izlenen tanılar bül-bleb ve kist-abse-enfeksiyon olarak izlendi. Çalışmadaki vakaların 90'ına cerrahi yöntem olarak video yardımlı cerrahi uygulanırken, 75 vakaya torakotomi ve 1 vakaya ise sternotomi uygulanmıştır. Torakotomi kullanılan vakalarda wedge sayısının multipl olma oranı VATS kullanılan gruba göre anlamlı olarak yüksek izlenmiştir. Yapılan diğer karşılaştırmalı analizlerde farklı cerrahi teknik kullanılan iki grup arasında anlamlı farklılık saptanmamıştır.

Sonuç: Kama rezeksiyonlar, klinik uygulamada göğüs cerrahları tarafından en sık kullanılan rezeksiyon şeklidir. Sıklıkla metastatik akciğer hastalıklarında ve daha nadir olarak interstisyel akciğer hastalıklarında tanısal amaçlı kullanılırken, özellikle büllöz akciğer hastalıklarında küratif amaçlı uygulanmaktadır.

Anahtar Sözcükler: Kama; küratif; rezeksiyon; tanısal.

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Original Article

The Relationship Between NT-proBNP Levels and Prognosis of the Patients Hospitalized in the Internal Medicine Clinic

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Keywords: Inpatients; NT-proBNP; prognosis; risk assessment.

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ABSTRACT

Objective: N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) is an important biomarker used in the diagnosis of heart failure. However, recent studies have shown that NT-proBNP is associated not only with cardiovascular diseases but also with other conditions such as pneumonia, renal failure, and malignancies. This study aims to investigate the impact of NT-proBNP on the prognosis of patients hospitalized in the internal medicine department.

Methods: A retrospective evaluation was conducted on 971 patients hospitalized between January 2022 and October 2023. Patients were divided into two groups: those who were discharged and those who were transferred to the Intensive Care Unit (ICU) or deceased, and their relationships with NT-proBNP levels were examined.

Results: Patients with high NT-proBNP levels had a significantly higher risk of being transferred to the ICU or dying (Discharged vs. ICU/Deceased: 3732.15±7297 vs. 10923±12572; p<0.001). ROC analysis identified a cutoff value of >1826 pg/ml, above which the risk of ICU admission or death was found to be 5.44 times higher (OR: 5.44). When analyzed separately in patients with and without cardiac symptoms, the prognostic impact of NT-proBNP levels was significant in both groups (p<0.001).

Conclusion: NT-proBNP can be used as an effective biomarker for predicting prognosis in both cardiac and non-cardiac diseases in patients hospitalized in internal medicine clinics.

INTRODUCTION

N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) is a biologically inactive protein that is produced in the heart chambers and released along with BNP during the breakdown of the proBNP protein.[1] BNP, which increases with the stretching of the heart muscle, is a peptide that regulates cardiovascular homeostasis by reducing renin and aldosterone secretion through diuresis and vasodilation.[2] These two molecules (BNP and NT-proBNP) are released into the bloodstream in nearly equal amounts during the breakdown of proBNP. However, because BNP has a relatively short biological half-life (approximately 20 minutes), whereas NT-proBNP has a longer half-life (approximately 60–120 minutes) and remains in circulation longer, NT-proBNP is a more easily measurable biomarker for the diagnosis and monitoring of heart failure compared to BNP.[3,4]

Various studies have shown that NT-proBNP is associated not only with heart failure but also with other conditions such as pneumonia, cerebrovascular events, malignancy, and end-stage renal failure.[5-10] These findings suggest that NT-proBNP is closely related to overall health status in addition to cardiovascular diseases.

Studies investigating the association of NT-proBNP with clinical conditions beyond cardiovascular diseases suggest that this biomarker has a broad range of applications for integration into clinical practice.[11,12] It has also been shown that NT-proBNP levels increase in conditions involving heightened inflammatory responses and acute phase reactants.[13] The aim of this study is to evaluate the relationship between NT-proBNP and the discharge status of patients hospitalized in the internal medicine ward, independent of comorbidities and reasons for admission. This examination aims to demonstrate the potential utility of NT-proBNP as a marker for determining the prognosis of patients in the ward and to integrate it more effectively into clinical practice, thereby contributing to future re-

search that will explore the significance of NT-proBNP in medical applications.

MATERIALS AND METHODS

This study was conducted retrospectively by evaluating patients who were hospitalized and followed up in the Internal Medicine ward between January 2022 and October 2023, and whose NT-proBNP values were measured. The study was approved by the institutional ethics committee (approval no: 116; 26/10/2023) and complied with the Declaration of Helsinki and good clinical practice guidelines.

Serum NT-proBNP levels, discharge status, primary diagnosis, and comorbidities were added to the study form by scanning the hospital information systems. The patients included in the study were evaluated in two groups. Group 1 consisted of patients who were discharged from the Internal Medicine ward in good health (control group), while Group 2 included patients who were transferred to the Intensive Care Unit or who died in the ward (study group). The NT-proBNP values and discharge statuses of patients in both groups were compared. Patients who left the ward voluntarily by signing a treatment refusal form or were referred to an inpatient ward other than the Intensive Care Unit were not included in the study due to the uncertainty of their prognostic status.

Statistical Analysis

The data were analyzed using the SPSS 25.0 software package. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of the data distribution. Descriptive statistical methods (mean, standard deviation, median, IQR, frequency, percentage) were used to evaluate the study data. The Independent t-test was used for the comparison of two groups with parametric distribution, while the Mann-Whitney U test was used for the comparison of two groups with non-parametric distribution. ROC analysis was used to determine the cutoff value. The Chi-square test was used for the analysis of categorical data. Statistical significance was evaluated at the level of $p<0.05$ for all values.

RESULTS

A total of 971 patients with a mean age of 68±17.69 years were included in the study. When the prognoses of the patients after hospitalization were examined, it was observed that 814 patients were discharged from the ward, 151 patients were transferred to the Intensive Care Unit, and 6 patients passed away. Due to the relatively low number of deceased patients, these patients were combined with those transferred to the Intensive Care Unit, forming a group of 157 patients. The relationship between the patients' NT-proBNP levels and their prognosis is presented in Table 1.

In Table 1, it is evident that there is a significant difference between the group of patients who were discharged and those who were either transferred to the ICU or deceased. The NT-proBNP levels of patients who were discharged and returned home were significantly lower compared to the other patient group (Discharged–ICU or Deceased: 3732.15±7297–10923±12572; $p<0.001$).

In Table 2, the distribution of previous diseases that are thought to potentially affect the NT-proBNP levels in the 971 patients is presented. The patients were divided into two groups: those with cardiac findings, such as a history of hypertension, coronary artery disease, and heart failure (659 patients), and those with no history of cardiac disease until the time of admission (312 patients). The NT-proBNP values were compared based on their discharge

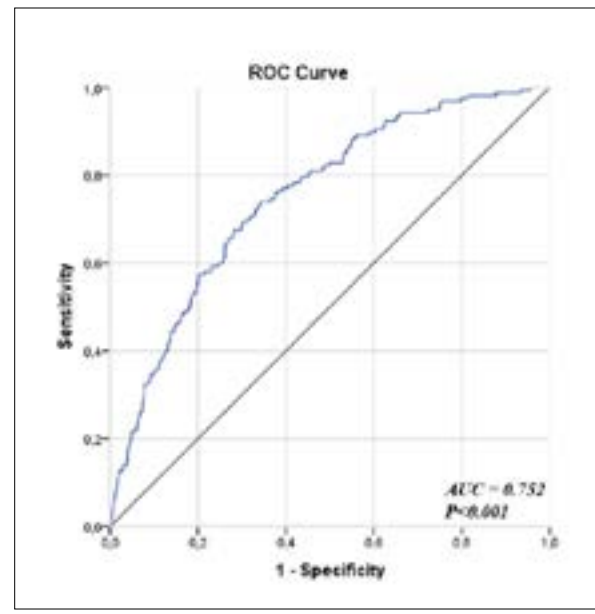

Figure 1. ROC curve regarding the effect of NT-proBNP levels on the prognosis of paitents.

Table 1. Effects of NT-proBNP values on post-hospitalization prognosis

	Dischaged (n:814)	ICU/Deceased (n:157)	p-value
NT-proBNP			
Mean±SD	3732.15±7297	10923±12572	<0.001
Median(IQR)	931 (2302)	5138(13788)	

Table 2. Chronic Diseases of Patients, Their Numbers, and Percentages

Condition	Number of Patients	Percentage (%)
Hypertension	580	59.70
Coronaryarterydisease	226	23.30
Heartfailure	186	19.20
Diabetesmellitus	370	38.10
Chronickidneydisease	194	20.00
Acutekidneyfailure	167	17.20
Liverfailure	31	3.20
COPD orAsthma	133	13.70
Pneumonia	125	12.90
Pulmonaryembolism	18	1.90
Malignancy	108	11.10
Pancreatitis	70	7.20
Anemia	93	9.60
Cerebrovascular accident	102	10.50
Dementia	111	11.40
Hypothyroidism	66	6.80
Hyperthyroidism	11	1.10
Rheumatologic diseases	33	3.40

Table 3. The effects of NT-proBNP levels on the prognosis after hospitalization in patients with and without cardiac complaints

	Cardiacproblem (-)			Cardiac problem (+)		
	Dischaged (n:272)	ICU/Deceased (n:40)	p Value	Dischaged (n:542)	ICU/Deceased (n:117)	p Value
Mean±SD	1275±3870	6754±9768	<0.001	4967±8243	12348±13131	<0.001
Median(IQR)	249 (793)	2330 (4922)		1547 (4349)	7435(18219)	

status from the ward (Table 3).

As seen in Table 3, NT-proBNP levels in discharged patients, regardless of whether they had cardiac findings or not, were significantly lower compared to those who were transferred to the ICU or who died (p<0.001). ROC analysis was performed to determine a cutoff value for NT-proBNP to ensure its usability in the clinic. The ROC curve resulting from the analysis is shown in Figure 1.

Table 4 presents the ROC curve analysis. The area under the ROC curve (AUC) was calculated to be 0.752. This value indicates that NT-proBNP has good discriminative ability as a prognostic marker. The cutoff value determined from the ROC curve analysis was found to be >1826. NT-proBNP levels above this value were associated with a high-risk prognosis. According to the analysis results, the sensitivity was calculated as 73.89%, and the specificity as 65.81%.

When patients were evaluated based on whether their NT-proBNP levels were above or below the cutoff value of 1826 pg/ml, it was observed that this had a significant impact on their discharge outcomes (Table 5).

When the discharge outcomes of patients are reviewed based on the determined cutoff value, it is observed that 41 patients, representing 7.1% of the 577 patients with a cutoff value of ≤1826, were in the ICU-deceased group. However, when the cutoff value is >1826, this rate significantly increases to 29.4% (116 out of 394 patients) (χ^2(1,

Table 4. ROC Curve Analysis Table

Area Under the ROC Curve (AUC)	0.752
Standard Error	0.0203
95% ConfidenceInterval	0.724to 0.779
z-value	12.409
p<0.0001	
Youden Index J	0.3969
Cutoff Point	>1826
Sensitivity	73.89
Specificity	65.81

Table 5. The Impact of the Determined Cut-off Value on Patient Discharge

NT-proBNP	Dischaged	ICU/Deceased	p
Cut-off ≤ 1826	536	41	<0.0001
Cut-off> 1826	278	116	

N=971)=81.17, p<0.00001). Additionally, the risk of ICU admission or mortality before discharge for patients with an NT-proBNP value>1826 pg/ml was found to be approximately 5.44 times higher than others (OR=5.44).

DISCUSSION

BNP is a protein that has been shown to increase when the heart ventricle walls are stretched or under pressure as a result of physiological and biochemical processes in many diseases, particularly heart failure.[7-10] This suggests that NT-proBNP may have a wide application area in its integration into clinical practice. In our study, the NT-proBNP levels measured at the time of hospital admission in patients who were subsequently discharged in good health from the internal medicine ward were significantly lower than the NT-proBNP levels at the time of admission of patients who were transferred to intensive care or who deceased after their condition became critical while hospitalized in the internal medicine clinic. Since this relationship has been demonstrated in both patients with and without previous cardiac complaints, it gives important messages in terms of the prognosis of patients.

In a study conducted by Fonarow and colleagues involving 48,629 individuals, it was found that BNP levels measured at hospital admission significantly predicted in-hospital mortality in patients with acute decompensated heart failure. The study divided BNP levels into four groups, and the in-hospital mortality rates were found to be 1.9% in those with BNP ≤430 pg/ml, while it was 6.0% in those with BNP ≥1,730 pg/ml. Consequently, the routine assessment of BNP levels has been shown to provide valuable prognostic information for risk stratification and management of these patients.[14] Similar to this study, there are various studies in the literature that examine the relationship between NT-proBNP levels and prognosis. While many studies focus on patients with heart failure symptoms, research exploring the relationship between NT-proBNP and other chronic diseases has also begun to emerge.

According to the results of a study conducted by Waldum and colleagues involving 2,076 patients, the risk of cardiovascular mortality significantly increases as NT-proBNP levels rise in heart failure patients with impaired renal function. Specifically, it was found that 59.1% of patients with impaired renal function had NT-proBNP levels above 2180 pg/ml, and the 2-year survival rate for this group was 57%; this rate was significantly lower than the 85% survival rate observed in patients with normal renal function.[15]

In another study by Nowak and colleagues, the potential of NT-proBNP, MR-proANP, and BNP to predict short- and long-term mortality in patients with community-acquired pneumonia was compared, and all three natriuretic peptides were found to be effective. NT-proBNP was shown to be an independent predictor of both short- and long-term mortality (hazard ratio: 1.004, 95% CI: 1.00–1.01, p=0.001, per 300 pg/ml increase). These findings suggest that NT-proBNP levels provide simple and robust predictions in patients with community-acquired pneumonia and that its prognostic accuracy is comparable to the pneumonia severity index.[13] While the relationship between NT-proBNP levels and prognosis in this study shows similarities to ours, the focus on patients diagnosed solely with community-acquired pneumonia differentiates this study from ours.

Another study conducted by Idris et al.[8] on a group of 125 patients showed that NT-proBNP levels had significant effects on 1-year mortality in patients with acute stroke. NT-proBNP levels in deceased patients (980.2±1249.9 pmol/L) were significantly higher than in survivors (125.4±244.9 pmol/L), suggesting the possibility of occult cardiac dysfunction, although the patients did not have obvious complaints of heart failure. Cox regression analysis performed in the study evaluated 1-year mortality using variables such as age, gender, creatinine, urea, ALT, alkaline phosphatase, and NT-proBNP. According to the results of the analysis, the most significant variable for 1-year mortality was log NT-proBNP (Wald 17.9, p<0.0001). Fifteen of 57 patients with a median NT-proBNP value above 42 pmol/L died within 1 year, whereas only 1 of 57 patients with a median value below this value died (p<0.001). Although this study is specific to ischemic stroke patients, unlike other studies, it consists of patients without significant heart failure.

In a study conducted by Benmachiche and colleagues involving 3,833 individuals, the in-hospital mortality rate and length of stay were found to be higher in the fifth quintile group with the highest NT-proBNP levels compared to other groups (20.3% vs. 6.5% and 20.8±24.0 days vs. 14.9±26.5 days, both p<0.001). After multivariate adjustment, the hazard ratio (HR) for in-hospital mortality in the fifth quintile group was determined to be 1.97 (1.57-2.46), and the adjusted length of stay was 20.4±1.0 days (p<0.001). As a result, patients with high NT-proBNP levels were found to be at a higher risk of in-hospital mortality and longer hospital stays, independent of their clinical characteristics.[11] The difference between this study and other studies is that NT-proBNP levels were not only limited to patients with heart failure or cardiac symptoms but

also included 2,177 other patients without any cardiac or pulmonary disease findings.

This study aligns with ours in that it includes not only patients with heart failure symptoms but also a significant number of patients without heart failure. Similarly, in our study, NT-proBNP levels were statistically significantly lower in patients who were discharged in good health compared to those in the other group, regardless of whether they had known heart failure or not.

In a study conducted by Kotanidou and colleagues, NT-proBNP levels were found to be a significant biomarker for predicting ICU mortality in 233 consecutive patients with non-cardiac critical illness. The study demonstrated that NT-proBNP levels at ICU admission were significantly higher in non-survivors. Additionally, it was shown that this biomarker was effective in predicting ICU mortality independent of APACHE II scores and cytokine levels.[12] While this study, like ours, includes all patient groups, our study focuses on patients discharged from the internal medicine ward, whereas their study addresses the impact on the prognosis of ICU patients.

When the results of these studies and ours are evaluated together, it can be said that NT-proBNP levels are important for determining the need for ICU admission, as in our study, and for predicting prognosis in the ICU. In some studies, NT-proBNP values have been divided into quintiles to indicate the severity of illness, while in others, the risk has been determined based on the degree of increase in proBNP levels.[12-15]

In our study, through ROC analysis aimed at determining the risk of ICU admission or discharge, we identified NT-proBNP>1826 pg/ml as the cutoff value with 73.89% sensitivity and 65.81% specificity. According to this cutoff value, the risk of ICU admission or death before discharge was found to be approximately 5.44 times higher in patients with NT-proBNP levels>1826 pg/ml (OR=5.44).

Although NT-proBNP levels are typically used as indicators of heart failure and other cardiac conditions, they can also increase in various non-cardiac diseases. These increases are due to non-cardiac factors and may be associated with different mechanisms. Sepsis is a condition characterized by organ dysfunction resulting from the body's excessive response to infection. In septic shock, elevated inflammatory cytokines and increased vascular permeability place additional stress on the heart, leading to increased NT-proBNP levels.[16,17]

In both acute and chronic renal failure, NT-proBNP levels can rise significantly. This increase results from impaired clearance of NT-proBNP through the kidneys or fluid accumulation due to renal failure, which subsequently impacts the heart and leads to elevated circulating levels.[15-18]

In patients with COPD, chronic hypoxia places stress on the right ventricle and can lead to pulmonary hypertension. Similarly, during a pulmonary embolism, the sudden increase in pressure on the right ventricle can increase NT-proBNP release.[19,20]

In cancer patients, NT-proBNP levels may rise due to the systemic effects of the malignancy itself and the cardiotoxic effects of chemotherapeutic agents. This increase is associated with mechanisms such as inflammation, oxidative stress, and direct cardiac damage.[9,21]

Our study is different from others in that it includes not only cardiac-related conditions but also other chronic diseases, and it evaluates these conditions as a whole. However, there are some limitations to this study. The retrospective nature of our data set and the limited sample size are considered weaknesses of the study.

Conclusion

In conclusion, this study demonstrates that NT-proBNP levels can be used to determine prognosis not only in cardiac diseases but also in patients admitted to internal medicine wards for various other reasons. The identified NT-proBNP cutoff value of >1826 pg/ml provides high accuracy in predicting the need for intensive care or the risk of mortality. These findings support the broader use of NT-proBNP in clinical practice.

Ethics Committee Approval

The study was approved by the Health Sciences University Istanbul Fatih Sultan Mehmet Training and Research Hospital Ethics Committee (Date: 26.10.2023, Decision No: 116).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: A.Ö., N.O.; Design: M.K., Y.S.; Supervision: Y.S., M.S.; Fundings: A.Ö., N.O.; Data collection &/or processing: M.K., N.O.; Analysis and/or interpretation: Y.S., A.Ö.; Literature search: M.S., N.O.; Writing: M.K., Y.S.; Critical review: A.Ö., N.O.

Conflict of Interest

None declared.

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Dahiliye Kliniğinde Yatan Hastaların NT-proBNP Değeri ile Prognoz Arasındaki İlişki

Amaç: N-terminal pro-B-tipi Natriüretik Peptid (NT-proBNP), kalp yetmezliği tanısında kullanılan önemli bir biyomarkerdir. Ancak son çalışmalar, NT-proBNP'nin yalnızca kardiyovasküler hastalıklarla değil, aynı zamanda pnömoni, böbrek yetmezliği ve maligniteler gibi diğer durumlarla da ilişkili olabileceğini göstermektedir. Bu çalışma, NT-proBNP'nin iç hastalıkları servisinde yatan hastaların prognozu üzerindeki etkisini araştırmayı amaçlamaktadır.

Gereç ve Yöntem: Ocak 2022-Ekim 2023 tarihleri arasında yatan 971 hasta retrospektif olarak değerlendirildi. Hastalar, taburcu edilenler ve Yoğun Bakım Ünitesi'ne sevk edilen ya da vefat edenler olarak iki gruba ayrıldı ve NT-proBNP seviyeleri ile ilişkileri incelendi.

Bulgular: NT-proBNP seviyeleri yüksek olan hastaların Yoğun Bakım Ünitesi'ne sevk edilme veya ölüm riski anlamlı derecede yüksek bulundu (Taburcu–YBU veya Ex: 3732.15±7297–10923±12572; p<0.001). ROC analizi sonucunda belirlenen kestirim değeri >1826 pg/ml idi ve bu değerin üzerinde olan hastalarda yoğun bakıma gitme veya ölüm riskinin 5.44 kat daha yüksek olduğu görüldü (OR: 5.44). Kardiyak bulgusu olan ve olmayan hastalarda ayrı ayrı değerlendirildiğinde, NT-proBNP düzeylerinin prognoz üzerindeki etkisinin her iki grupta da belirgin olduğu saptandı (p<0,001).

Sonuç: NT-proBNP, hem kardiyak hem de kardiyak olmayan hastalıkların prognozunu belirlemede etkili bir biyomarker olarak iç hastalıkları kliniğinde yatan hastaların prognozunu öngörmede kullanılabilir.

Anahtar Sözcükler: NT-proBNP; prognoz; risk belirleme; yatan hastalar.

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Original Article

Effects of Different Anesthetic Agents on Postoperative Cognitive Functions in Laparoscopic cholecystectomy

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Keywords: Postoperative cognitive dysfunction, Mini-Cog test, desflurane, sevoflurane, propofol

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ABSTRACT

Objective: In this study, it was aimed to compare the effects of inhalation anesthesia applied with sevoflurane or desflurane and intravenous anesthesia with propofol on early postoperative cognitive functions.

Methods: This study included patients with the ASA I-III classes, aged between 30-70 years and who underwent elective laparoscopic gallbladder surgery. The cognitive function levels of the patients were determined by performing the Mini-Cog test the day before the surgery. The patients were randomly divided into three groups as Group I (Desflurane), Group II (Sevoflurane), and Group III (Propofol). After induction of anesthesia with propofol and remifentanil rocuronium, endotracheal intubation was performed in all patients. In addition to the remifentanil infusion administered to all patients during the maintenance of anesthesia, anesthesia depth was provided with desflurane, sevoflurane inhalation or propofol infusion, with a bispectral index (BIS) of 40-60. The Modified Aldrete Recovery Scores (MARS) were measured and recorded at the postoperative 5th, 10th, 20th, and 30th minutes in all patients. Pain levels were evaluated with a visual analog scale (VAS) at the 10th, 20th, and 30th minutes postoperatively. The Mini-Cog test was repeated by the same physician at the postoperative 24th hour and compared with the preoperative values.

Results: There was no difference in demographic characteristics, duration of surgery and anesthesia, postoperative MARS and VAS values between the three groups (for all, $p>0.05$). While there was no significant difference between the preoperative and postoperative Mini-Cog test scores in the Desflurane and Propofol groups ($p>0.05$), it was observed that the Mini-Cog test in the sevoflurane group was significantly lower than in the Propofol group and Desflurane group ($p=0.002$ and $p=0.012$, respectively).

Conclusion: It was concluded that desflurane and propofol did not have negative effects on cognitive functions, while sevoflurane had a negative effect on postoperative cognitive functions.

INTRODUCTION

Postoperative cognitive dysfunction can lead to varying degrees of morbidity, from mild concentration disorders to memory loss. This results in a low quality of life after surgery. Furthermore, postoperative cognitive dysfunction was associated with mortality at 3 months and 1 year.[1-3]

Although the pathogenesis of postoperative cognitive dysfunction is not fully known, old age, pre-existing neurological diseases, cardiovascular disease, and alcohol use were considered as risk factors.[4] On the other hand, the effects of anesthetic drugs on postoperative cognitive functions and recovery have been the subject of research for many years.[5]

Sevoflurane and desflurane among inhalation anesthetics, and propofol among intravenous anesthetics, provide rapid recovery. The effects of these three popular anesthetic agents on postoperative cognitive functions may differ with their effects on recovery.[6]

Neuropsychological tests have been developed for rapid and practical evaluation of cognitive functions. In order to both standardize the examination and reduce time loss, pre- and postoperative cognitive functions can be evaluated with these tests, and how the postoperative cognitive functions are affected can be measured.

The aim of this study was to investigate the effects of different general anesthesia agents and techniques on postoperative cognitive functions in elective laparoscopic cholecystectomy operations.

MATERIALS AND METHODS

Before the beginning of the study, ethics approval was obtained from the local ethics committee (Dr. Lutfi Kirdar City Hospital ethics committee, approval date: 25.09.2019, number: 2019/514/162/8). This study was conducted in accordance with the principles of the Declaration of Helsinki. A total of 101 patients in ASA I-III physical condition, aged 30-70 years, literate, and without any neurological or psychological disease, and who were scheduled for elective laparoscopic cholecystectomy were included in the study. The patients were enrolled in the study after they were informed about the objectives of the study and their written consent was obtained.

Patients with neurological or psychiatric diseases affecting the central nervous system and cognitive functions, and patients using any medication affecting the central nervous system were excluded from the study.

All patients included in the study were evaluated in the general surgery service the day before the surgery. Age, gender, marital status, education level, and smoking status of the patients were recorded. The Mini-Cog test [7] was applied and scored. The patients were randomly divided into three groups as Group I (Desflurane), Group II (Sevoflurane), and Group III (Propofol).

Electrocardiography (ECG), pulse oximetry, non-invasive arterial blood pressure, and bispectral index (BIS) monitoring were performed in the operating room. Anesthesia was induced with propofol 2 mg/kg and remifentanil 1 µg/kg, muscle relaxation was achieved with rocuronium 0.6 mg/kg, and the patients were intubated endotracheally. The patients were ventilated perioperatively with a 50% air-oxygen mixture with EtCO2: 35-45 mmHg. In the maintenance of anesthesia with remifentanil (0.05-1 µg/kg/min) infusion, desflurane at a concentration of 4%-6%, or sevoflurane inhalation at a concentration of 1%-2.5%, or propofol (6-10 mg/kg/hour) infusion was administered with a BIS of 40-60 for depth of anesthesia.

At the end of the operation (while the gallbladder was taken out and the port entrances were closed), all anesthetics were discontinued, and the standard postoperative analgesia protocol (1 mg/kg tramadol iv bolus and 1 g paracetamol infusion) was applied. The recovery of the patients who were taken to the recovery room was evaluated at the 5th, 10th, 20th, and 30th minutes postoperatively using the Modified Aldrete Recovery Scoring (MARS). Pain assessments were made with a visual analog scale (VAS) at the 10th, 20th, and 30th minutes postoperatively. The Mini-Cog test was repeated by the same physician at the postoperative 24th hour and compared with the preoperative values.

To understand the difference between the preoperative Mini-Cog value (pre-Mini-Cog) and the postoperative Mini-Cog value (post-Mini-Cog), a new variable we named the "adaptation cog" was created. This variable was found by subtracting the preoperative Mini-Cog value from the postoperative Mini-Cog value. The value found was marked -1 if negative, 0 if equal, and +1 if positive. Based on this variable, the change in patients was divided into 3 groups as positive (+1), negative (-1), and ineffective (0).

Statistical Analysis

The data obtained in the study were statistically analyzed using IBM® SPSS® (The Statistical Package for the Social Sciences) Statistics version 25.0.

The variables were characterized using mean values. Percentage values were used for qualitative variables. Normal distributions were reported as mean±SD. The ANOVA Welch test was used to measure the difference between groups. Tamhane's T2 test was used for comparison between groups. Pearson Chi-square test was used to analyze the qualitative variables and show that the data were homogeneously distributed. $p<0.05$ values were considered statistically significant.

RESULTS

Before the beginning of the study, ethics approval was obtained from the local ethics committee (Dr. Lutfi Kirdar City Hospital ethics committee, approval date: 25.09.2019, number: 2019/514/162/8). This study was conducted in accordance with the principles of the Declaration of Helsinki. A total of 101 patients in ASA I-III physical condition, aged 30-70 years, literate, and without any neurological or psychological disease, and who were scheduled for elective laparoscopic cholecystectomy were included in the study. The patients were enrolled in the study after they were informed about the objectives of the study and their written consent was obtained.

Patients with neurological or psychiatric diseases affecting the central nervous system and cognitive functions, and patients using any medication affecting the central nervous system were excluded from the study.

All patients included in the study were evaluated in the general surgery service the day before the surgery. Age, gender, marital status, education level, and smoking status of the patients were recorded. The Mini-Cog test[7] was applied and scored. The patients were randomly divided into three groups as Group I (Desflurane), Group II (Sevoflurane), and Group III (Propofol).

Electrocardiography (ECG), pulse oximetry, non-invasive arterial blood pressure, and bispectral index (BIS) monitoring were performed in the operating room. Anesthesia was induced with propofol 2 mg/kg and remifentanil 1 µg/kg, muscle relaxation was achieved with rocuronium 0.6 mg/kg, and the patients were intubated endotracheally. The patients were ventilated perioperatively with a 50% air-oxygen mixture with $EtCO_2$: 35-45 mmHg. In the maintenance of anesthesia with remifentanil (0.05-1 µg/kg/min) infusion, desflurane at a concentration of 4%-6%, or sevoflurane inhalation at a concentration of 1%-2.5%, or propofol (6-10 mg/kg/hour) infusion was administered with a BIS of 40-60 for depth of anesthesia.

Table 1. Distribution of demographic characteristics of the groups

		Desflurane	Sevoflurane	Propofol	Total	p value
Gender						
Male	(n, %)	14, 13.90	10, 9.90	10, 9.90	34, 33.70	0.315
Female	(n, %)	22, 21.80	23, 22.80	22, 21.80	67, 66.30	
Education						
Literate	(n, %)	1, 1.00	5, 5.00	0, 0.00	6, 5.90	0.139
Primary school	(n, %)	25, 24.80	18, 17.80	21, 20.80	64, 63.40	
High School	(n, %)	8, 7.90	6, 5.90	9, 8.90	23, 22.80	
University	(n, %)	2, 2.00	4, 4.00	2, 2.00	8, 7.90	
Marital Status						
Single	(n, %)	2, 2.00	2, 2.00	3, 3.00	7, 6.90	0.802
Married	(n, %)	34, 33.70	31, 30.70	29, 28.70	94, 93.10	
Smoking						
No	(n, %)	26, 25.70	19, 18.80	18, 17.80	63, 62.40	0.065
Yes	(n, %)	10, 9.90	9, 8.90	13, 12.90	32, 31.70	
Ex-Smoker	(n, %)	0, 0.00	5, 5.00	1, 1.00	6, 5.90	
ASA Class						
I	(n, %)	11, 10.90	7, 6.90	8, 7.90	26, 25.70	0.429
II	(n, %)	20, 19.80	15, 14.90	17, 16.80	52, 51.50	
III	(n, %)	5, 5.00	11, 10.90	7, 6.90	23, 22.80	

Abbreviations: N: number; ASA: American Society of Anesthesiologists.

At the end of the operation (while the gallbladder was taken out and the port entrances were closed), all anesthetics were discontinued, and the standard postoperative analgesia protocol (1 mg/kg tramadol iv bolus and 1 g paracetamol infusion) was applied. The recovery of the patients who were taken to the recovery room was evaluated at the 5th, 10th, 20th, and 30th minutes postoperatively using the Modified Aldrete Recovery Scoring (MARS). Pain assessments were made with a visual analog scale (VAS) at the 10th, 20th, and 30th minutes postoperatively. The Mini-Cog test was repeated by the same physician at the postoperative 24th hour and compared with the preoperative values.

To understand the difference between the preoperative Mini-Cog value (pre-Mini-Cog) and the postoperative Mini-Cog value (post-Mini-Cog), a new variable we named the "adaptation cog" was created. This variable was found by subtracting the preoperative Mini-Cog value from the postoperative Mini-Cog value. The value found was marked -1 if negative, 0 if equal, and +1 if positive. Based on this variable, the change in patients was divided into 3 groups as positive (+1), negative (-1), and ineffective (0).

Statistical Analysis

The data obtained in the study were statistically analyzed using IBM® SPSS® (The Statistical Package for the Social Sciences) Statistics version 25.0.

The variables were characterized using mean values. Percentage values were used for qualitative variables. Normal distributions were reported as mean±SD. The ANOVA Welch test was used to measure the difference between groups. Tamhane's T2 test was used for comparison between groups. Pearson Chi-square test was used to analyze the qualitative variables and show that the data were homogeneously distributed. $p<0.05$ values were considered statistically significant.

DISCUSSION

In this study, no significant difference was found between the preoperative and postoperative Mini-Cog test scores in the desflurane and propofol groups. However, the Mini-Cog test scores decreased significantly in the sevoflurane group.

Postoperative cognitive impairment is a condition characterized by impaired memory and concentration. The goal of evaluating postoperative cognitive functions is to measure the expected and unexpected long-term effects of anesthesia and surgery on cognitive functions. In order for these adverse effects to be as minimal as possible, uneventful induction and maintenance of anesthesia should be ensured. The aim is to return to preoperative

Table 2. Comparison of age, anesthesia and surgery times, pain and recovery scores between the groups

	Desflurane	Sevoflurane	Propofol	Total	p value
Age (years)					
n	36	33	32	101	0.526
Mean±SD	51.86±8.96	53.9±10.4	53.4±10.3	53.03±9.82	
Surgery time (min)					
n	36	33	32	101	0.394
Mean±SD	82.14±14.36	91.2±17.4	86.09±10.4	86.6±14.9	
Anesthesia time (min)					
n	36	33	32	101	0.081
Mean±SD	95.6±14.12	101.5±19.5	98.59±10.2	97.5±16.9	
VAS10					
n	36	33	32	101	0.076
Mean±SD	3.89±2.08	4.06±1.78	3.94±1.95	3.97±1.82	
VAS20					
n	36	33	32	101	0.091
Mean±SD	4.39±2.38	4.82±1.26	4.28±2.16	4.57±2.02	
VAS30					
n	36	33	32	101	0.102
Mean±SD	4.58±2.29	4.81±1.4	4.38±1.99	4.47±2.03	
MARS5					
n	36	33	32	101	0.122
Mean±SD	5.52±1.09	5.18±1.15	5.25±1.01	5.34±1.10	
MARS10					
n	36	33	32	101	0.089
Mean±SD	7.64±1.07	7.33±1.41	7.26±1.29	7.36±1.27	
MARS20					
n	36	33	32	101	0.139
Mean±SD	9.05±1.22	8.97±1.38	8.96±1.21	8.99±1.29	
MARS30					
n	36	33	32	101	0.079
Mean±SD	9.75±0.55	9.77±0.33	9.53±0.51	9.72±0.49	
Total					
n	36	33	32	101	
%	35.60%	32.70%	31.70%	100.00%	

Abbreviations: N: number; SD: standart deviation; min: minutes; VAS: Visual Analog Scale; MARS: Modified Aldrete Recovery Score.

Table 3. Preoperative and postoperative Mini-Cog values of the patients

	Desflurane	Sevoflurane	Propofol	Total	p
Pre-Mini-Cog					
n	36	33	32	101	0.394
Mean±SD	4.13±0.96	4.36±0.78	3.91±1.2	4.13±1.02	
Post-Mini-Cog					
n	36	33	32	101	0.338
Mean±SD	4.16±1.0	3.72±1.42	3.96±1.3	4.00±1.24	

Abbreviations: N: number; SD: standart deviation; Mini-Cog: Mini Cognitive Assessment.

performance as soon as possible and to avoid permanent cognitive impairment.[2]

The causes of postoperative neurologic dysfunction are still unclear. The general opinion is that there are changes in the activity of the central nervous system due to the

Table 4. Mini-Cog variation (adaptation Cog) by anesthetic agents and differences between anesthetic agents

	Maintenance agent	Mean difference	p	N	Mean	Standard deviation
Desflurane	Sevoflurane	0.449*	0.012	36	0.06	0.583
	Propofol	-0.069	0.934			
Sevoflurane	Desflurane	-0.449*	0.012	33	-3.9	0.659
	Propofol	-0.519*	0.002			
Propofol	Desflurane	0.069	0.934	32	0.13	0.492
	Sevoflurane	0.519*	0.002			

Abbreviations: N: number; p: p value; *: statistically significant difference.

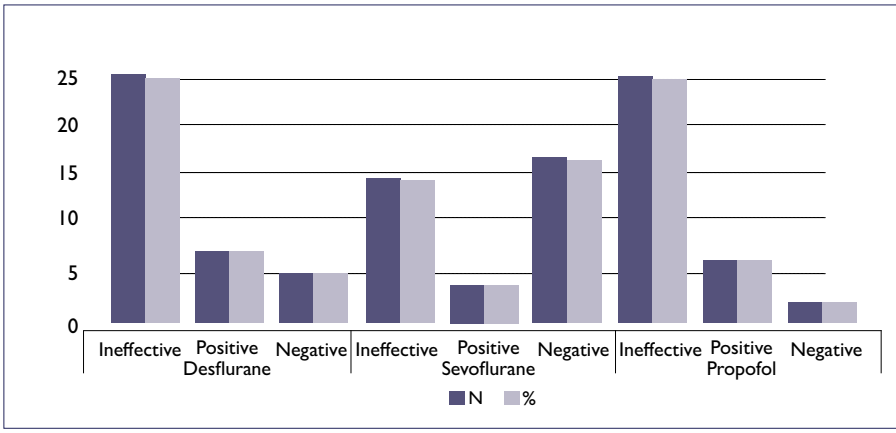

Figure 1. Anesthetic agent-based number and proportions of the adaptation Cog variable.

residual effects of the proven negative effects of anesthetic agents in postoperative cognitive dysfunction. In the study by Hussain et al.[8] investigating the effects of general anesthesia on dementia in elderly patients, general anesthesia was found to pose an increased risk of postoperative delirium and postoperative neurocognitive disorders compared to the population that did not receive general anesthesia.

It has been shown that anesthesia and surgery cause an increase in biomarkers in plasma suggestive of neuronal damage. Therefore, in addition to pre-existing neurological disease, hypoxia during the operation and advanced age, many other factors may be the cause of postoperative cognitive impairment.[9]

The choice of anesthetic drugs may also affect postoperative cognitive status, as residual levels of inhaled anesthetics may produce changes in central nervous system activity. Among inhaler anesthetics, desflurane and sevoflurane are known to provide early recovery due to their low blood-gas partition coefficients. However, this situation does not fully reflect their effects on cognitive functions.

Different results were obtained in studies investigating the effects of these two inhalation anesthetics on postoperative cognitive functions in different surgical procedures. For example, in a study by Bilotta et al.,[10] it was shown that desflurane provided earlier cognitive improvement in overweight patients who underwent craniectomy. In another study, it was shown that although postoperative recovery was faster in those treated with desflurane than those treated with sevoflurane, the effects of the two inhalation agents on cognitive functions were similar in patients over 65 years of age who had knee or hip surgery.[11]

Green et al.[12] compared the effects of desflurane and sevoflurane on neurocognitive functions after urological interventions in patients over 65 years of age but found no significant difference. It was reported that postoperative neurocognitive disorders can be induced, especially in elderly patients and in the presence of systemic inflammatory diseases. While the similar feature of these two studies is that the study groups consisted of elderly patients over 65 years of age, the characteristic of the patient groups in Bilotta's study was that they were overweight. Therefore, due to the low fat/blood partition coefficient of desflurane, it can be removed from the body faster in obese patients and may affect cognitive functions less.

All inhalation and intravenous anesthetic agents have different effects that are not yet known, in addition to their known effects on the central nervous system. Therefore, when investigating the negative effects of these agents on postoperative cognitive functions, not only their pharmacodynamic properties but also their pharmacokinetic properties should be considered.

Zhang et al.[13] investigated the improvement of neurocognitive functions after major cancer surgery in elderly patients and showed that the incidence of delayed neurocognitive recovery was lower in those treated with propofol compared to sevoflurane. As in the study by Zhang et al., BIS was used in our study to standardize the depth of anesthesia and the degree of sedation in all three groups, ensuring the concentration adequacy of the anesthetic agents and eliminating individual differences as much as possible. Consistent with Zhang et al.'s study, it was concluded in our study that cognitive functions were affected more in the sevoflurane group than in the other two groups.

However, a systematic review showed that propofol has a greater adverse effect on postoperative cognitive functions than sevoflurane in elderly patients with lung cancer.[14]

Xing et al.[15] investigated the early and late postoperative effects of sevoflurane and propofol anesthesia combined with remifentanil in intracranial tumors (subtentorial gliomas). Both types of anesthesia methods were found to be equally effective on postoperative neurocognitive functions.

Guo et al.[16] evaluated sevoflurane and propofol anesthesia in terms of cerebral oxygenation and neurocognitive dysfunction. According to the results of the study, which included patients aged 40-75 years who underwent abdominal surgery for more than two hours, it was determined that while sevoflurane and propofol did not cause a significant difference in terms of postoperative neurocognitive function, cerebral oxygenation was better preserved in the sevoflurane group.

In a study by Royse et al.[17] in which they evaluated early cognitive dysfunction in cardiac operations, it was found that propofol caused significant postoperative cognitive dysfunction compared to desflurane and had a significant effect on prolongation of hospital stay.

It was observed that the effects of sevoflurane, desflurane, and propofol on postoperative cognitive functions have not been clearly demonstrated. The results of many clinical studies differ from each other.

The effects of sevoflurane, desflurane, and propofol on postoperative cognitive functions were generally studied in pairwise comparative studies. Comparisons between anesthetic agents in each study yielded different results, albeit minimally. This may be due to the variety of tests used. In our study, the Mini-Cog test, which has been introduced more recently in clinical use, was used rather than the Mini Mental State test used in most of the other studies mentioned. Although the Mini Mental State test includes longer analyses than the Mini-Cog test, language differences may adversely affect the reliability of the test. It has been observed that the Mini-Cog test is more practical, is not affected by language differences, and shows no difference from the Mini Mental State test in measuring cognitive functions in clinical use.[18] It can be thought that the tests used may also be effective in the differing effects of sevoflurane, desflurane, and propofol on cognitive functions between studies.

The results of this study indicate that postoperative cognitive functions are affected more in the sevoflurane group than in the propofol and desflurane groups. High concentrations of sevoflurane (>1.5 MAC) may impair the autoregulation of cerebral blood flow (CBP), leading to a decrease in CBP. In order to provide 40%-60% BIS indicators in the preoperative period, sevoflurane levels >1.5 MAC may have been used in some cases, which could make it difficult to control cerebral blood flow regulation and explain the decline in postoperative neurocognitive functions. Sevoflurane tends to reach inspired concentration more slowly than desflurane. This indicates that induction and recovery may be slower. Additionally, sevoflurane potentiates muscle relaxants, both in terms of pharmacological effect and duration of action. Since the clock drawing part of the Mini-Cog test that we used in the evaluation may also be affected by muscle strength, the low results may have been related to the effect of sevoflurane. More studies are needed on this situation.

Conclusion

In conclusion, it was thought that desflurane or propofol may be more advantageous than sevoflurane in terms of postoperative cognitive dysfunction and that they may be preferred in the selection of anesthetic agents, especially in patients with preoperative neurological problems. However, it was concluded that further clinical studies are needed to reach clearer results.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 25.09.2019, Decision No: 2019/514/162/8).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: N.N.A., E.B.; Design: N.N.A., E.B., B.Ç.; Supervision: B.Ç., E.B.; Fundings: B.Ç.; Materials: N.N.A., E.B.; Data collection &/or processing: N.N.A.; Analysis and/or interpretation: N.N.A., E.B.; Literature search: N.N.A., E.B.; Writing: N.N.A., E.B.; Critical review: E.B., B.Ç., N.N.A.

Conflict of Interest

None declared.

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Laparoskopik Kolesistektomide Farklı Anestetik Ajanların Postoperatif Kognitif Fonksiyonlar Üzerine Etkileri

Amaç: Bu çalışmada, sevofluran veya desfluran ile uygulanan inhalasyon anestezisi ile propofol ile uygulanan intravenöz anestezinin postoperatif erken dönem kognitif fonksiyonlar üzerine etkilerinin karşılaştırılması amaçlandı.

Gereç ve Yöntem: Bu çalışmaya ASA I-III sınıfı, 30-70 yaş arası, elektif laparoskopik safra kesesi ameliyatı geçiren hastalar dahil edildi. Ameliyattan bir gün önce Mini-Cog testi yapılarak hastaların kognitif fonksiyon düzeyleri belirlendi. Hastalar rastgele Grup I (Desfluran), Grup II (Sevofluran) ve Grup III (Propofol) olmak üzere üç gruba ayrıldı. Propofol ve remifentanil roküronyum ile anestezi indüksiyonu yapıldıktan sonra tüm hastalara endotrakeal entübasyon uygulandı. Anestezi idamesi sırasında tüm hastalara uygulanan remifentanil infüzyonunun yanı sıra bispektral indeksi (BIS) 40-60 olan desfluran, sevofluran inhalasyonu veya propofol infüzyonu ile anestezi derinliği sağlandı. Tüm hastaların postoperatif 5., 10., 20. ve 30. dakikalarda Modifiye Aldrete Recovery Skorları (MARS) ölçüldü ve kaydedildi. Ağrı düzeyleri postoperatif 10., 20. ve 30. dakikalarda görsel analog skala (VAS) ile değerlendirildi. Mini-Cog testi ameliyat sonrası 24. saatte aynı hekim tarafından tekrarlanarak ameliyat öncesi değerlerle karşılaştırıldı.

Bulgular: Üç grup arasında demografik özellikler, ameliyat ve anestezi süresi, ameliyat sonrası MARS ve VAS değerleri açısından fark yoktu (hepsi için $p>0.05$). Desfluran ve Propofol gruplarında ameliyat öncesi ve ameliyat sonrası Mini-Cog test skorları arasında anlamlı fark görülmezken ($p>0.05$), sevofluran grubunda Mini-Cog testinin Propofol grubuna göre ve Desfluran grubuna göre anlamlı derecede düşük olduğu görüldü (sırasıyla $p=0.002$ ve $p=0.012$).

Sonuç: Desfluran ve propofolün kognitif fonksiyonlara olumsuz etkisinin olmadığı, sevofluranın ise postoperatif kognitif fonksiyonlara olumsuz etkisinin olduğu sonucuna varıldı.

Anahtar Sözcükler: Desfluran; Mini-Cog testi; postoperatif bilişsel işlev bozukluğu; propofol; sevofluran.

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Original Article

Persistent Right Umbilical Vein: Clinical Outcomes and Prognostic Factors in Prenatal Diagnosis

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Keywords: Fetal anomalies; perinatal outcomes; persistent right umbilical vein; prenatal ultrasound.

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ABSTRACT

Objective: To evaluate clinical outcomes and associated anomalies in fetuses diagnosed with persistent right umbilical vein (PRUV) during routine prenatal ultrasound at a tertiary perinatology clinic.

Methods: This retrospective study included 11 cases of PRUV diagnosed between October 2022 and January 2024. Data were collected on maternal demographics, gestational age at diagnosis, associated anomalies, and neonatal outcomes. Ultrasound examinations were performed using B-mode and color Doppler, with fetal echocardiography to assess cardiac abnormalities. Cases were classified as isolated PRUV or PRUV with associated anomalies.

Results: PRUV was detected in 11 out of 10,176 pregnancies (0.1%). Seven cases were isolated PRUV, while four cases had associated anomalies, including cardiovascular and genitourinary defects. One case with extrahepatic PRUV and severe cardiovascular abnormalities was discontinued. The remaining 10 cases, including those with isolated PRUV, resulted in healthy live births. Six births were by cesarean section, and four were spontaneous deliveries. The presence of additional malformations was associated with more complex prenatal management and a poorer prognosis.

Conclusion: Isolated PRUV is usually associated with favorable outcomes, but the presence of additional anomalies, particularly cardiovascular defects, has a significant impact on management and prognosis. Comprehensive prenatal imaging, including echocardiography, is essential in PRUV cases to inform clinical decisions. Larger studies are needed to further elucidate the long-term outcomes of PRUV.

INTRODUCTION

A rare vascular anomaly that occurs when the left umbilical vein regresses during embryonic development and the right umbilical vein remains open is called Persistent Right Umbilical Vein (PRUV).[1] Normally, the left umbilical vein does not close and carries oxygenated blood to the fetus, but in PRUV, the left umbilical vein closes and the right umbilical vein continues to function. This condition is usually detected during routine prenatal ultrasound examinations in the second trimester.[2]

The incidence of PRUV varies across studies but is generally estimated to be between 1/250 to 1/1250 pregnancies.[3] However, the actual prevalence may be higher as the anomaly can easily be missed on standard ultrasound examinations. Advances in imaging techniques, including color Doppler and 3D ultrasound, have improved the ability to diagnose PRUV.[3]

PRUV is often considered an isolated finding, meaning it occurs in the absence of other fetal anomalies, and in such cases the prognosis is generally favorable.[4] However, PRUV may also be associated with other malformations, in particular cardiac defects and gastrointestinal, genitourinary, and skeletal anomalies.[1] This association emphasizes the importance of a detailed anatomical examination of the fetus and fetal echocardiography as soon as a PRUV

is detected.[1]

The etiology of PRUV remains unclear, although some studies suggest possible factors such as folic acid deficiency or teratogenic exposure.[3] In addition, some researchers suggest that thrombosis or external pressure on the left umbilical vein could lead to persistence of the right umbilical vein.[3]

In this study, we aim to evaluate the prognostic outcomes of fetuses diagnosed with PRUV, including any associated fetal malformations or chromosomal abnormalities, using a retrospective analysis of cases diagnosed by routine prenatal ultrasound examinations.[3,5]

MATERIALS AND METHODS

This study was conducted to retrospectively evaluate the clinical outcomes of fetuses diagnosed with PRUV during routine prenatal ultrasound examinations. Data were collected from all patients who underwent prenatal ultrasonography between October 2022 and January 2024 at the Perinatology Clinic of our institution.

Study Participants

In this study, we included pregnant women who were diagnosed with PRUV during routine ultrasound examinations in the last two trimesters. Cases with chromosomal abnormalities or other major fetal malformations were excluded.

Ultrasound Evaluation

In all patients, the venous system was examined using a Voluson E8 GE ultrasound machine (GE Medical Systems, Milwaukee, WI, USA) equipped with a convex 4-8 MHz transabdominal transducer. Two-dimensional color Doppler imaging was used to assess the target vessels. Three basic criteria were considered in the diagnosis of PRUV:

1. Abnormal course of the portal vein towards the stomach (Fig. 1),

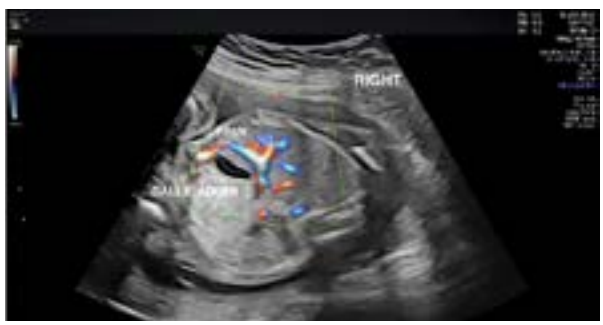

Figure 1. Prenatal ultrasound image showing a persistent right umbilical vein (PRUV) in a transverse section of the fetal abdomen. The PRUV can be seen in the direction of the right portal vein as indicated by the color Doppler flow. The gallbladder can be seen medial to the PRUV. This finding is characteristic of PRUV in which the umbilical vein remains on the right side instead of the usual left side. The use of Doppler imaging helps visualize the abnormal vascular flow pattern and aids in diagnosis.

2. Presence of an umbilical vein on the right side of the gallbladder,

3. Connection of the umbilical vein with the portal veins.

In addition, the medial location of the gallbladder in relation to the umbilical vein served as a further diagnostic marker. To detect possible cardiac anomalies, fetal echocardiography was performed in all cases.

Data Collection

For each case, maternal demographic characteristics (age, gravidity, parity), gestational age at diagnosis, and any associated fetal anomalies were recorded. Cases were classified as either isolated PRUV (without other anomalies) or PRUV with associated anomalies. All cases were followed up until delivery, and neonatal outcomes, including gestational age at delivery, mode of delivery, and postnatal findings, were documented. The results of invasive diagnostic tests for fetal chromosome analysis were recorded, if available. Information about newborns was obtained from the families by telephone.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee at which the studies were conducted (Clinical Research Ethics Committee of Ankara Etlik City Hospital No. 1 [Decision No.: AEŞH-EK-2024-008, date: 10/01/2024]) and with the 2013 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical Analysis

Descriptive statistics were used to present the data, including the average gestational age at diagnosis and the incidence of associated malformations. The incidence of PRUV was calculated as a percentage of the total number of pregnancies examined. Statistical analyses were performed using SPSS software (version 26.0), and results with a p-value below 0.05 were considered statistically significant.

RESULTS

Among 10,176 pregnancies evaluated at the perinatology clinic, PRUV was detected in 11 cases, which corresponds to an incidence of 0.1%. The general week of diagnosis of these patients was the same as the week of admission to our hospital and ranged from 16 to 33 weeks. One out of 11 patients had a twin pregnancy, while the others had singleton pregnancies (Table 1). One out of 11 patients had an extrahepatic PRUV, while 10 had an intrahepatic PRUV. The ductus venosus was present in all patients except for the extrahepatic PRUV.

Seven of the 11 patients had isolated PRUV, and four had concomitant abnormalities. One patient had cardiovascular abnormalities (extrahepatic PRUV), two had genitourinary system anomalies, and one had a single umbilical

Table 1. Characteristics of the cases, malformations associated with PRUV

Age (years)	GA at diagnosis (weeks)	Additional findings	GA at delivery (weeks)	Birth Weight (gr)	Delivery Type	Gender	Neonatal Outcome	Type of PRUV	Presence of Ductus Venosus	Karyotype
35	16	Isolated	34.6	2500	Caesarean section	Male	Healty	Intrahepatic	Yes	46 XY
23	21.6	Bilateral renal pelvis dilatation	35.0	2540	Caesarean section	Male	Healty	Intrahepatic	Yes	
29	33.1	Isolated (FGR)	38.0	2170	Caesarean section	Male	Healty	Intrahepatic	Yes	
32	20.6	Tetralogy of Fallot (Dextrocardia, Inlet VSD, Pulmonary Artery Atresia)	21.0	425	Terminated	Male	Terminated	Extrahepatic	None	46 XY
26	20	Isolated	35.0	2660	Caesarean section	Male	Healty	Intrahepatic	Yes	
32	25	Isolated	38.0	3050	Spontaneous	Female	Healty	Intrahepatic	Yes	
28	21	Isolated	39.0	3100	Spontaneous	Female	Healty	Intrahepatic	Yes	
34	27	Isolated	37.0	2750	Caesarean section	Male	Healty	Intrahepatic	Yes	
28	22	SUA	39.0	2950	Spontaneous	Female	Healty	Intrahepatic	Yes	
36	20	Bilateral renal pelvis dilatation	38.0	3400	Spontaneous	Female	Healty	Intrahepatic	Yes	46 XX
34	21	Isolated	36.0	2460	Caesarean section	Female-Male	Healty	Intrahepatic	Yes	

Abbreviations: GA; Gestational age; PRUV: Persistent right umbilical vein; FGR: Fetal growth restriction; VSD: Ventricular septal defect; SUA: Single umbilical artery.

artery. None of the patients had teratogenic exposure, and only one patient did not take folic acid in early pregnancy.

Four of the 11 patients were delivered by normal spontaneous delivery (NSD), and six by cesarean section (C/S). One patient with concomitant dextrocardia was also terminated. Six patients delivered at term, while four had a premature delivery. All fetuses were healthy, with the exception of the fetus that was terminated in neonatal follow-up.

DISCUSSION

This study provides valuable insight into the clinical relevance of PRUV, a rare vascular anomaly commonly detected on routine prenatal ultrasound. The incidence of PRUV in our cohort remains low, consistent with previous findings, but its clinical significance cannot be underestimated. PRUV can occur either as an isolated anomaly or together with other congenital abnormalities, which has a significant impact on prognosis and management.

Our findings are consistent with previous literature on the incidence of PRUV, which ranges from 0.08% to 0.5% of pregnancies.[6-8] In our study, the majority of PRUV cases were isolated, and the prognosis in such cases tends to be favorable, as also found in other studies. When PRUV is isolated, it is often considered a benign variant of normal vascular anatomy.[8,9] However, when it is associated with other anomalies, particularly cardiovascular malformations, the prognosis becomes more complex.[3,9] While our findings align with previous studies, the incidence of abnormalities associated with intrahepatic PRUV in our study is higher (36%) than in other studies.[6,8,10] This result may be related to our being a referral center.

PRUV was defined by Jeanty et al.[11] in two types: intrahepatic and extrahepatic. If the umbilical vein is directly connected to the inferior vena cava and the right atrium, it is called an extrahepatic PRUV. In this type, there is usually no ductus venosus, and the prognosis is generally poor.[8,12] The most common type of PRUV is the intrahepatic type (95%), and there is usually a ductus venosus.[12,13] In agreement with the literature, in our study only one of 11 cases had an extrahepatic PRUV that did not have a ductus venosus. This case was terminated because of severe cardiovascular abnormalities that had a poor prognosis, which is consistent with the studies.

The presence of a single umbilical artery (SUA) alongside PRUV further complicates fetal outcomes. As Mohapatra et al.[10] point out, the co-occurrence of SUA and PRUV increases the likelihood of additional malformations, particularly in the cardiovascular system. These findings emphasize the need for detailed fetal echocardiography in all PRUV cases to detect possible cardiovascular abnormali-

ties.[5,9] This correlation was not observed in our findings. Among the 11 cases, only one involved SUA, and no other congenital abnormalities were identified. A larger sample size may be needed to align our results with those reported in the literature.

The most common hypotheses for the etiology of PRUV are early thrombosis of the left umbilical vein, teratogenic exposure, and folic acid deficiency in the first trimester.[5,6] Interestingly, most of our patients had no history of teratogenic exposure, and all but one had taken folic acid in the first trimester. This supports previous research suggesting that folic acid deficiency does not play a major role in the development of PRUV in all cases.[5,8]

The management of PRUV should be based on the presence or absence of additional anomalies. Isolated cases of PRUV generally do not require invasive procedures as they are associated with a good prognosis.[6,7,9] However, when PRUV is detected together with other malformations, especially in the cardiovascular or urinary systems, further genetic testing and detailed anatomical scans are indicated to better predict the outcome of the newborn.[5,10]

Conclusion

In summary, although isolated PRUV is usually a benign finding, the presence of associated anomalies significantly alters the management and prognosis of affected pregnancies. Comprehensive prenatal imaging, including detailed ultrasonography and echocardiography, is essential to accurately diagnose PRUV and determine the best course of action for each individual case. Further studies with larger cohorts are needed to better understand the pathophysiology of PRUV and its long-term impact on neonatal health.

Ethics Committee Approval

The study was approved by the Ankara Etlik City Hospital Ethics Committee (Date: 10.01.2024, Decision No: AEŞH-EK-2024-008).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: S.Ö., A.A., F.B.F., M.L.D., Ş.Ç.; Design: S.Ö., A.A., F.B.F., M.L.D., Ş.Ç.; Supervision: S.Ö., A.A., F.B.F., M.L.D., Ş.Ç.; Data collection &/or processing: F.B.F.; Analysis and/or interpretation: M.L.D.; Literature search: A.A.; Writing: S.Ö., A.A.; Critical review: S.Ö., Ş.Ç.

Conflict of Interest

None declared.

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Persistan Sağ Umbilikal Ven: Prenatal Tanıda Klinik Sonuçlar ve Prognostik Faktörler

Amaç: Bu çalışmanın amacı, üçüncü basamak bir perinatoloji kliniğinde yapılan rutin prenatal ultrason sırasında persistan sağ umbilikal ven (PSUV) tanısı konan fetüslerde klinik sonuçları ve ilişkili anomalileri değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif çalışma, Ekim 2022 ile Ocak 2024 tarihleri arasında PSUV tanısı konan 11 vakayı içermektedir. Anne demografik verileri, tanı anındaki gestasyonel yaş, ilişkili anomaliler ve neonatal sonuçlarla ilgili veriler toplanmıştır. Kardiyak anomalileri değerlendirmek amacıyla B-mod ve renkli Doppler ile ultrason muayeneleri yapılmış ve fetal ekokardiyografi ile desteklenmiştir. Vakalar, izole PSUV ya da ilişkili anomalili PSUV olarak sınıflandırılmıştır.

Bulgular: PSUV, 10.176 gebeliğin 11'inde (%0.1) tespit edilmiştir. Yedi vaka izole PSUV iken, dört vakada kardiyovasküler ve genitoüriner defektler dahil olmak üzere ek anomaliler görülmüştür. Ekstrahepatik PSUV ve ciddi kardiyovasküler anomalilere sahip bir vaka sonlandırılmıştır. İzole PSUV vakaları dahil olmak üzere kalan 10 vaka sağlıklı canlı doğumlarla sonuçlanmıştır. Altı doğum sezaryen ile, dört doğum ise spontan gerçekleşmiştir. Ek malformasyonların varlığı, daha karmaşık doğum öncesi yönetim ve daha kötü bir prognoz ile ilişkilendirilmiştir.

Sonuç: İzole PSUV genellikle olumlu sonuçlarla ilişkilendirilirken, özellikle kardiyovasküler defektler gibi ek anomalilerin varlığı, yönetim ve prognoz üzerinde önemli bir etkiye sahiptir. PSUV vakalarında kapsamlı prenatal görüntüleme, ekokardiyografi dahil olmak üzere, klinik kararları yönlendirmek için hayati öneme sahiptir. PSUV'nun uzun vadeli sonuçlarını daha iyi anlamak için daha geniş kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Fetal anomaliler; perinatal sonuçlar; persistan sağ umbilikal ven; prenatal ultrason.

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Original Article

Learning Curves in Transabdominal Pre-Peritoneal (TAPP) Herniorrhaphy: Comparison of Transabdominal Extraperitoneal (TEP) Experience and Supervisor-led Learning

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Keywords: Learning curve; laparoscopic hernia repair; TAPP; TEP.

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ABSTRACT

Objective: Inguinal hernia (IH) is one of the common diseases encountered in general surgery. Laparoscopic techniques are recommended and preferred surgical methods for inguinal hernia today due to their advantages. There are various published studies regarding the learning curve (LC) of the TAPP technique, one of the laparoscopic methods. In our study, we aimed to compare the LC of TAPP herniorrhaphy performed by a surgeon without supervisor support after TEP experience with that of a surgeon without laparoscopic hernia experience under supervision.

Methods: In our study, patients who underwent laparoscopic inguinal hernia repair at our clinic between 2011 and 2024 were analyzed. Patients operated on by a surgeon who transitioned to TAPP herniorrhaphy without supervision after gaining experience in TEP were designated as Group-1, while patients operated on by a surgeon performing TAPP herniorrhaphy under supervision were designated as Group 2. In both groups, the first 100 patients who underwent primary TAPP herniorrhaphy were retrospectively evaluated for operative times, conversion rates to open surgery, and complications, with learning curve data generated.

Results: In this study, a total of 128 patients (64 patients in each group) who underwent TAPP herniorrhaphy for primary unilateral inguinal hernia were evaluated. There was no significant difference between the two groups in demographic features ($p>0.05$). No significant difference was found between the groups according to the Nyhus classification ($p>0.05$). No difference was observed between the groups in terms of postoperative complications ($p>0.05$). In the analyses performed for the LC, it was seen that the ideal number of surgeries for Group-1 was 19, and for Group-2 it was 26, and it was not statistically significant ($p>0.05$).

Conclusion: The learning curve in TAPP surgeries performed under supervision showing similar results to those of surgeons experienced in TEP indicates the potential importance of supervisory support in the learning process.

INTRODUCTION

IH affect approximately 220 million people worldwide, and each year, 20 million individuals undergo surgery due to hernia in the groin area. IH, which account for more than 75% of abdominal hernias, have a lifetime prevalence of 27% to 32.9% in men, while this rate remains lower in women, ranging from 3% to 12.9%.[1,2]

Today, various surgical techniques are available for the repair of IH, including open and laparoscopic approaches. In laparoscopic surgery, particularly advancements recorded in the last 30 years have enabled the development of techniques such as TAPP and TEP repair.[3,4] The European Hernia Society (EHS) guidelines recommend open Lichtenstein and laparoscopic inguinal hernia techniques (TEP and TAPP) as the best evidence-based treatment options for the repair of primary unilateral groin hernia, provided

that the surgeon has sufficient experience and the necessary resources for the specific procedure.[5]

According to guidelines from the EHS and the International Endohernia Society (IEHS), both new techniques are advantageous in terms of all parameters related to pain when compared to open surgery. Accordingly, the guidelines suggest that laparoscopic hernia repair should be the first-line treatment, especially in patients where quick postoperative recovery is particularly important (grade A). Furthermore, the guidelines propose that an endoscopic procedure should be recommended for the working population, particularly for bilateral hernias, from a socioeconomic perspective (grade A).

There is ongoing debate about which method is preferable. Despite numerous peer-reviewed studies showing the advantages of low postoperative complication rates, short hospital stays, low costs, reduced recurrence rates and postoperative pain, early return to work, and improvements in quality of life and demonstrating that these techniques can be safely performed by surgeons worldwide, the adoption of laparoscopic techniques has remained limited until recently.[6,7] Despite the proven benefits of this new, revolutionary technique, its clinical application remains insufficient in many countries.[8-10] It raises the question of why so many surgeons do not prefer or adopt laparoscopic inguinal hernia repair. Among the discussed reasons are the technical difficulty of laparoscopic surgery and challenges related to the LC.

Various studies have assessed the LC in laparoscopic inguinal hernia repair, indicating that it can vary between 20 and 250 cases.[11-15] However, there is no general consensus on the exact number of cases that a surgeon must perform to achieve proficiency in the LC.[[12] The assessment of the LC is generally evaluated through parameters such as operative time, postoperative complications, and technical difficulties.[16]

The purpose of this study is to evaluate and compare the TAPP technique LC in two different parameters, with supervision and TEP technique experience.

MATERIALS AND METHODS

Patients who presented to our clinic with a hernia diagnosis between April 2011–December 2011 and November 2022–June 2024 and underwent elective surgery using the TAPP method by two different surgeons were retrospectively evaluated.

Inclusion criteria

- Unilateral hernias
- Age between 18–75 years
- BMI<35 kg/m²

Exclusion criteria

- Bilateral hernias
- Recurrent hernias
- Patients with giant hernias
- Patients transitioning from TEP to TAPP during surgery
- Emergency patients (irreducible, incarcerated)
- Patients using anticoagulants
- Patients with a history of midline inferior surgery

The patients were divided into two groups: Group 1 consisted of a surgeon experienced in TEP without the presence of a supervisor, during the period of April–December 2011, while Group 2 comprised of a surgeon performing TAPP herniorrhaphy with a supervisor during the November 2022–June 2024 period.

In Group 2, 22 patients who did not meet the inclusion criteria were excluded from 86 patients undergoing TAPP herniorrhaphy, leaving 64 patients included in the study. Of those excluded, 15 had bilateral hernias, 4 were recurrent cases, and 3 were transferred to the supervisor.

For Group 1, 100 patients were initially included to match the number of cases with 64 patients in Group 2 from the start of TAPP. Of these, 36 patients were excluded (3 reverted from TEP to TAPP, 20 were bilateral, and 13 were recurrent cases), resulting in 64 patients in Group 1.

Learning curve (LC) evaluation parameters included the duration of surgery, the conversion to a different method (open) from TAPP, and intraoperative and postoperative complications.

Patients' demographic characteristics, hernia type, duration of surgery, intraoperative complications (vascular and organ injury, hemorrhage), conversion to a different method, the use and duration of drains, postoperative outcomes, length of stay, hemorrhage, hematoma, seroma, cord edema, wound infection, mesh infection, and early recurrence by the 1st month were evaluated. The Nyhus classification was used for hernia classification.[17]

Surgery duration was defined as the time from the first skin incision to the removal of the camera port. Intraoperative complications were defined as major vascular injury (testicular or epigastric artery), ductus deferens, and organ damage. Postoperative complications like hematoma or seroma were defined as the accumulation of blood or fluid in any subcutaneous tissue area down to the scrotal region. Recurrence occurring within the first 4 weeks was defined as early recurrence.

Group 1: The surgeon acting as a supervisor had laparoscopy experience in the LC process, performed more than 200 Total Extraperitoneal (TEP) procedures, over 300 laparoscopic cholecystectomies, and more than 400 Lichtenstein inguinal hernia repairs, but had no experience with laparoscopic TAPP herniorrhaphy and operated without a mentor, performed by a single surgeon.

Group 2: Performed by a single surgeon without experience in laparoscopic TEP and TAPP, having performed more than 300 Laparoscopic Sleeve Gastrectomies, over 350 laparoscopic cholecystectomies, and more than 200 Lichtenstein inguinal hernia repairs, but without experi-

ence in laparoscopic TAPP herniorrhaphy, operated under the guidance of an experienced TAPP supervisor.

All procedures were conducted according to the principles of the 1964 Helsinki Declaration and its later amendments, with informed consent obtained from all patients who were included in the study. Ethical Committee approval was obtained with the number 2024/109 on 18.07.2024.

Surgical technique

All surgeries were performed using the generally described (3 trocar-laparoscopic) TAPP method [18–20]. Differently, a standard mesh size of 15*15 was used in all cases, and the peritoneal opening was closed with tacks.

Statistical Analysis

Descriptive statistics of the data used median, mean, standard deviation, frequency, and ratio values. The distribution of variables was measured with Kolmogorov-Smirnov and Shapiro-Wilk tests. The Mann-Whitney U test was used to analyze quantitative independent data with abnormal distribution. The chi-square test was used to analyze qualitative independent data, and the Fisher test was used when chi-square test conditions were not met. SPSS 27.0 software was used for analysis.

RESULTS

Out of a sample of 186 individuals, a total of 128 patients who met the study criteria were included, with 64 patients in Group 1 and 64 in Group 2. When patients in both groups were compared, no significant differences were found in terms of age, gender, ASA score, hernia side, and hernia types ($p>0.05$). Only the BMI values of Group 2 patients were significantly higher (24.03 vs. 25.78, $p<0.05$).

In both groups, no patients required hospital stay longer than 2 days. The average length of stay in Group 1 was found to be longer and statistically significant compared to Group 2 (1.13 vs. 1.03, $p<0.05$). The average surgery duration was significantly longer in Group 2 compared to Group 1 (38.56 vs. 35.34, $p<0.05$).

The detailed demographic information of all patients is shown in Table 1. The distribution of patients based on surgery duration is presented in Figures 1-2.

Complications

When all patients were evaluated, a complication rate of 22.66% was observed. In the second group, the rate of seroma was found to be higher compared to the first group (1 vs. 7), although this was not statistically significant ($p>0.05$). In Group 2, out of 7 patients with seroma, 6 resolved spontaneously, and 1 required aspiration as there was no improvement at the 6-week check-up, with no need for additional surgery. In Group 1, there was 1 hematoma that did not require interventional treatment, while no hematoma was observed in Group 2. Cord edema was seen in a total of 20 patients, with 11 cases (1.19%) in Group 1 and 9 cases (13.73%) in Group 2, mak-

Table 1. Demographic characteristics of the patients

	Total n=128	Group 1 n=64 (50%)	Group 2 n=64 (50%)	p-value
Age, Mean±SD	43.73±11	43.98±11.69	42.75±10.33	0.53 t
Gender, n(%)				
Male	118 (92.19)	60 (93.75)	58 (90.63)	0.74 X^2
Female	10 (7.81)	4 (6.25)	6 (9.38)	
ASA, n(%)				
ASA I	65 (50.78)	29 (45.31)	36 (56.25)	0.21 X^2
ASA II	59 (46.9)	34 (53.13)	25 (39.06)	
ASA III	4 (3.13)	1(1.56)	3 (4.69)	
BMI, Mean±SD	24.91±3.17	24.03±2.44	25.78±3.57	**0.0016**[t]
Duration of surgery (min), Mean±SD	36.95±7.43	35.34±7.47	38.56±7.10	**0.0137**[m]
Hospitalization time (day), Mean±SD	1.08±0.27	1.13±0.33	1.03±0.18	**0.048**[t]
Hernia site N (%)				
Right	73(57.03)	38(59.37)	35(54.69)	0.72 X^2
Left	55(42.97)	26(40.63)	29(45.31)	
Hernia type				0.85 X^2
Direct herni (D)	37(28.91)	19(29.69)	16(25.0)	
İndirect herni (ID)	73(57.03)	36(56.25)	37(57.81)	
D-ID	20(17.19)	9(14.06)	11(17.19)	
Femoral	3(2.34)	1(1.56)	2(3.12)	

[m]Mann-whitney u test; X^2:Chi-square test; Fisher's Exact test/t t-Test ; SD: Standard deviation; ASA: American Society of Anesthesiologist; BMI: Body Mass Index; D: direct; ID: Indirect.

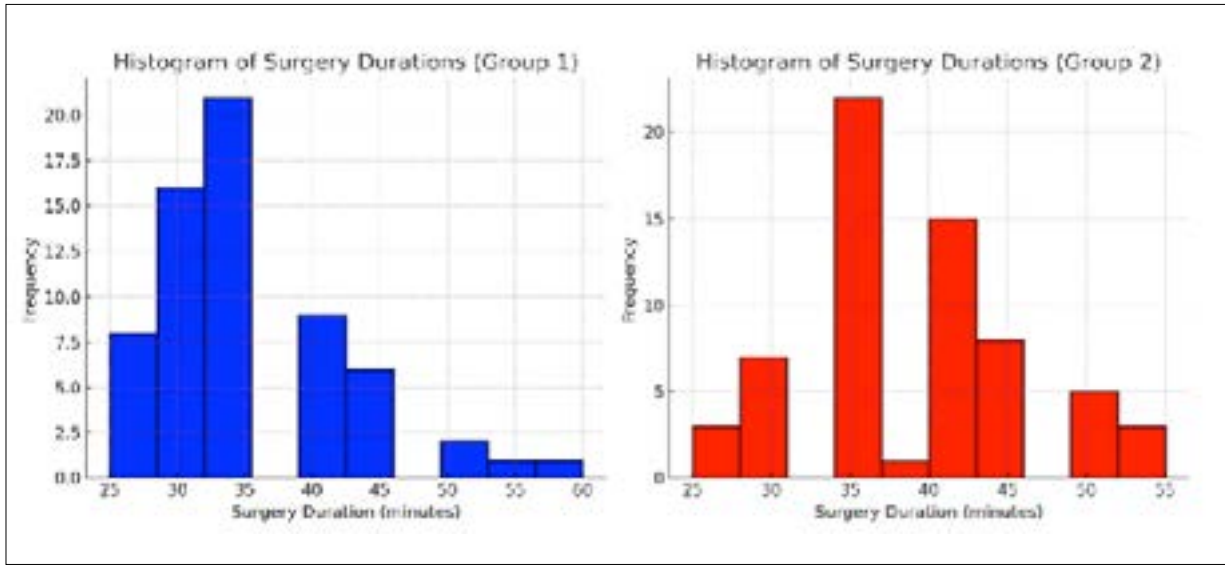

Figure 1. Comparison of surgery duration between Group 1 and Group 2 in a histogram.

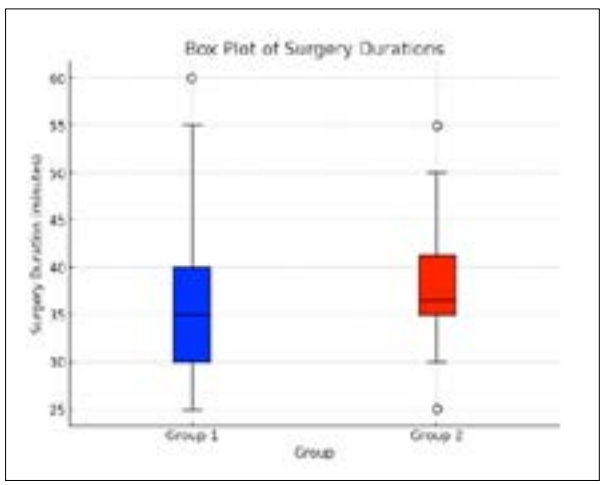

Figure 2. Boxplot of surgery duration for Group 1 and Group 2.

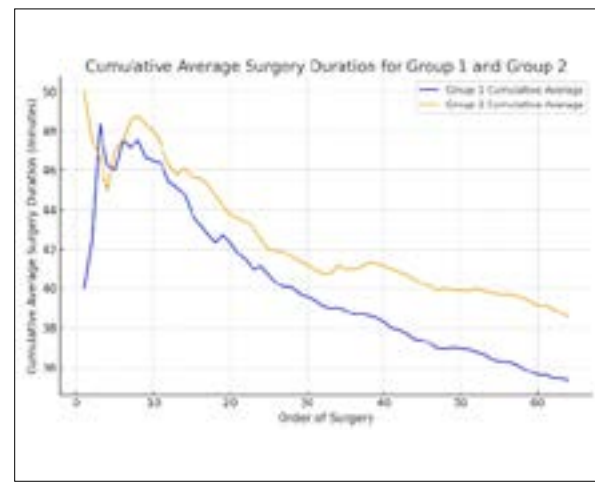

Figure 3. Comparison of cumulative mean surgery times of Group 1 and Group 2.

Table 2. Complications in 2 groups

	Total n=128	Group1 n=64 (50)	Group2 n=64 (50)	p-value
Postoperative complications N (%)	29 (22.66)	13 (20.31)	16 (25.00)	0.67 X^2
Scrotal hematom	1 (0.78)	1 (1.56)	0 (0)	1 X^2
Seroma	8 (6.25)	1 (1.56)	7 (10.68)	0.067 X^2
Cord edema	20 (15.63)	11 (17.19)	9 (13.73)	0.8 X^2

X^2 Chi-square test / Fisher's Exact test

ing up 15.63% overall. There were no cases of cord or organ injury, major vascular injury, or severe bleeding that required transfusion. Re-operation was not performed. Detailed information is summarized in Table 2.

When the effects of patients' age, gender, BMI, and type of hernia on surgery duration were analyzed, it was observed that age, gender, and BMI did not affect surgery duration ($p>0.05$). When the effects of hernia types on surgery duration were compared according to Nyhus, Nyhus type 3a had the shortest duration at 30.61 minutes, while Ny-

Table 3. Mean surgery durations according to Nyhus classification

Nyhus Classification	Surgery Duration mean±std)	Number of Patients
2	36.84±5.83 minutes	56
3a	30.61±4.80 minutes	33
3b	45.59±6.59 minutes	17
3a+2	38.47±4.58 minutes	15
3a+3b	48.75±8.54 minutes	4
3a+3c	37.50±3.54 minutes	2
2+3c	35.00±N/A minutes	1

Std: Standard deviation.

Table 4. Regression analysis results showing the effects of Nyhus classification and other variables on surgery duration

Variable	Coefficient	p-value
Nyhus Complex	8.2744	0.0
Age	-0.0656	0.2306
Gender (Male/Female)	2.1221	0.3256
BMI	0.1163	0.5293

BMI Body mass index.

hus type 3a+3b was found to have the longest duration at 48.75 minutes (Table 3). When we categorized Nyhus classification into simple (uncomplicated 3a and 2) and complicated (other groups), a significant difference was observed between the two groups, with times of 30.61±4.8 minutes vs. 42.49±7.05 minutes ($p<0.005$) (Table 4).

Learning Curve

We aimed to identify the point where the ideal LC stabilizes. "The LC was defined as the period during which the surgery duration stabilized."

This was done by analyzing how surgery times change over time using moving averages or cumulative averages, and by detecting the point where cumulative average times stabilize. In Group 1, the point where the cumulative average surgery time fell below a certain threshold and stabilized was the 19th surgery. In Group 2, it was identified as the 26th surgery. When the two groups were compared, no statistically significant difference was observed in the LC between Group 1 and Group 2, whereas the surgery time in Group 1 was statistically significantly shorter than in Group 2 ($p<0.005$) (Fig. 3).

DISCUSSION

The concept of the 'LC' was first defined in 1936 by T.P. Wright in the aircraft manufacturing sector.[12] Initially used in various fields outside of healthcare, the term began to be applied in medicine following the emergence of minimally invasive surgery in the 1980s. Traditionally, in surgical branches, resident training is based on a master-apprentice relationship and is supervised by a supervisor according to the basic training principles of the branches. In surgery, the term 'LC' is used to describe the process of acquiring surgical skills necessary to perform a procedure safely, adequately, and effectively.[21]

The guidelines of the EHS advocate for open Lichtenstein and laparoscopic inguinal hernia techniques (TEP and TAPP) as the best evidence-based treatment options for the repair of primary unilateral groin hernias, provided that the surgeon is adequately experienced and that the necessary resources for the procedure are available.[5]

The LCs and complication rates of surgeons who frequently perform the procedure will differ from those who operate occasionally, such as residents and surgical assistants.[22] There is evidence indicating that even after 400 cases, the operation time, conversion rate, and short-term complication rate continue to decrease.[23]

Many factors can affect the LC in surgery, including previously acquired individual and institutional experiences, especially in laparoscopic operations. Patient selection for laparoscopy, details of the technique, the number of annual surgeries performed, and training can also be significant. In this context, there may be differences in the LC between experienced surgeons learning a new technique and younger surgeons working in a hospital where TAPP has already been fully standardized and applied as a routine procedure.[11]

Numerous studies can be found in the literature describing the LC in laparoscopic inguinal hernia repair. Studies include variable data from 20 to 250 cases.[12-15] However, there is no general consensus regarding the exact number of cases a surgeon must perform to achieve the LC. Some publications indicate that the operation times for experienced surgeons are longer than those for seasoned surgeons and that a reduction occurs after around 50 cases.[11]

In our study, the average number of cases required for the LC was found to be 19 for Group 1 surgeons with TEP experience, while it was determined to be 26 for Group 2 surgeons who had no prior TAPP experience. Although no statistical difference was observed between the two

groups, it shows that TEP experience is beneficial in the learning of laparoscopic hernia repair. Compared to the literature, the LC with supervisor assistance appears to be superior to that of many studies. Maybe watching the operation outside the team by the experienced surgeon could be safe before starting.

The average operation time for TAPP in the literature is highly variable, ranging from 20 to 64 minutes across different studies.[3,11,24] Another study reported that the operation time was longer due to the closure of the peritoneum with sutures (54-65 minutes).[12] There are publications indicating significantly long learning phases, stating that it takes about 30 minutes to close the opened peritoneum with sutures, as required by the surgical technique.[11]

In our study, the operation times were observed to be shorter than those reported in the literature, at 35.34 minutes for Group 1 and 38.56 minutes for Group 2. We believe the shorter operation times compared to other publications may be due to TEP and laparoscopic experience, the surgery being performed under supervisor assistance, and the effective closure of the peritoneal incision with tacker (Fig. 1, Table 1).

The literature includes reports that large inguinal defects and advanced scrotal hernias contribute to prolonged operation times.[5,19,25,26] In our study, the operation times for direct hernia type 3a and indirect type II according to the Nyhus classification were statistically significantly shorter than those of other hernia types ($p<0.05$).

Selecting cases primarily categorized as type 3a and type 2 during the learning phase may be more suitable and motivating for new surgeons.

For a surgeon experienced in laparoscopy but without laparoscopic hernia experience, it has been determined that after 26 repetitions of TAPP herniorrhaphy, the average operation time shows a decrease and stabilizes, similar to what is achieved by someone with TEP experience after 19 cases, with no extra difference found in terms of complications.

Conclusion

Surgeons who have adequate laparoscopic experience but lack laparoscopic hernia repair experience can quickly learn TAPP herniorrhaphy under supervisor assistance. Surgeons with TEP experience may prefer to transition to TAPP herniorrhaphy without supervisor assistance. Selecting patients with uncomplicated hernias (Type 2) or direct hernias (Type 3A) can positively affect the surgeon's LC process.

Limitations

The study was conducted retrospectively. In this study, peritoneal flaps were closed with clips in all cases. Intracorporeal sutures require a separate learning process concerning operation time. Therefore, it is important to note that surgical skill may vary among surgeons. To provide a more comprehensive and accurate analysis of the development of the LC, multicenter studies comparing a large number of surgeons and socioeconomically heterogeneous populations should be conducted.

Ethics Committee Approval

The study was approved by the Dogus University Hospital Ethics Committee (Date: 18.07.2024, Decision No: 2024/109).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Y.Ö.; Design: Y.Ö., Y.B:K.; Supervision: Y.Ö., Y.B:K.; Data collection &/or processing: Y.Ö.; Analysis and/or interpretation: Y.Ö., Y.B:K.; Literature search: Y.Ö., Y.B:K.; Writing: Y.Ö.; Critical review: Y.Ö., Y.B:K.

Conflict of Interest

None declared.

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Transabdominal Pre-peritoneal (TAPP) Öğrenme Eğrisinde: Transekstraperitoneal (TEP) Deneyimi ile Supervisor Eşliğinde Öğrenimin Karşılaştırılması

Amaç: İnguinal herni, tedavisinde açık ve laparoskopik gibi farklı cerrahi tekniklerin kullanıldığı, genel cerrahinin sık karşılaşılan hastalıklarından biridir. Laparoskopik yöntemler, sahip olduğu avantajları nedeniyle kasık fıtığı için günümüzde önerilen ve tercih edilen ameliyat tekniklerindendir. Laparoskopik yöntemlerden biri olan TAPP tekniği öğrenme eğrisi ile ilgili yayınlanmış değişik çalışmalar vardır. Çalışmamızda, TEP deneyiminden sonra süpervisör desteği olmayan cerrah ile laparoskopik fıtık deneyimi olmayan bir cerrahın süpervisör eşliğinde TAPP herniorafinin öğrenme eğrisini karşılaştırmayı amaçladık.

Gereç ve Yöntem: Çalışmamızda, kliniğimizde 2011–2024 tarihleri arasında laparoskopik kasık fıtığı ameliyatı olan hastalar incelendi. TEP deneyimine sahip olup, süpervizör olmadan TAPP herniorafisine geçen cerrahın hastaları Grup 1 olarak, süpervizör eşliğinde TAPP herniorafisi uygulayan cerrahın hastaları ise Grup 2 olarak tanımlandı. Her iki grupta primer TAPP herniorafisi uygulanan ilk 100 hastanın ameliyat süreleri, açık cerrahiye geçiş oranları ve komplikasyonlar retrospektif olarak değerlendirildi ve öğrenme eğrisi verileri oluşturuldu. Bilateral veya nüks fıtık vakaları çalışma kapsamı dışında tutuldu.

Bulgular: Bu çalışmada, her iki grupta da tek taraflı kasık fıtığı nedeniyle TAPP herniorafisi uygulanan toplam 128 hasta (her grupta 64 hasta) değerlendirildi. Her iki grupta da hastaların yaş, cinsiyet dağılımı, ASA skoru, yatış süresi ve fıtık tarafı açısından anlamlı bir fark saptanmadı ($p>0.05$). Direk (D), İndirekt (ID), D-ID ve Femoral (F) ayrımı ile Nyhus sınıflamasına göre gruplar arasında anlamlı bir farklılık bulunmadı. Grup 2'de vücut kitle indeksi (VKİ) istatistiksel olarak anlamlı derecede yüksek bulundu ($p<0.005$). Postoperatif komplikasyonlar açısından gruplar arasında farklılık gözlenmedi ($p>0.05$). Öğrenme eğrisi karşılaştırıldığında, Grup 1'de öğrenme eğrisinin 19 ameliyatta, Grup 2'de ise 26 ameliyatta tamamlandığı görüldü. Grup 2'de ameliyat sayısı sayısal olarak daha yüksek olmasına rağmen, istatistiksel olarak anlamlı bir fark izlenmedi ($p>0.05$).

Sonuç: Süpervizör eşliğinde yapılan TAPP ameliyatlarında öğrenme eğrisinin, TEP deneyimli cerrahlarla benzer sonuçlar göstermesi, öğrenme sürecinde süpervizör desteğinin potansiyel önemini işaret etmektedir.

Anahtar Sözcükler: Laparoskopik inguinal herni onarımı; öğrenme eğrisi; TAPP; TEP.

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Original Article

Evaluation of Radiation Safety Knowledge and Radiation Protection Awareness of Physicians Working in Surgical Units

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Keywords: Fluoroscopy; radiation awareness; radiation protection; radiation safety; surgical units.

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ABSTRACT

Objective: The use of radiation in medical diagnosis and surgical procedures is increasing with developing technology. During these routine interventions and procedures, physicians' decision-making through radiation safety awareness and application of radiation protection knowledge daily will protect themselves, their team, and patients from unnecessary radiation exposure and the negative effects of radiation. We aim to determine awareness and knowledge levels.

Methods: Our research was based on evaluating answers to the questionnaire applied to physicians working in the Surgical Units of the hospital. The questionnaire consists of 3 parts. The 1st part of the research questionnaire consisted of 7 questions aimed to collect general information about the physicians participating in the study. The 2nd part of the research questionnaire consisted of 13 questions aimed at analyzing the use of acquired radiation protection awareness in daily practice in the outpatient clinic and operation room. The 3rd part of the research questionnaire consisted of 12 questions aimed to analyze the basic radiation safety and radiation protection knowledge.

Results: A total of 172 physicians from surgical units participated in this questionnaire, 96 of them were assistants. In the analysis of 2nd part radiation protection awareness questions, an awareness level of 50% or more was observed in 10 answers. In the analysis of 3rd part general radiation safety and radiation protection knowledge questions, a correct answer level of 50% and more was observed in 6 answers.

Conclusion: Radiation protection awareness is teamwork as well as an individual effort. The results of this questionnaire we conducted within our hospital clearly emphasized that our hospital's chief physician, clinic chiefs, and all physicians in surgical units have high awareness of radiation safety. Knowledge about radiation protection has created optimum working conditions in outpatient clinics and operation rooms.

INTRODUCTION

In addition to the radiation sources that naturally exist around us, the radiation produced from artificial (man-made) radioactive sources through developing technology has been integrated into many areas of our daily lives. X-rays and γ (gamma) rays, used in medicine for diagnosis and treatment, are electromagnetic wave types of radiation emitted from artificial radioactive sources.[1]

The amount of ionizing radiation dose received from medical interventions is considered as the majority of radiation dose received from artificial sources in the general population exposure.[2] Ionizing radiation is used in a variety of medical procedures, including angiography, fluoroscopy, computed tomography (CT), and radiographic imaging.[3]

Ionizing radiation has adverse biological effects on living organisms that may vary depending on the type of radiation, absorbed dose, and duration of exposure, which is the dose rate.[4,5] The biological effects of ionizing radiation vary depending on the type of radiation and the magnitude of its energy. Sievert is the unit of equivalent radiation dose, effective dose. For example, a standard chest X-ray (CXR) corresponds to approximately 0.02 mSv of effective radiation.[1]

One Sv is the amount of radiation necessary to produce the same effect on living organisms as 1 Gray (Gy) of high-penetration X-rays. Quantities that are measured in Sv represent the biological effects of ionizing radiation.[6] When comparing a chest CT scan and a standard CXR, despite both techniques irradiating the lungs, the effective

dose from CT can be several hundred times that of a CXR, depending on the CT protocol technique. While the effective dose for standard CXR is 0.02 mSv, effective dose values ranging from 5.1 mSv[7] to 10–40 mSv[8] for lung CT have been reported in different studies.[9]

Considering these exposures, it is recommended that patients should be informed about the risks of radiation exposure while being informed about the necessity and benefits of diagnostic and interventional procedures.[9] The radiation risk of 1 mSv is not equal for a 10-year-old child, a 25-year-old adult, or a 70-year-old adult. Also, that biological risk is not the same for a man or a woman.[10]

Follow-up and investigation of a patient's radiological procedure history will be beneficial for individual patient radiation protection, as it can provide clinical information that will not require another radiological examination for that patient. Avoiding unnecessary repetition of medical imaging involving radiation exposure achieves a 100% dose reduction, even if the dose from the previous imaging is not taken into account.[11] Patient dose tracking is a concept created within the International Atomic Energy Agency (IAEA) and led to the implementation of the IAEA's Smart Card project.[12-14] Many different European countries have implemented this monitoring system, and experiences from Finland are presented documenting the impact of individual patient monitoring in strengthening justification and optimization processes.[11,15]

In light of this information, physicians have a great duty and responsibility to protect people from radiation exposure resulting from medical practices. Three basic elements defined as radiation protection principles by the International Committee on Radiation Protection (ICRP)—Justification, Optimization (As Low As Reasonably Achievable-ALARA), and Dose Limitations—must be taken into consideration in clinical management.[16]

The importance of physician awareness in radiation protection and radiation safety is also evident during the management of the fluoroscopic imaging process in the operating room. We can categorize the principles of fluoroscopy protection for teams working in the operating room under four headings: distance and position (distance 'D'), duration (exposure 'E'), use of barrier (barrier 'B'), and technical features of the device (technique 'T').[17]

In operating rooms, the distance rule is the easiest to comply with and the most effective method of protection from radiation, as radiation decreases inversely proportional to the square of the distance. To minimize the number of scattered photons, the fluoroscopy device should be positioned appropriately and the operating room team should stand on the correct side of the fluoroscopy. The X-ray tube must be under the table. When taking a lateral image, the team should be positioned on the opposite side of the X-ray tube. By increasing the distance between the X-ray tube and the patient, both the patient's dose and the team's exposure dose will decrease.[17]

The duration of radiation exposure is directly proportional to the amount of radiation to be received. Therefore, in preoperative planning, determining the location of fluoroscopy inside the operation room, marking the area to be shot on the patient's body if possible, and mastering the actual medical images of the patient, as well as keeping the last image on the screen or recording the previous images by using the technological features of the fluoroscopic device, will prevent the repetition of shooting during the case.[17]

Additionally, all shielding equipment and barriers must be available in the operating room and must be worn whenever fluoroscopy is used. This equipment prevents radiation exposure at different rates depending on the regions where they are used. Lead-coated (0.15 mm) glasses reduce the amount of radiation reaching the eye by 70%. It was found that exposure was reduced by 2.5 times after thyroid shielding was used. A lead apron increases protection by 16 times in the anterior-posterior plane and 4 times in the lateral plane. Lead alloy-coated gloves are difficult to use but can reduce exposure by up to 35%.[18]

The main purpose of the study is to evaluate the radiation safety and radiation awareness of physicians working in surgical units through the questions in the questionnaire created by us, to analyze and determine levels of this awareness on both their approaches to patients coming to the outpatient clinic during imaging requests involving radiation, and the importance and attitudes they take to protect the patient, the operating room team, and themselves during the use of fluoroscopy in the operating room.

The second aim of the study is to analyze the radiation safety and awareness knowledge of physicians working in surgical units with the questionnaire created by us, through the basic radiation protection and radiation safety questions.

MATERIALS AND METHODS

Our research was based on the evaluation of answers to the questionnaire that was applied to physicians working in the Surgical Units of Kartal Dr. Lütfi Kırdar City Hospital. This research is planned to be completed between 01/04/2024 and 01/06/2024, including the application of the questionnaire to the physicians working in the Surgical Units of Kartal Dr. Lütfi Kırdar City Hospital and the evaluation of their answers.

The 1st part of the research questionnaire consisted of questions aimed to collect general information about the physicians participating in the study. The questions to be answered by the participants are: gender, age, clinical title, the department they work in, years of experience in that department, their observative analysis of radiation exposure percentage regarding the environment they are working in, and their radiation protection training status. Seven questions in total.

The 2nd part of the research questionnaire consisted of questions aimed at analyzing the use of acquired radiation

protection awareness in daily practice in the outpatient clinic and operation room. The questions to be answered by the participants are divided into categories.

The first category of 6 questions is aimed at determining the physician's level of awareness of radiation exposure and radiation protection when ordering medical imaging examinations for patients coming to the outpatient clinic.

The second category of 7 questions is aimed at determining the level of awareness of radiation exposure and radiation protection in cases where fluoroscopy is performed in the operating room.Thirteen questions in total.

The 3rd part of the research questionnaire consisted of questions aimed at analyzing the basic general radiation safety and radiation protection knowledge. The content of questions aims to determine the knowledge about: General principles of radiation protection, Factors affecting radiation protection, Imaging techniques that include radiation, Shielding equipment in the operating room and their characteristic features, Annual allowed dose limits, Fluoroscopic techniques and characteristic features, Radiation protection techniques during performing fluoroscopy. Twelve questions in total.

The questionnaire was administered to designated clinical units, and questionnaire responses were collected and analyzed. Then, radiation protection awareness and radiation safety knowledge levels were determined from the analysis of the answers.

In Part 1, the results were declared as percentages for each marked answer for seven demographic questions.

In Part 2, percentages of each answer were declared for each of the 13 questions marked for one of the following: yes, no, or sometimes.

In Part 3, the percentage of correct answers marked for each of the 12 questions was declared.

To determine the percentages of the questionnaire responses, frequency charts via descriptive statistics were used. The statistical analysis of the questionnaire was performed with SPSS 17.0.

Ethical approval for this study was obtained from Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee, taken on 27.03.2024 (No:2024/010.99/2/37), and this study was conducted in accordance with the Declaration of Helsinki.

RESULTS

We presented the evaluation of the answers to the 3 different sections that make up our questionnaire in tables. The demographic structure of the questionnaire participants is represented in Table 1.

172 physicians participated in the study. 37 of the participants were women and 135 were men. Age distribution: 96 people between 21-30, 44 people between 31-40, 20 people between 41-50, 11 people between 51-60, 1 people over 60. Distribution and rates of experience: 66,9% (115) for 1-5 years, 18% (31) for 6-15 years, 8,1% (14) for 16-25 years, 7% (12) for 26-35 years, none for >36 years. Interdepartment distribution: 22,7% (39) for Orthopedics and Traumatology, 17,4% (30) for Ear Nose and Throat Diseases, 12,8% (22) for Plastic and Reconstructive Surgery, 10,5% (18) for Urology, 8,7% (15) for Neurosurgery, 8,1% (14) for General Surgery, 8,1% (14) for Anesthesiology and Reanimation, 6,4% (11) for Cardiovascular Surgery, 4,7% (8) for Thoracic Surgery and 0,6% (1) for Pediatric Surgery. Distribution of percentage of the radiation exposure possibility in work from the point of

Table 1. Demographic structure of the questionnaire participants

Gender (W, M)	37 (21.5 %)	135 (78.5 %)			
Age	55.8% (96), age 21-30	25.6% (44), age 31-40	11.6% (20), age 41-50	6.4% (11), age 51-60	0.6% (1), age >60
Title	65.1% (112), Assistant	20.9% (36), Specialist	1.2% (2), Assistant Professor	8.7% (15), Associate Professor	4.1% (7), Professor
Experince	66.9% (115), 1-5 years	18% (31), 6-15 years	8.1% (14), 16-25 years	7% (12), 26-35 years	None, >36 years
Department	22.7% (39), Orthopedics and Traumatology	17.4% (30), Ear Nose and Throat Diseases	12.8% (22), Plastic and Reconstructive Surgery	10.5% (18), Urology	8.7% (15), Neurosurgery
	8.1% (14), General Surgery	8.1% (14), Anesthesiology and Reanimation	6.4% (11), Cardiovascular Surgery	4.7% (8), Thoracic Surgery	0.6% (1), Pediatric Surgery
Percentage of radiation exposure possibility	54.1% (93), 0-20%	23.3% (40), 21-40%	13.4% (23), 41-60%	6.4% (11), 61-80%	2.9% (5), 81-100%
Participation in radiation protection training	Yes 4.7% (8)		No 95.3% (164)		

Table 2. Evaluation of radiation protection and radiation safety awareness in the outpatient clinic and in the operation room.

Question	Yes	No	Sometimes
1. After the examination, before a new imaging procedure order for the patient, I check the system when was the last time any imaging procedure was applied.	83.7%	4.1%	12.2%
2. After the examination, before a new imaging procedure order that will cause radiation exposure for the patient, I also check by asking the patient when the patient last had one of these tests. (private or other centers)	84.8%	5.8%	9.4%
3. When I monitor the patient from the system, I look at the summary document showing the applications involving radiation to which the patient is exposed for diagnosis and treatment purposes.	23.4%	62.6%	14%
4. Without affecting the diagnosis and treatment process, if the previous imaging examination performed on the patient involved radiation exposure, I would consider re-evaluating the need for a new examination that would cause radiation exposure and postponing it if it is not urgent.	70.9%	10.5%	18.6%
5. Without affecting the diagnosis and treatment process, I focus on the examination that will cause the least radiation exposure fort he patient.	82.6%	7.6%	9.9%
6. During examination if the patient insists on an imaging procedure that involves radiation exposure, I explain to the patient that this examination is not necessary and that procedure will cause a radition exposure.	75.6%	10.5%	14%
7. If fluoroscopic imaging technique will be used during the surgical operation, I always use the shielding equipment in the room.	51.2%	15.9%	32.9%
8. When using the fluoroscopic imaging technique during the surgical operation, if I do not have shielding equipment, and if my duty/position is appropriate, I keep distance from the floroscopic device or leave the room.	60.9%	15.4%	23.7%
9. When using the fluoroscopic imaging technique during the surgical operation, even if I have shielding equipment, and if my duty/position is appropriate, I keep distance from the floroscopic device or leave the room.	43.5%	26.8%	29.8%
10. When using the fluoroscopic imaging technique during a surgical operation, I warn my colleagues who do not have shielding equipment, to use the equipment or leave the room during the shooting.	73.4%	12.4%	14.2%
11. When using the fluoroscopic imaging technique during the surgical operation, I pay attention to the duration and necessity of use, use techniques that will reduce the number of shots, and take care to make transactions under optimum conditions.	70.8%	10.1%	19%
12. While fluoroscopic imaging technique is used during the surgical operation, in case of suspicion of a radiation accident, I contact the operating room nurse in charge and I write a report stating the situation.	67.7%	23.4%	9%
13. While fluoroscopic imaging technique is used during the surgical operation, in case of suspicion of a radiation accident, I follow up the report that I write and examine the analysis report.	49.4%	34.5%	16.1%

view the participants: 54,1% (93) for 0-20%, 23,3% (40) for 21-40%, 13,4% (23) for 41-60%, 6,4% (11) for 61-80%, and 2,9% (5) for 81-100%. And last distribution of participation in radiation protection training: Yes 4,7% (8), and No 95,3% (164).

Evaluation of questions about radiation protection and radiation safety awareness in the outpatient clinic and in the operation room is represented in Table 2.

The distribution of 'yes' answer percentages for 13 questions is as follows. 1st question 83,7%, 2nd question 84,8%, 3rd question 23,4%, 4th question 70,9%, 5th question 82,6%, 6th question 75,6%, 7th question 51,2%, 8th

Table 3. Evaluation of radiation protection and radiation safety knowledge

Question	% of Correct Answer
1. Which is not one of the general principles of radiation protection determined by the International Commission on Radiological Protection (ICRP)?	46.1
2. Which is one of the most important factors in radiation protection?	90.6
3. Which is the radiological imaging technique that causes radiation exposure?	98.2
4. Which is the radiological imaging technique that does not cause radiation exposure?	96.5
5. Which is not one of the shielding equipment for radiation exposure during surgical operations?	21.9
6. Which of the following is the maximum permissible exposure dose limit for 1 year for members of the public, according to the recommendation of the International Commission on Radiological Protection (ICRP)?	42.7
7. Which of the following is the main source of radiation exposure for the operation room team when using fluoroscopic imaging technique during surgery?	18.1
8. Which of the following is the most appropriate place to be positioned in the room when lateral imaging is performed with fluoroscopy during the surgical operation, even if I have shielding equipment and I cannot keep a distance from the patient due to my duty/position?	11.5
9. For which of the following organs radiation exposure can be dangerous?	90
10. Radiation dose decreases as distance increases. What is the formula for the decrease in radiation with distance? (d = distance between employee and primary beam)	56.9
11. Which of the following is the safe distance between employee and the fluoroscopic device, as recommended by the International Atomic Energy Agency (IAEA)?	58.3
12. How much greater is the radiation exposure that the patient received during fluoroscopic application compared to received from a chest X-Ray?	31.9

question 60,9%, 9th question 43,5%, 10th question 73,4%, 11th question 70,8%, 12th question 67,7%, 13th question 49,4%.

The distribution of 'no' answer percentages for 13 questions is as follows. 1st question 4,1%, 2nd question %5,8, 3rd question %62,6, 4th question %10,5, 5th question %7,6, 6th question 10,5%, 7th question 15,9%, 8th question 15,4%, 9th question 26,8%, 10th question 12,4%, 11th question 10,1%, 12th question 23,4%,13th question 34,5%.

The distribution of 'sometimes' answer percentages for 13 questions is as follows. 1st question 12,2%, 2nd question 9,4%, 3rd question 14%, 4th question 18,6%, 5th question 9,9%, 6th question 14%, 7th question 32,9%, 8th question 23,7%, 9th question 29,8%, 10th question 14,2%, 11th question 19%, 12th question 9%, 13th question 16,1%.

In the analysis of 2nd part radiation protection awareness questions, an awareness level of 50% or more was observed in 10 answers. This percentage rate is given based on the 'yes' answer given to the questions. In total, an awareness level of 50% or more was observed in 10 answers, and an awareness level of 70% or more was observed in 7 answers.

The evaluation of questions about radiation protection and radiation safety knowledge is represented in Table 3. The distribution of correct answer percentages for 12 questions is as follows. 1st question 46,1%, 2nd question 90,6%, 3rd question 98,2%, 4th question 96,5%, 5th question 21,9%, 6th question 42,7%, 7th question 18,1%, 8th question 11,5%, 9th question 90%, 10th question 56,9%, 11th question 58,3%, 12th question 31,9%.

In the analysis of 3rd part general radiation safety and radiation protection knowledge questions, a correct answer level of 50% or more was observed in 6 answers. This percentage rate is given based on the correct answer given to the questions. In total, it was observed that there were 6 questions with over 50% correct answers and 4 questions with over 90% correct answers.

DISCUSSION

Within the scope of the study, our questionnaire results show that the radiation protection awareness is high and the basic knowledge of radiation protection is sufficient for our physicians working in surgical units within our hospital.

It is clear that many benefits are provided by our physicians working in surgical units as a result of their attention to minimum radiation exposure as the primary goal. With awareness and knowledge of radiation protection during fluoroscopic applications, the physician protects themself, the team in the operation room, and the patient from un-

necessary radiation dose exposure. Moreover, due to radiation protection awareness and knowledge, before medical imaging examination orders, the physician protects the patient from unwanted radiation dose exposure and prevents unnecessary use of hospital radiation resources.

Radiation protection awareness is a team effort as well as an individual, and this is a win-win situation. The results of this questionnaire we conducted within our hospital clearly emphasized this. The fact that our hospital's chief physician, clinic chiefs, and all physicians in surgical units have high awareness of radiation protection has created optimum working conditions in outpatient clinics and operation rooms.

The importance given by the chief physician and clinic chiefs to radiation safety and radiation protection in the meetings, and the protocols and approaches they created regarding medical imaging and interventions involving radiation in the clinics they manage in line with this awareness, have yielded results as seen in the questionnaire analysis.

Conclusion

In addition, the care shown by the chief physician and all clinic chiefs during this questionnaire participation process once again demonstrated their attention to this issue. Developing awareness about radiation safety and radiation protection should be supported by attention to in-clinic practices and maintenance as well as the management of the training process.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 27.03.2024, Decision No: 2024/010.99/2/37).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: N.Ç., S.K.G.; Design: N.Ç., S.K.G.; Supervision: Ş.K.G., R.D.; Data collection &/or processing: N.Ç., S.K.G., R.D.; Analysis and/or interpretation: N.Ç., S.K.G.; Literature search: N.Ç.; Writing: N.Ç.; Critical review: N.Ç., S.K.G., R.D.

Conflict of Interest

None declared.

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Cerrahi Birimlerde Çalışan Hekimlerin Radyasyon Güvenliği Bilgisi ve Radyasyondan Korunma Farkındalığının Değerlendirilmesi

Amaç: Radyasyonun tıbbi teşhis, prosedür ve cerrahi tedavide kullanımı, gelişen tekniklerle birlikte artmıştır. Bu rutin müdahale ve işlemler sırasında hekimlerin radyasyon güvenliği bilinciyle karar vermesi ve radyasyondan korunma bilgilerini günlük olarak uygulaması, kendilerini, ekiplerini ve hastalarını gereksiz radyasyon maruziyetinden ve radyasyonun olumsuz etkilerinden koruyacaktır. Amacımız, bu farkındalık ve bilgi düzeylerini belirlemektir.

Gereç ve Yöntem: Araştırmamız, Kartal Dr. Lütfi Kırdar Şehir Hastanesi Cerrahi Birimlerinde görev yapan hekimlere uygulanan ankete verilen yanıtların değerlendirilmesi üzerine kurulmuştur. Anket 3 bölümden oluşmaktadır. Araştırma anketinin 1. bölümü, çalışmaya katılan hekimler hakkında genel bilgi toplamayı amaçlayan 7 sorudan oluşmuştur. Araştırma anketinin 2. bölümü, poliklinik ve ameliyathanede edinilen radyasyondan korunma bilincinin günlük pratikte kullanımını analiz etmeyi amaçlayan 13 sorudan oluşmuştur. Araştırma anketinin 3. bölümü, temel radyasyon güvenliği ve radyasyondan korunma bilgilerini analiz etmeyi amaçlayan 12 sorudan oluşmuştur.

Bulgular: Bu ankete cerrahi birimlerden, 96'sı asistan olmak üzere, 172 hekim katılmıştır. İkinci bölüm radyasyondan korunma farkındalığı sorularının analizinde, 10 yanıtta %50 ve üzerinde farkındalık düzeyi gözlendi. Üçüncü bölüm genel radyasyon güvenliği ve radyasyondan korunma bilgisi sorularının analizinde, 6 cevapta %50 ve üzeri doğru cevap düzeyi gözlendi.

Sonuç: Radyasyondan korunma bilinci, bireysel bir çaba olduğu kadar bir ekip işidir. Hastanemizde yürüttüğümüz bu anketin sonuçları açıkça vurguluyor ki, hastanemiz başhekimi, klinik şefleri ve cerrahi ünitelerdeki tüm hekimlerin radyasyon güvenliği konusunda farkındalıklarının yüksek olması ve radyasyondan korunma konusunda bilgi sahibi olmaları, poliklinik ve ameliyathanelerimizde optimum çalışma koşullarını oluşturmuştur.

Anahtar Sözcükler: Cerrahi birimler; floroskopi; radyasyon farkındalığı; radyasyon güvenliği; radyasyondan korunma.

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Original Article

Clinical and Demographic Characteristics of Patients Diagnosed with Primary Ciliary Dyskinesia with CCDC40 Homozygous Mutation

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ABSTRACT

Objective: Primary ciliary dyskinesia (PCD) is a rare genetic disorder caused by defective ciliary function, resulting in chronic respiratory infections and other systemic issues. CCDC40 encodes a protein crucial for assembling and functioning ciliary dynein arms, vital for ciliary movement. Mutations in CCDC40 can significantly exacerbate PCD symptoms. This study analyzed the clinical and demographic profiles of pediatric patients with PCD due to homozygous CCDC40 mutations.

Methods: A retrospective analysis was conducted of 13 patients at the Marmara University Division of Pediatric Pulmonology, focusing on their demographics, clinical symptoms, high-speed video microscopy (HSVM) findings, nasal nitric oxide (nNO) levels, PICADAR scores, sputum culture results, and respiratory function tests. Statistical analyses were performed using the SPSS software.

Results: The cohort had a median age of 17 years (25–75p, 11.5–21.5 years), with typical onset of symptoms at birth and a median diagnostic delay of 7 years (25–75p, 2–13.5 years). Notably, 84.6% of patients had consanguineous parents. The common symptoms included recurrent cough (100%), bronchiectasis (92.3%), and rhinosinusitis (92.3%). The median PICADAR score of the patients was 8 (25–75p, 5–11.5), and the median nasal NO value was 17.3 nl/min (25–75p, 7.7–114.5). HSVM analysis revealed immotile cilia and abnormal movement patterns in 53.8% and 30.7% of patients, respectively. Sputum cultures identified Haemophilus influenzae (92.3%) as the predominant pathogen.

Conclusion: The results highlight the importance of early diagnosis and intervention in managing PCD, particularly for those with CCDC40 mutations who may experience more severe respiratory complications than other genetic variants.

INTRODUCTION

Primary ciliary dyskinesia (PCD) encompasses a group of rare, genetically diverse, clinically variable disorders characterized by defective ciliary function. The global prevalence of PCD is estimated to be approximately 1 in 10,000 individuals.[1] Ciliary dysfunction results in impaired mucociliary clearance, which predisposes affected individuals to chronic infections of both the upper and lower respiratory tracts.[1] Beyond respiratory symptoms, PCD is associated with additional systemic manifestations, including laterality defects, male infertility, and hydrocephalus, in rare instances. To date, more than 50 genes have been implicated in PCD.[2]

At least 12% of PCD cases are attributed to defects in the inner dynein arm (IDA) and microtubular disorganization (MTD). The vast majority of these cases result from mutations in CCDC39 and CCDC40.[3] CCDC40 encodes a protein essential for the assembly and function of ciliary dynein arms, structures responsible for cilia movement.[4] Mutations in this gene typically result in a loss of ciliary motility, leading to severe clinical manifestations of PCD.

Around 50% of the individuals affected by CCDC40 mutations show defects in laterality, while male patients also experience infertility caused by immobile sperm tails with structural abnormalities.[5,6]

This study aimed to examine the clinical and demographic profiles, diagnostic procedures, and respiratory function measurements in subjects with homozygous mutations in the CCDC40 gene associated with PCD.

MATERIALS AND METHODS

Study Design and Population

This retrospective study was conducted at Marmara University Pediatric Pulmonology Division and included patients diagnosed with CCDC40 homozygous PCD. The patient data were collected from medical records from (1999–2024), including demographic, clinical, and respiratory function test results, high-speed video microscopy (HSVM) findings, nasal nitric oxide (nNO) levels, and sputum culture results. Ethical approval was obtained from the Marmara University Ethics Committee (Protocol No:18.10.2024.1333), with informed consent waived due to the retrospective nature of the study. The Declaration of Helsinki was always followed.

Inclusion and Exclusion Criteria

Patients with a confirmed diagnosis of CCDC40 homozygous PCD based on genetic testing and complete clinical data were included. Individuals with incomplete clinical, laboratory, or genetic data were excluded from the analysis.

Data Collection

Demographic information such as age, gender, and age at diagnosis was collected. Clinical data including chronic cough, recurrent respiratory infections, sinusitis, bronchiectasis, otitis media, dextrocardia, and fertility status were retrospectively extracted from medical records.

Respiratory Function Tests

Pulmonary function was assessed using spirometry, measuring parameters such as forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio.[7] These results were compared with predicted values based on age, gender, and height.[7] Pulmonary function data were retrieved from patient records and analyzed for trends in disease severity.

PICADAR Questionnaire

Patients were interviewed and scored for probable PCD using the PICADAR questionnaire.[8,9] PICADAR, a scoring tool with seven predictor variables, assigns integer values (1–4) to each clinical factor's presence based on regression coefficients. A threshold of 5 points optimized sensitivity (0.90) and specificity (0.75).[9] The maximum score of 14 indicated a 99.80% likelihood of PCD. Scores of 10 or higher showed a 92.6% probability, while scores of 5 or more indicated an 11.10% chance of PCD.[9]

Immunofluorescence Analysis

Respiratory epithelial cells were obtained via transnasal brush biopsy (Cytobrush Plus; Medscand Medical, Malmö, Sweden), suspended in RPMI medium, and air-dried on glass slides at the outpatient clinic of Marmara University.[10] The samples were then sent to the University of Münster's IF Laboratory for analysis. IF analysis involved treating cells with 4% paraformaldehyde, 0.2% Triton X-100, and 1% skim milk, followed by incubation with primary antibodies for 3-4 hours and secondary antibodies for 30 min at room temperature.[10]

Antibodies targeted proteins of the ODAs (DNAH5) and nexin-dynein regulatory complex (GAS8) in the ciliary axoneme. Double labeling was performed using monoclonal mouse anti-DNAH5 and polyclonal rabbit anti-GAS8 (HPA041311) primary antibodies at 1:500 dilution and Goat Anti-mouse Alexa Fluor 488 and anti-rabbit Alexa Fluor 546 secondary antibodies at 1:1000 dilution. Hoechst 33342 (Sigma-Aldrich) stained the cell nuclei.[10] Confocal images were captured with a Zeiss laser scanning microscope (Axiovert 200 LSM510 META) and processed using Zeiss LSM510 software.

High-Speed Video Microscopy Analysis

Nasal epithelial cells were collected using nasal brushing.[11] Participants were excluded if they had used nasal steroids or decongestants within four weeks or exhibited acute respiratory tract infection symptoms during that period. The ciliated cells were transferred to RPMI 1640-Medium at 37°C and maintained using a heater plate (Tpi-TSX, Tokyo, Japan).

HSVM with Sisson-Ammons Video Analysis software (SAVA, MI, USA) measured ciliary movement frequency.[11] Measurements were taken with an inverted phase-contrast Nikon Eclipse TS100 microscope (Nikon, Japan) using a 40x objective and a digital high-speed video camera (Basler acA1300-200um, Germany). Digital image sampling was 640×480 pixels at 120-150 frames per second (fps). Recordings lasted one minute with 15-second intervals. Both the top and side views of the ciliary beat were analyzed in real time and slow motion.[11]

Ciliary beat patterns (CBP) were categorized as 'normal,' 'virtually immotile,' 'stiff beating with reduced amplitude,' 'circular gyrating motion,' and 'ciliary beat frequency'.[11] The HSVM results were compared to clinical symptoms and other diagnostic features.

Nasal Nitric Oxide (nNO) Measurement

Nasal nitric oxide levels were measured using a chemiluminescence analyzer following American Thoracic Society/European Respiratory Society standard guidelines.[12] Patients performed breath-holding or exhalation techniques while nNO was measured from one nostril.[12]

In patients suspected of PCD, nNO levels below 77 ppb, measured with a chemiluminescence NO analyzer during mouth breathing, exhibit over 95% specificity and sensitiv-

ity for PCD diagnosis.[12] nNO levels were compared with established normal ranges and between patients.

Radiological Assessment

Chest X-rays and high-resolution computed tomography (HRCT) scans were reviewed for all patients. Bronchiectasis severity and the presence of situs abnormalities (such as situs inversus) were noted.[13]

Sputum Culture Analysis

Sputum samples were collected from patients during routine clinical visits. The microbiological profile was analyzed by performing sputum cultures to identify bacterial pathogens, with particular focus on common PCD-associated organisms such as Pseudomonas aeruginosa (PA), Haemophilus influenzae, and Staphylococcus aureus (SA). The frequency of positive cultures and chronic colonization were evaluated in relation to clinical outcomes.

Statistical Analysis

All statistical analyses were performed using (statistical software, e.g., SPSS). Descriptive statistics were used to summarize continuous variables (mean±standard deviation) and categorical variables (frequencies and percentages). Comparative analyses of demographic, clinical, and functional characteristics were performed using Student's t-test for continuous variables and chi-square or Fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Thirteen pediatric patients with CCDC40 homozygous PCD constituted the cohort for the current analysis. Of all patients, 9 (69.2%) were females. The median patient age was 17 years (25–75p, 11.5–21.5 years). The median age of symptom onset was 0 years (25–75p, 0–0 years), and the median age at diagnosis was 7.0 years (25–75p, 2–13.5 years). No parent was diagnosed with PCD, whereas two siblings had PCD.

Approximately 84.6% of patients (11/13) exhibited parental consanguinity. All patients (13/13) presented with recurrent wet cough, 69.2% of patients (9/13) manifested otitis media, 92.3% of patients (12/13) demonstrated bronchiectasis, and 92.3% of patients (12/13) displayed rhinosinusitis. Sixty-one percent of patients (8/13) experienced neonatal respiratory distress, and 61% of patients (8/13) presented with situs inversus totalis. Clinical and demographic characteristics of the patients are presented in Table 1.

The median PICADAR score of the patients was 8 (25–75p, 5–11.5), and the median nasal NO value was 17.3 nl/min (25–75p, 7.7–114.5). Immunofluorescence (IF) analysis of respiratory biopsy specimens obtained from four patients revealed that two patients had an outer dynein arm (ODA) defect and two patients had an IDA and MTD defect, along with genetic tests.

High-speed video microscopy (HSVM) analysis revealed immotile cilia in 53.8% of patients (7/13) and abnormal

Table 1. Clinical and demographic characteristics of CCDC40 homozygous PCD patients

ID	Gender / Age (year)	Neonatal respiratory distress	Chronic rhinitis	Recurrent otitis and sinusitis	Situs inversus totalis	Bronchiectasis consanguinity	Parental	PICADAR (nl/dk)	Nno findings (37°)	HSVM
ID-1	F/26	-	+	-	-	+	+	3	36	immotile
ID-2	F/25	+	+	+	-	+	+	7	NA	immotile
ID-3	F/22	+	+	+	+	+	+	12	4	NA
ID-4	M/21	-	+	+	-	+	+	4	655	abnormal pattern
ID-5	F/17	+	+	-	+	+	+	11	22	immotile
ID-6	F/20	-	+	+	+	+	+	8	9	immotile
ID-7	F/16	+	+	+	-	+	+	8	305	abnormal pattern
ID-8	F/17	-	+	+	+	+	+	6	11	immotile
ID-9	M/15	+	+	-	+	+	+	11	0	abnormal pattern
ID-10	M/13	+	+	+	+	+	-	12	51	abnormal pattern
ID-11	M/10	+	+	+	+	+	+	12	13	NA
ID-12	F/7	+	-	+	+	+	+	11	NA	immotile
ID-13	F/6	-	+	+	-	NA	-	4	NA	immotile

NA: not available; F: female; M: male; Nno: Nasal Nitric Oxide; HSVM: High-Speed Video Microscopy Analysis.

movement patterns (stiff movements) in 30.7% (4/13) patients. HSVM sampling could not be performed in two patients because consent could not be obtained.

Five patients showed normal spirometry results, five had mild obstructive impairment, and two adult patients had severe small airway obstruction. The youngest patients in the obstructive impairment group were 10 and 13 years of age, whereas the remaining three were 17 years of age or older.

Successful collection of at least two culture samples was achieved in 12 patients. A pathogenic species was confirmed when identical pathogens were identified in a minimum of two cultured specimens from the same patient. Haemophilus influenzae was the most commonly isolated pathogen (n:12/13, 92.3%), followed by PA (n:5/13, 38.5%) and methicillin-resistant SA (n:2/13, 15.4%). Three of the 5 patients with PA were adults.

DISCUSSION

This study provides a comprehensive analysis of clinical, demographic, and diagnostic characteristics in patients with CCDC40 homozygous PCD. Our cohort consisted of 13 patients. The early onset of symptoms (median age: 0 years) and a median diagnostic delay of seven years reflect the diagnostic challenges associated with PCD. Diagnostic delays are commonly reported in PCD due to the nonspecific nature of early symptoms, such as neonatal respiratory distress and chronic cough, often attributed to other more common conditions.[14-16] Concurrently, the absence of a gold standard diagnostic test contributes to a delay in diagnosis.[8]

Consanguineous marriages were observed at a high rate in our cohort (84.6%), supporting the idea that CCDC40 mutations are associated with autosomal recessive inheritance, especially in populations with a high rate of consanguineous marriage.[16]

Clinical features including chronic wet cough, sinusitis, chronic middle ear disease, situs anomalies, and history of neonatal respiratory distress (NRD) are observed more frequently than in general patients.[15] Prominent clinical features included NRD (61%), early-onset persistent chronic cough (100%), rhinosinusitis (92.3%), and situs inversus totalis (61%). NRD and situs inversus totalis were also observed at slightly higher rates than reported in previous studies.[15] The higher ratio of situs inversus totalis may be due to CCDC40 being expressed specifically in the embryonic node and midline, which are important tissues controlling left-right patterning.[5]

The prevalence of NRD in PCD remains uncertain; it has been reported to vary considerably in the literature, ranging from 15% to 91%.[17] However, it is reported that these data are generally of poor quality.[18] In the large international dataset, including data from Türkiye, 55% of children with PCD had a history of NRD.[18] The increased NRD frequency in our patient cohort likely results from the more severe pulmonary symptoms linked to CCDC40 mutations. Literature case series have documented more severe NRD in PCD patients with this genetic variant.[19]

The PICADAR score, a predictive tool for low-resource settings, was used to evaluate the probability of PCD.[9] A score of 14 corresponds to a 99.8% probability of PCD, and a score of 10 corresponds to a probability of 92.6%.[9] In our cohort, all five individuals had a median score of ≥8, suggesting moderate clinical suspicion in this cohort, aligning well with the overall diagnostic presentation. Importantly, the consistently low nNO levels (median: 17.3 nl/min) reaffirm its utility as a reliable diagnostic marker for PCD, particularly in resource-limited settings where genetic testing may not be readily accessible.[15]

Immunofluorescence (IF) analysis has emerged as a valuable diagnostic tool for PCD, offering high specificity and rapid results compared to traditional methods.[20] In patients diagnosed with homozygous CCDC40-related PCD, IF examination revealed the absence of the inner dynein arm protein in both ciliary structures and spermatozoa.[14] In our study cohort, although IDA defects were observed in two patients, consistent with the literature, two patients exhibited ODA defects. Nevertheless, several studies have reported that the genes that primarily affect IDA are crucial for the assembly and localization of ODA.[21] Our findings may be related to this phenomenon.

HSVM plays a crucial role in diagnosing PCD.[22] Studies show that, when performed by experts, HSVM accurately detects PCD with high sensitivity and specificity, in line with multidisciplinary assessments and ERS guidelines.[22] In our patients' HSVM analysis, the majority exhibited immotile cilia or abnormal cilia movement patterns, thereby confirming the clinical diagnosis of PCD. The utility of HSVM, particularly due to its capacity for rapid result generation, was demonstrated through the identification of immotile cilia in 3 patients presenting with bronchiectasis and low PICADAR scores, without necessitating the delay associated with genetic testing.

PCD patients with CCDC40 mutations have been reported to show worse lung disease compared to those with ODA defects.[23] Respiratory function tests were normal in the younger age group of our patients, whereas obstructive and severe respiratory failure were observed in older patients. The spirometry findings, which showed normal to mild obstructive impairment in the majority of pediatric patients but more severe obstruction in adult patients, suggest progressive airway disease in PCD.[24]

In addition, although it is thought that the youngest ages of 10 and 13 years in our patients with obstructive impairment groups may be associated with poor lung function prognosis due to CCDC40 homozygosity, larger sample sizes are required to draw definitive conclusions. Furthermore, our findings indicated that pulmonary function in patients with PCD typically declines as they age, which aligns with existing research. This underscores the critical need for early detection and treatment to mitigate the

disease's progression.[23]

Primary ciliary dyskinesia patients are susceptible to recurrent bacterial infections due to impaired mucociliary clearance.[25] The most common pathogens in PCD airways include Haemophilus influenzae, SA, Moraxella catarrhalis, and PA.[25] In sputum cultures taken from our patient group, Haemophilus influenzae and PA were observed at high rates, similar to the literature where PA is more common in adult patients. Studies have not shown a correlation between persistent SA infection and declining pulmonary function in PCD patients.[26] Recent findings suggest that the prevalence of SA infection in pediatric and adolescent patients with PCD is between 35% and 46%.[27]

In our study, two adults with methicillin-resistant SA colonization had severe obstructive pulmonary function and concurrent PA colonization. Owing to the small sample size, a definitive causal link between methicillin-resistant SA and deteriorating respiratory function could not be confirmed, although the co-occurrence of methicillin-resistant SA and PA may have worsened the condition.

Conclusion

In conclusion, this cohort of CCDC40 homozygous PCD patients demonstrates a characteristic clinical phenotype, including early onset of symptoms, frequent respiratory infections, and progressive lung disease. The combination of clinical, functional, and genetic assessments proved essential for accurate diagnosis and management. Given the progressive nature of lung disease in PCD, particularly in adulthood, early diagnosis and aggressive management of respiratory infections and structural lung disease are crucial to improving long-term outcomes.

Ethics Committee Approval

The study was approved by the Marmara University Hospital Ethics Committee (Date: 25.10.2024, Decision No: 18.10.2024.1333).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Y.G.; Design: A.P.E.; Supervision: B.K.; Materials: Ş.K., N.M.Ç.; Data collection &/or processing: C.A.Y., E.E.B.; Analysis and/or interpretation: F.Ö., M.M.A.Y.; Literature search: M.S.; Writing: M.Y.K.; Critical review: E.E.E.

Conflict of Interest

None declared.

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CCDC40 Homozigot Mutasyonu Olan Primer Siliyer Diskinezi Tanısı Almış Hastaların Klinik ve Demografik Özellikleri

Amaç: Primer siliyer diskinezi (PSD), silyer fonksiyonun bozulmasıyla karakterize nadir bir genetik hastalıktır ve silyer fonksiyon bozukluğu, kronik solunum yolu enfeksiyonlarına ve diğer sistemik sorunlara yol açar. CCDC40, silyer hareketten sorumlu olan dynein kollarının işlevi için gerekli bir protein kodlar. Bu genin mutasyonları, PSD'nin şiddetli klinik bulgularına neden olabilir. Bu çalışma, CCDC40 homozigot mutasyonları olan pediatrik PSD hastalarının klinik ve demografik özelliklerini retrospektif olarak incelemeyi amaçlamıştır.

Gereç ve Yöntem: Marmara Üniversitesi Pediatrik Pulmonoloji polikliniğinde takipli 13 hasta çalışmaya alındı. Hastaların demografik verileri, klinik semptomları, yüksek hızlı video mikroskopisi (HSVM) bulguları, nazal nitrik oksit (nNO) ölçümleri, PICADAR skorları, balgam kültürü sonuçları ve solunum fonksiyonu testleri retrospektif olarak incelenmiştir. İstatistiksel analizler SPSS yazılımı kullanılarak yapıldı.

Bulgular: Çalışma grubunun medyan yaşı 17 yıl (25–75p, 11.5–21.5 yıl) olup, semptom başlangıç yaşı medyan 0 yıl (25–75p, 0–0 yıl) idi. Tanıda medyan gecikme süresi 7 yıl (25–75p, 2–13.5 yıl) idi. Hastaların %84.6'sında akraba evliliği mevcuttu. Yaygın semptomlar arasında kronik balgamlı öksürük (%100), bronşektazi (%92.3) ve rinosinüzit (%92.3) saptandı. Hastaların median PICADAR skoru 8 (25–75p, 5–11.5), median nazal NO değeri ise 17.3 nl/dk (25–75p, 7.7–114.5) olarak bulundu. HSVM analizinde hastaların %53.8'inde immotil silyalar, %30.7'sinde ise anormal hareket paterni saptandı. Balgam kültürlerinde en yaygın patojen Haemophilus influenzae (%92.3) idi.

Sonuç: PSD'nin yönetiminde erken tanı ve müdahale önemlidir. Özellikle CCDC40 mutasyonları olan hastalar, diğer genetik varyantlara kıyasla daha şiddetli solunum komplikasyonları yaşayabilirler.

Anahtar Sözcükler: CCDC40 mutasyonu; nazal nitrik oksit; primer siliyer diskinezi; yüksek hızlı video mikroskopi.

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Original Article

Evaluation of the Reasons for Requesting Ammonia Tests in the Pediatric Clinic Over the Last Five Years

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Keywords: Ammonia; autism; epilepsy; hyperammonemia; neuromotor retardation.

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ABSTRACT

Objective: Ammonia is a neurotoxic substance that is produced as a consequence of protein metabolism. It is converted to urea in the liver and subsequently eliminated by the kidneys. Hyperammonemia is defined as values that exceed 60 µmol/L outside of the neonatal period. Hyperammonemia in children is frequently caused by genetic and metabolic conditions, drug use, and liver disease or drug use in adults.

Methods: The results of patients treated at our hospital in the past five years and whose blood levels exceeded 60 µmol/L were evaluated in our single-center retrospective study. The age, gender, ammonia levels, and reasons for obtaining ammonia of the patients were analyzed.

Results: The purpose of the study was to investigate the reasoning behind the request for ammonia testing in pediatric patients at the hospital. The results showed that the reasons for requesting testing varied between children under and over 1 month of age. Although metabolic disorders are usually evaluated in newborns, infections, liver dysfunction, and drug side effects are predominant in children over the age of one month. The retrospective design and single-center aspect of the study have been noted as major limitations.

Conclusion: Hyperammonemia may be an adverse effect of neurological diseases in pediatric patients, and medications used to treat seizures can cause hyperammonemia. This should be kept in mind in patients presenting with seizures, especially those with changes in consciousness.

INTRODUCTION

Ammonia is a toxic chemical produced during the metabolic processing of proteins in the human body. Ammonia, a compound that is naturally produced in the body, is converted into urea, a less harmful product, in the liver via the urea cycle (ornithine cycle) and is eliminated from the body through the kidneys. The breakdown of ammonia is critically important, particularly for the protection of the central nervous system. Elevated ammonia levels are referred to as hyperammonemia. In accordance with the accepted clinical categorization, blood ammonia concentrations above 150 µmol/L in neonates and exceeding 60 µmol/L in adults are referred to as hyperammonemia.[1]

Hyperammonemia is related to several metabolic and genetic disorders characterized by increased ammonia levels in the bloodstream. Hyperammonemia in neonates has been linked to genetic metabolic problems, such as urea cycle disorders (e.g., ornithine transcarbamylase deficiency), organic acidemias (e.g., propionic acidemia and methylmalonic acidemia), and mitochondrial disorders. Urea cycle disorders are characterized by a lack of one or more enzymes involved in the conversion of ammonia to urea, which could result in defective ammonia metabolism, particularly in the liver, leading to accelerated accumulation of harmful amounts.[2]

In adults, hyperammonemia is primarily associated with conditions such as liver failure, particularly cirrhosis and acute liver failure, which may result in hepatic encephalopathy. Liver damage reduces urea cycle function, leading to decreased ammonia metabolism. Additionally, certain medications, such as valproic acid, in addition to kidney disease, may elevate ammonia levels.[3]

Increased ammonia concentrations are harmful to the central nervous system. Ammonia can traverse the blood-brain barrier, impacting energy metabolism in neuronal cells and leading to a decrease in ATP, the primary mol-

ecule for intracellular energy transfer. The process may lead to irreversible damage, especially in pediatric patients, manifesting as neurological symptoms such as lethargy, disorientation, and coma.[4] Increased ammonia levels disrupt glutamate metabolism in the brain, leading to excitotoxicity that damages neurons and results in neurotoxicity.[5]

As a result, hyperammonemia is a critical condition that requires urgent diagnosis and intervention, especially in pediatric metabolic diseases. Determination of blood ammonia levels, especially in patients presenting to neonatal and pediatric emergency departments with unexplained encephalopathy or neurological symptoms, is of great importance for the early diagnosis of potentially reversible metabolic disorders.

In this study, the reasons for measuring ammonia levels in pediatric patients at the hospital in the last five years were examined and their contributions to the diagnosis and treatment process of hyperammonemia were evaluated.

MATERIALS AND METHODS

The study was conducted by retrospectively examining hospital system data. The study started following the approval of the ethics committee. The study was approved by the Lütfi Kırdar City Hospital Ethics Committee (Approval date: 25.10.2024-Approval number: 2024/010.99/9/34). The research was conducted applying the hospital automation system records and patient records. The study was conducted in accordance with the Helsinki Declaration.

Patients under 18 years of age, for whom blood ammonia levels were requested in polyclinics and inpatient services within the Department of Pediatrics from October 1, 2020, to October 31, 2024, and the results were above 60 mmol/L were included in the study. Individuals aged 18 and above and the results under 60 mmol/L were excluded from the study.

The number of ammonia requests, the number of patients, ammonia levels, demographic characteristics, reasons for admission, and final diagnoses of the patients were recorded in the data collection form as study data.

Statistical Analysis

Data were analyzed with IBM SPSS V23. Compliance with normal distribution was examined with the Kolmogorov-Smirnov Test. Mann-Whitney U test was used to compare data that did not comply with normal distribution in pairs. Pearson chi-square test, Yates correction, and Fisher's Exact tests were used to examine the relationship between categorical data, and multiple comparisons were made with Bonferroni correction.

Table 1. Distribution of gender, age, diagnosis code, reason for test request and ammonia levels of patients for whom ammonia was requested in the pediatric clinic

	Average Deviation / Frequency	Median (min-max) / Percentage
Nationality		
Türkiye	401	95.9
Syrian	16	3.8
Iraq	1	0.2
Gender		
Male	236	56.5
Female	182	43.5
Diagnosis Code		
F82	151	36.3
E88.8	30	7.2
G40.9	30	7.2
Others	205	49.3
Test Request		
Seizure	124	30.6
Neuromotor retardation	64	15.8
Autism	46	11.4
Other	173	42.2
Age		
Under the age of 1 month	37	8.9
Above 1 month	381	91.4
Amonia level		
≤250 mmol/lt	393	94
>250 mmol/lt	25	6
Amonnia levels	126.03±130.72	87.84 (60.36-1235.46)
Age 4.51±6.69	2.5 (0.08-104.83)	

Mean±standard deviation and median (minimum-maximum) were used to display quantitative data. Frequency and percentage were used to display categorical data. The significance level was taken as $p<0.05$.

RESULTS

The study included 285 admissions among 255 patients who met the criteria and requested ammonia testing. One hundred forty-six (51.2%) of all admissions were male; the mean age was 67.2±69.7 months (Table 1).

A total of 1450 desired outcomes from 1080 patients were assessed. Among these, 420 patients had 556 results above 60 mmol/L, and the study included the results of these patients.

In this study, the demographic characteristics of 418 patients for whom ammonia tests were requested were analyzed. 95.9% (n=401) of the patients were Turkish nationals, 3.8% (n=16) were Syrian nationals, and 0.2% (n=1) was of Iraqi nationality. When analyzing the gender distribution, 56.5% (n=236) of the patients were male and 43.5% (n=182) were female. When the age distribution was examined, 8.9% (n=37) of the patients were in the newborn group aged 1 month and below, and 91.1% (n=381) were in the age group over 1 month. These data show that ammonia test requests are mostly made for boys of Turkish nationality, aged over 1 month (Table 1).

Gender distribution is similar between male and female patients: 56.5% of the patients are male (n=236) and 43.5% are female (n=182). This proportional distribution between genders reveals that there is no significant difference between male and female patients in the frequency of requesting ammonia testing.

The most common diagnosis code found with the ammonia test request was F82, which demonstrated up 36.3% of the time (n=15). Following this code, codes E88.8 and G40.9 both demonstrated up 7.2% of the time (n=30). People with alternative diagnosis codes represented 49.3% (n=205). According to this distribution, the number of requests for ammonia measurements is high, especially among children with diagnosis code F82 (neurodevelopmental disorders).

Upon investigating the reasons for requesting an ammonia test, it was observed that seizures (30.6%), neuromotor retardation (15.8%), autism diagnosis (11.4%), and other clinical reasons (42.2%) were the most frequently cited. Further, the most prevalent findings associated with testing orders are infection (25%), valproic acid use (47.5%), test error (hemolysis or prolonged waiting) (13.8%), and other factors. These data suggest that neurological symptoms and valproate use are significant factors in the motivations for requesting ammonia testing.

Neuromotor retardation (25%) was the most frequently requested reason for testing in patients aged 1 month and younger when grouped by age. Conversely, the group older than 1 month experienced an increase in test demand for reasons such as autism (12.2%) and seizures (31.4%). These age groups' distinct reasons for requesting testing indicate that the necessity of ammonia measurement is influenced by age-related clinical conditions.

The median ammonia value of patients in the 1 month and younger age groups was 85 µmol/L, whereas the value in the group aged over 1 month was 88.32 µmol/L. There was no statistically significant difference in ammonia value depending on age ($p=0.564$). The median ammonia value was 86.38 µmol/L in male patients and 89.25 µmol/L in females when evaluated according to gender. A statistically significant difference between gender and ammonia value was not observed ($p=0.216$). These results indicate that ammonia levels do not vary significantly by age and gender variables (Fig. 1).

The ammonia values were examined in two groups: ≤250 µmol/L and >250 µmol/L. 94% of the patients (n=393) had an ammonia value below 250 µmol/L, while 6% of the patients (n=25) had an ammonia value above 250 µmol/L. The majority of patients showed ammonia levels that were within the normal range, with only a small number of patients having pathological levels (Fig. 2).

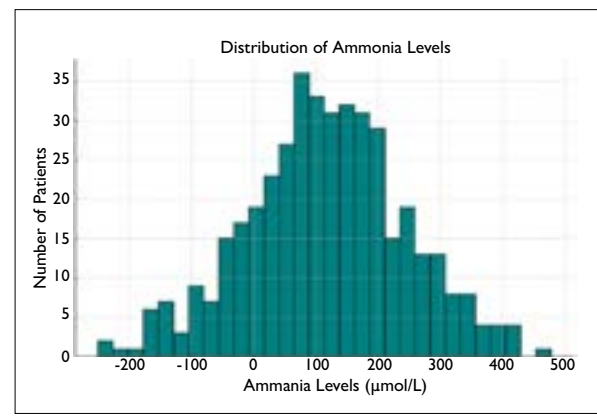

Figure 1. Distribution of ammonia levels.

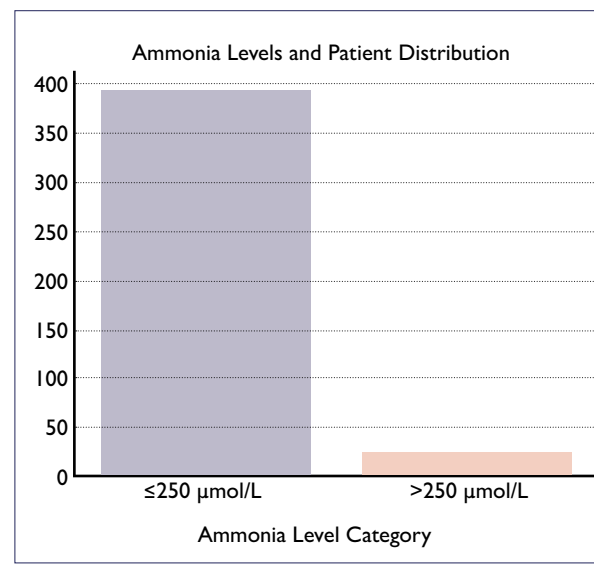

Figure 2. Ammonia Levels and patient distribution.

DISCUSSION

The clinical and demographic characteristics of pediatric patients who submitted inquiries for ammonia testing at the hospital were investigated in this study. The findings emphasize significant differences in reasons for ammonia testing based on age, particularly when contrasting infants under one month of age with older children.

Ammonia testing is primarily requested in neonates to diagnose metabolic disorders, including organic acidemias and urea cycle defects. In this age group, hyperammonemia is frequently associated with inherited metabolic diseases (IMDs), which may result in life-threatening symptoms such as lethargy, seizures, and coma. Ammonia can accumulate rapidly in newborns because of their immature metabolic pathways, requiring early testing. In cases of suspected IMDs in the neonatal period, Kadıoğlu Yılmaz et al.[6] also observed a higher frequency of ammonia test requests.

Ammonia testing is more frequently associated with acquired conditions in children over one month of age, such as liver dysfunction, medication effects, and infections. The literature underlines that valproate-induced hyperammonemia is a prevalent etiology in older children who have gone through antiepileptic therapy. Valproate may result in elevated ammonia levels, which require monitoring to avoid neurotoxic effects, by inhibiting the urea cycle. This is consistent with our research, which demonstrated that valproate was a significant contributor to hyperammonemia in patients over one month of age.[7]

Ammonia testing was requested for 30.6% of the cases in our study due to neurological symptoms, such as seizures and abnormal mental conditions. This is in line with the results of Ali and Nagalli (2023), who highlight the importance of hyperammonemia in neurotoxicity as a result of its capacity to disrupt neurotransmitter balance and cross the blood-brain barrier. Consequently, ammonia testing is essential in the diagnostic method for pediatric patients who exhibit unexplained neurological symptoms.[8]

Ammonia levels are also significantly influenced by age, with neonates having naturally higher baseline levels as a result of their immature liver function. Our research confirmed the findings of Ribas et al.[9] that ammonia levels were generally in the lower range for older children, which is suggestive of the maturing of metabolic processes with age.

The high frequency of misleading results in ammonia testing is another important discovery in our study. This phenomenon can be influenced by pre-analytical factors such as sample handling and transport conditions. Maranda et al.[10] demonstrated that clinical decisions can be influenced by falsely elevated ammonia levels resulting from improper sample handling. It is essential to implement rigorous sample processing protocols in order to reduce the likelihood of inaccurate results.

This study has several limitations that must be considered when interpreting the results:

• The study is retrospective, depending on historical records and data. Prospective studies may facilitate more regulated data collection and standardized protocols.

• The data was obtained from a singular institution, potentially limiting the generalizability of the findings to other hospitals or regions. Multi-center studies might provide diverse data and comprehensive insights into ammonia testing practices across diverse pediatric populations and healthcare settings.

• Some patient subgroups, especially those with rare illnesses or specific etiologies for hyperammonemia, showed only a small number of cases.

• Sample handling, transport, and processing affect ammonia levels. Despite efforts to reduce errors, sample processing delays and improper storage may have caused ammonia measurements to be inaccurate. This may affect the study's hyperammonemia prevalence.

• This study focused on establishing ammonia testing frequencies and associated clinical characteristics but did not conduct a longitudinal follow-up of patients to evaluate outcomes associated with hyperammonemia. As a result, we cannot assess the effect of the measured ammonia levels on long-term patient health or treatment efficacy.

• The study provides facts about the clinical characteristics of patients undergoing ammonia testing; however, it fails to consider all potential confounders, such as underlying comorbidities and concurrent medications, which may have affected ammonia levels. A more thorough analysis with controlled variables may produce additional conclusions.

• Ammonia reference values can differ significantly with age, and there is no generally accepted threshold for hyperammonemia in different pediatric age categories. The absence of standardization may influence the interpretation of ammonia levels and could introduce variability in the assessment of hyperammonemia across various age groups.

Recognizing these limitations allows for the design of future studies that may involve prospective, multicenter approaches with standardized sample handling protocols and extended follow-up to more accurately evaluate clinical outcomes associated with ammonia levels in pediatric patients.

Conclusion

This study emphasizes the importance of ammonia testing in pediatric patients, particularly in the detection of metabolic disorders in neonates and the management of drug-induced hyperammonemia in older children. The findings, despite their retrospective, single-center design, highlight the necessity of age-specific guidelines and standardized protocols in ammonia testing. Future research using longitudinal follow-ups and multicenter data may provide more information, helping clinicians to enhance diagnostic accuracy and improve patient outcomes related to hyperammonemia.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 25.10.2024, Decision No: 2024/010.99/9/34).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.Ö.E., B.Y.; Design: E.Ö.E., B.Y.; Supervision: Y.A.; Fundings: Y.Ç., Y.A.; Data collection &/or processing: B.Y.; Analysis and/or interpretation: E.Ö.E., B.Y.; Literature search: E.Ö.E., Y.Ç.; Writing: E.Ö.E., B.Y.; Critical review: Y.A.

Conflict of Interest

None declared.

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Son 5 Yılda Pediatri Kliniğinde Amonyak Test İstemi Nedenlerinin Araştırılması

Amaç: Amonyak, protein metabolizması sonucunda oluşan nörotoksik bir bileşiktir, karaciğerde üreye dönüştürülür ve böbreklerle atılır. Yenidoğan dönemi dışında 60 µmol/L'yi aşan değerler hiperamonyemi olarak değerlendirilir. Çocuklarda genetik ve metabolik durumlar, ilaç kullanımı; erişkinlerde ise karaciğer hastalığı veya ilaç kullanımı en sık hiperamonyemi nedenleridir.

Gereç ve Yöntem: Tek merkezli retrospektif çalışmamızda, son 5 yılda hastanemizde bakılıp 60 µmol/L'yi aşan hasta sonuçları değerlendirildi. Hastaların yaş, cinsiyet, amonyak değerleri ve amonyak istenme nedenleri incelendi.

Bulgular: Bu çalışmada, hastanemizde pediatrik hastalarda amonyak testi isteme nedenleri incelenmiştir. Bulgular, 1 ay altı ve üstü çocuklar arasında test isteme nedenlerinde farklılıklar olduğunu göstermiştir. Yenidoğanlarda testler genellikle metabolik bozukluklar için yapılırken, 1 ay üstü çocuklarda karaciğer fonksiyon bozuklukları, ilaç yan etkileri ve enfeksiyonlar ön plandadır. Çalışmanın retrospektif tasarımı ve tek merkezli olması ise önemli sınırlamalar olarak belirtilmiştir.

Sonuç: Pediatrik hastalarda nörolojik hastalıkları temelinde hiperamonyemi olabileceği gibi nöbet nedeni ile kullanılan ilaçlar da hiperamonyemiye neden olabilir. Bu durum nöbetle başvuran, özellikle bilinç durum değişikliği olan hastalarda akılda tutulmalıdır.

Anahtar Sözcükler: Amonyak; epilepsi; hiperamonyemi; nöromotor retardasyon; otizm.

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Original Article

Relaparotomy After Cesarean Section: A Tertiary Center Experience

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Keywords: Cesarean section; hypogastric artery ligation; intraperitoneal bleeding; relaparotomy; uterine atony.

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ABSTRACT

Objective: We aimed to contribute to the literature by studying the risk factors for post-cesarean relaparotomy, the morbidities that occur, and the practices performed during relaparotomy.

Methods: This retrospective study included cases of relaparotomy after cesarean section performed at a training and research hospital between January 2014 and January 2021. All cases who underwent relaparotomy within 60 days after cesarean section within a 7-year period were included in the study. We divided all cases into three groups with regard to the timing of relaparotomy after cesarean section: within the first 24 hours, between day 1 and day 10, and after day 10.

Results: A total of 24,293 cesarean sections were performed in our hospital. The relaparotomy rate after cesarean section was 0.18% in our clinic. Emergency cesarean sections accounted for 60.8% of our study group. The most common indication for relaparotomy was postpartum hemorrhage due to uterine atony with 41.3%. Uterine atony was followed by peritoneal bleeding with 28.2%. Hypogastric artery ligation was performed in 18 (39.1%) patients. Relaparotomy after cesarean section was most performed within the first 24 hours. Maternal mortality was not observed after relaparotomy.

Conclusion: Post-cesarean relaparotomy is becoming increasingly important due to the increasing number of cesarean sections. The most common reasons for relaparotomy are uterine atony and intraperitoneal bleeding. Most relaparotomies are performed within the first 24 hours after cesarean section. The complication rate increases as the interval between cesarean section and relaparotomy increases.

INTRODUCTION

Cesarean section is the most common obstetric procedure in daily practice. Recently, there has been a significant increase in cesarean section rates in many countries.[1] Although cesarean sections are effective in saving the lives of mothers and babies when needed for obstetrically indicated reasons, at the population level, cesarean section rates above 10% are not associated with reductions in maternal and neonatal mortality.[2] Despite recent advances in surgical techniques and blood transfusion facilities that have increased the safety of cesarean sections, the procedure still carries significantly higher maternal and fetal risks compared with vaginal delivery.[3,4]

Relaparotomy refers to surgeries performed within 60 days of the initial surgery. It is a rare but serious complication that may lead to prolonged hospital stay, wound infection, blood transfusion, near-miss, hysterectomy, and even maternal death.[5] This situation can be life-threatening and is one of the most serious and feared events in the post-cesarean period.[6] The main conditions leading to relaparotomy include uterine atony, intra-retroperitoneal bleeding, pelvic abscess, rectus hematoma, and bowel and bladder injury.[7-10] Although relaparotomy is sometimes necessary to prevent near misses, it should be noted that it itself increases maternal mortality and morbidity.[7]

There are very few studies on relaparotomy after cesarean section.[4,11] Relaparotomy cases remain one of the most

feared and deadly cases for obstetricians. This study aims to contribute to the literature by examining the risk factors for post-cesarean relaparotomy, the morbidities that occur, and the practices performed during relaparotomy.

MATERIALS AND METHODS

This retrospective study included cases of relaparotomy after cesarean section performed at a training and research hospital between January 2014 and January 2021. Prior to the initiation of this study, approval was obtained from the Human Research Ethics Committee of our institution (Registry number: 160 and Date: September 22, 2021). The Helsinki Declaration principles were adhered to throughout our study. Hospital electronic records and patient charts were reviewed for all data. Maternal age, gravida, parity, gestational week, and history of cesarean section were recorded. Indications for cesarean section, indications for relaparotomy, and procedures performed during relaparotomy were recorded separately. The mean amounts of erythrocyte suspension, fresh frozen plasma, cryoprecipitate, random platelet, and fibrinogen transfused to the cases were also recorded.

All cases who underwent relaparotomy within 60 days after cesarean section within a 7-year period were included in the study. We divided all cases into three groups with regard to the timing of relaparotomy after cesarean section: within the first 24 hours, between day 1 and day 10, and after day 10.

Statistical Analysis

Statistical analyses were performed with SPSS (Statistical Package for Social Sciences) for Windows 15.0 (SPSS, Inc., Chicago, IL, USA), Epi Info, and Excel programs. Descriptive statistics included median with minimum and maximum, and count (%) as appropriate.

RESULTS

From January 2014 to January 2021, a total of 24,293 cesarean sections were performed in our hospital. The demographic data of the patients revealed that the mean age was 32±6.6 (18–47) years, gravidity was 2.7±1.58 (1–6), parity was 2±1.03 (1–5), and gestational age was 35.6±3.3 (29–42) weeks. The most common indications for cesarean section among patients who underwent relaparotomy were a history of previous cesarean section and severe preeclampsia and HELLP syndrome.

In our study cohort of 24,293 patients who underwent cesarean sections, 46 patients (0.18%) underwent relaparotomy. Notably, emergency cesarean sections constituted 60.8% of the cases in this group. In our clinic, 42 patients underwent relaparotomy through a Pfannenstiel incision and 4 through a vertical incision. The most common indication for relaparotomy was postpartum hemorrhage due to uterine atony (41.3%), followed by peritoneal bleeding (28.2%). Uterine atony patients received uterine massage and medical treatments before relaparotomy. In 8.7% of cases, relaparotomy was performed secondary to pelvic abscess (Table 1).

Table 1. Indications for relaparotomy

Indication	n=46	Ratio
Uterine atony	19	41.3%
Intraperitoneal bleeding	13	28.2%
Rectus hematoma	5	10.9%
Pelvic abscess	4	8.7%
Retroperitoneal bleeding	2	4.3%
Bladder injury	1	2.2%
Ileus	1	2.2%
Evisceration	1	2.2%

Table 2. Procedures performed in relaparotomy

Procedure	n=46	Ratio
Hypogastric artery ligation + B-lynch suture	9	19.5%
Hematoma evacuation (aspiration-irrigation)	8	17.5%
Uterine artery ligation + B-lynch suture	6	13%
Hypogastric artery ligation	4	8.7%
Abscess drainage	4	8.7%
Hypogastric artery ligation + Uterine artery ligation	3	6.5%
Uterine incision repair	3	6.5%
Hypogastric artery ligation + Uterine artery ligation + B-lynch	2	4.3%
suture Hysterectomy	2	4.3%
Inferior epigastric artery ligation + B-lynch suture	2	4.3%
Fascia repair	1	2.2%
Bladder repair	1	2.2%
Bowel repair	1	2.2%

Hysterectomy was performed in 2 of the 46 cases of relaparotomy. Hypogastric artery ligation was performed in 18 patients (39.1%). In 8 patients (17.3%), aspiration and irrigation were performed after peritoneal hematoma drainage (Table 2). No active bleeding site was observed in these cases, and no additional surgical procedures were performed.

Relaparotomy after cesarean section was most frequently performed within the first 24 hours (Table 3). The most common indications within the first 24 hours were postpartum hemorrhage due to peritoneal bleeding and atony. The median number of erythrocyte suspension units transfused was 4 (0–14). Similarly, fresh frozen plasma was administered with a median of 4 units (0–13). Cryoprecip-

Table 3. Timing of relaparotomy after cesarean section

	n=46	Ratio
In the first 24 hours		
Postpartum hemorrhage	15	32.6%
Peritoneal bleeding	14	30.4%
1st to 10th day		
Rectus hematoma	5	10.8%
Postpartum hemorrhage	4	8.7%
Pelvic abscess	2	4.3%
Peritoneal bleeding	1	2.2%
Ileus	1	2.2%
>10th day		
Pelvic abscess	2	4.3%
Evisceration	1	2.2%
Bladder injury	1	2.2%

itate and random platelet transfusions had medians of 1 unit each (0–5/0–16). Fibrinogen was given with a median dose of 2 grams (0–13). No maternal mortality was observed after relaparotomy.

DISCUSSION

This study analyzed patients who underwent relaparotomy after cesarean section. Most cases of relaparotomy after cesarean section were associated with previous lower segment cesarean section or severe preeclampsia-HELLP syndrome. The majority of relaparotomy cases were caused by uterine atony or intraperitoneal bleeding.

Previous studies reported the incidence of relaparotomy after cesarean section to be 0.07–0.72%.[7,10,11] In our study, we found an incidence of 0.18%, consistent with the literature. The most common indication for cesarean section before relaparotomy was a history of previous cesarean section, similar to other studies.[11-13] The most common causes of relaparotomy were atony and intraperitoneal bleeding.

The literature indicates that factors such as surgeon experience, duration of operation, type of anesthesia, complications during cesarean section, high postoperative pulse rate, and cesarean section performed outside working hours are risk factors for relaparotomy.[4,11,14-16] These factors explain the variation in relaparotomy rates between hospitals.

Although some clinics do not report maternal mortality in post-cesarean relaparotomy cases, other studies report maternal mortality rates as high as 9–25%. No maternal mortality was observed in our study group. We believe that differences in case numbers, cesarean section rates, surgical experience, hospital characteristics (such as blood bank and surgical equipment), and rapid intervention in cases contribute to these differences.

The incidence of hysterectomy in relaparotomy also varies widely among clinics. Our hysterectomy rate was 4.3%, lower than reported in some other studies. In the 2017 study by Elkhateeb et al.,[16] the rate of hysterectomy during relaparotomy was observed to be the highest at 46.9%. In two other studies conducted in 2013 and 2020, the rate of hysterectomy during relaparotomy was similarly reported as 26% and 26.1%, respectively.[11,17] The rate closest to our study and the lowest reported in the literature was observed in the 2021 study by Weissmann-Brenner et al.[18] at 6.3%.

Studies have shown that emergency indications for cesarean delivery are significant factors contributing to relaparotomy.[17] Emergency cesarean delivery has higher morbidity and mortality rates than elective cesarean delivery.[19] In our study group, 60.8% of relaparotomy cases occurred after emergency cesarean delivery.

The study has some limitations, including its retrospective nature and the lack of concrete data on the amount of bleeding during cesarean section and the difference in the doctors performing the cesarean section. However, the strength of the study lies in the large number of cases and the management of these cases in a tertiary clinic by an experienced multidisciplinary team.

Conclusion

Post-cesarean relaparotomy is becoming increasingly important due to the rising number of cesarean sections. The most common reasons for relaparotomy are uterine atony and intraperitoneal bleeding. Most relaparotomies are performed within the first 24 hours after cesarean section. The complication rate increases as the interval between cesarean section and relaparotomy increases.

We believe that increased surgical experience, close monitoring of vital signs, and careful observation of vaginal bleeding in the first 24 hours will allow early intervention and reduce maternal mortality and morbidity.

Ethics Committee Approval

The study was approved by the Zeynep Kamil Gynecology and Pediatrics Training and Research Hospital Ethics Committee (Date: 22.09.2021, Decision No: 160).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: A.Ö.; Design: A.B.A.D., A.Ö.; Supervision: A.Ö., A.E.; Fundings: A.B.A.D., A.E.; Materials: A.B.A.D., A.E.; Data collection &/or processing: A.B.A.D.; Analysis and/or interpretation: A.Ö.; Literature search: A.Ö., A.B.A.D.; Writing: A.Ö.; Critical review: A.B.A.D.

Conflict of Interest

None declared.

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Sezaryen Sonrası Relaparotomi: Tersiyer Merkez Deneyimi

Amaç: Sezaryen sonrası relaparotomilerin risk faktörlerini, meydana gelen morbiditeleri ve işlem sırasında uygulanan yöntemleri inceleyerek literatüre katkıda bulunmayı amaçladık.

Gereç ve Yöntem: Bu retrospektif çalışma; Ocak 2014 ile Ocak 2021 tarihleri arasında bir eğitim ve araştırma hastanesinde gerçekleştirilen sezaryen sonrası relaparotomi vakalarını içermektedir. Bu 7 yıllık dönem içinde sezaryen sonrası 60 gün içinde relaparotomi olan tüm vakalar çalışmaya dahil edildi. Vakalar sezaryen sonrası relaparotomi zamanlaması açısından üç gruba ayrıldı; ilk 24 saat içinde, 1. gün ile 10. gün arasında ve 10. günden sonra.

Bulgular: Hastanemizde toplamda 24,293 sezaryen gerçekleştirildi. Sezaryen sonrası relaparotomi oranı kliniğimizde %0.18 olarak kaydedildi. Acil sezaryenler, çalışma grubumuzun %60.8'ini oluşturdu. Relaparotomi için en sık endikasyon, %41.3 ile uterin atoniye bağlı postpartum kanamaydı. Uterin atoniyi %28.2 ile intraperitoneal kanama takip etti. Hipogastrik arter ligasyonu, hastaların %39.1'inde uygulandı. Sezaryen sonrası relaparotomi, çoğunlukla ilk 24 saatte gerçekleştirildi. Relaparotomi sonrası maternal mortalite gözlemlenmedi.

Sonuç: Sezaryen sayısının artması sonucu sezaryen sonrası relaparotomi giderek daha önemli hale gelmektedir. Relaparotominin en yaygın nedenleri uterin atoni ve intraperitoneal kanamadır. Çoğu relaparotomi, sezaryen sonrası ilk 24 saat içinde gerçekleştirilir. Sezaryen ile relaparotomi arasındaki süre arttıkça komplikasyon oranı da artmaktadır.

Anahtar Sözcükler: Hipogastrik arter; intraperitoneal kanama; relaparotomi; sezaryen; uterin atoni.

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Original Article

Comparison of Benign and Malignant Lesions in NOSES After Laparoscopic Colorectal Surgery: A Prospective Study

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Keywords: Benign colorectal tumors; Laparoscopic colorectal surgery; Malignant colorectal tumors; Minimally invasive surgery; Natural orifice specimen extraction surgery.

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ABSTRACT

Objective: Natural orifice specimen extraction surgery (NOSES) is defined as the removal of the specimen through natural orifices following laparoscopic colorectal surgery, and it is an important component of minimally invasive surgery. This study aims to compare the extraction of resected malignant and benign lesions through natural orifices after laparoscopic colorectal surgery.

Methods: Among 45 patients undergoing laparoscopic colorectal resection with planned NOSES between January 2019 and March 2020, 36 patients underwent NOSES. Transanal and transvaginal routes were utilized for extraction following laparoscopic resection. The transvaginal route was used in gynecologic cases and if there was a hysterectomy. Patients were divided into two groups based on the diagnosis of malignant or benign lesions. Demographic characteristics, perioperative and postoperative findings, as well as pathology and specimen sizes, were examined.

Results: Lesion localization was predominantly in the rectosigmoid region in the malignant group and in the rectum in the benign group. There was a statistically significant difference between the groups ($p<0.05$). The maximum specimen size was higher in the malignant group ($p>0.05$), whereas the maximum lesion size was larger in the benign group ($p<0.05$). Mesenteric dissection distribution was higher in the malignant group ($p<0.05$). There were significant differences between the patient groups in terms of specimen extraction site distribution and anvil localization ($p<0.05$). Transanal extraction and extracorporeal anastomosis were more common in the malignant group, whereas transvaginal extraction and intracorporeal anastomosis were more common in the benign group.

Conclusion: NOSES can be safely performed for both malignant and benign colorectal lesions. Despite larger lesion sizes in benign lesions in comparison to malignant ones, specimen sizes are smaller. Therefore, they are easier to extract through natural orifices after laparoscopic resection. Moreover, benign lesions can be dismembered into smaller sizes for extraction, in contrast with the case for malignant lesions.

INTRODUCTION

For approximately 40 years, laparoscopic colorectal surgery has been proven to be superior to conventional techniques.[1,2] The most significant disadvantage of laparoscopic surgery and the part responsible for complications is the mini-laparotomy incision for specimen extraction.[3] There has been a need for a minimally invasive approach to optimize surgical outcomes and improve recovery. However, this generally entails a long learning curve since it might necessitate intracorporeal anastomosis. The pinnacle of minimally invasive surgery is the natural orifice specimen extraction surgery (NOSES).[1,4] Thus, NOSES provides less pain, faster recovery, shorter hospitalization time, better cosmetic results, and lower risk of incisional hernia.[5,6] After laparoscopic colorectal surgery, specimen extraction can be done in two ways depending on the extraction site: transanal and transvaginal. Transanal extraction can be further classified based on the extraction site, such as transcolonic, transrectal, and transanal. Transcolonic extraction is rarely performed. Transcolonic extraction, which involves extracting the specimen from the colon by making use of colonoscopy after ileocolic resection, is controversial in terms of its feasibility.[7,8] Transanal and transrectal extraction are more commonly performed.[9] Transvaginal extraction is a route used only

in female patients.[10,11] Although there are studies in the literature examining the advantages and disadvantages of the NOSES method for malignant colorectal cancer cases, there is no clinical study comparing malignant and benign cases.[12,13] This study was conducted to compare transvaginal and transanal extractions of benign and malignant colorectal lesions. Therefore, it may be a useful study in terms of contributing to the literature.

MATERIALS AND METHODS

This study was conducted as a prospective clinical study in the general surgery clinic of a tertiary university hospital between January 2019 and March 2020. Approval was obtained from the hospital's medical ethics committee (Ethics committee approval number; 2019/514/146/2-28.01.2020). Informed consent was obtained from the patients before surgery. The study was conducted in accordance with the declaration of Helsinki. The type of pathology, specimen size, tumor stage (excluding metastasis), history of previous surgery, segment of resection, patient's gender, and body mass index were not considered. Patients under 18 years of age, those with metastases, those who did not consent, and those with virginity and anal-vaginal anomalies were excluded from the study. Laparoscopic colorectal resections were performed using established standard methods. In malignant lesions, the meso was partially dissected parallel to vascular structures with sealing devices to facilitate extraction without compromising vascular integrity before removing large-volume specimens. Patients were operated under general anesthesia in the modified Lloyd-Davies position. The transanal and transvaginal extraction sites were cleansed with povidone-iodine solution. Laparoscopic colorectal resections were performed using standard, well-established techniques. Transanal route was the first choice for specimen extraction after laparoscopic resection, and if unsuccessful, transvaginal route was attempted in female patients. If both were unsuccessful, the specimen was extracted through an abdominal wall incision. Patients were divided into two groups, malignant and benign, based on the diagnosis. In the comparison of anvil localization of both groups; in the malignant group, 12 anvils were placed extracorporeally, 10 anvils were placed intracorporeally, and the lesions of these 10 patients were located in the rectum and their anastomoses were at a lower level. In the comparison of anvil localization of both groups; in the benign group, 12 had anvil extracorporeal and in 3 had anvil intracorporeal, the lesions of these 11 patients were rectal and their anastomoses were at a lower level. The increase in intracorporeal placement of anvil in the benign group is due to the diagnosis of endometriosis. Demographic data, body mass index (BMI), American Society of Anesthesiologists Association (ASA) score, accompanying comorbidities, previous abdominal surgery, diagnosis, tumor location, type of operation, type of colectomy, number of trocars, additional organ resection, method of specimen extraction, method of anvil placement, operation time, blood loss, type of anastomosis, postoperative day 1 visual analog pain score (VAS), time to oral intake, length of hospital stay, complications, and pathology report (type, specimen size, length of lesion) of the patients were analyzed. In the pathological evaluation of the groups, the type of lesion, the maximum diameter of the specimen (including the entire resected pathological lesion and the specimen), and the maximum diameter of the lesion itself (measuring only the pathological lesion within the resected specimen) were examined. Patients diagnosed with rectal prolapse in the benign group were excluded from the statistical analysis due to the absence of a measurable lesion diameter. A total of 45 patients, for whom NOSES was planned after laparoscopic colorectal resection, were involved in this study (Fig. 1). Conversion was performed in seven patients for various reasons (ureteral invasion, proximal colon ischemia, inability to locate tumor in sigmoid colon, inability to determine distal part of tumor, and advanced local tumor in three patients). Moreover, two patients were not suitable for NOSES due to the short length of the distal rectum. Conventional laparoscopic colectomy followed by specimen extraction through a suprapubic incision was performed in these patients. The analysis was conducted on the data obtained from 36 successful NOSES cases. Of the malignant group, 11 had rectosigmoid tumors, 9 had sigmoid colon tumors, one had a rectum tumor, and one had a right colon tumor. In the benign group, 7 patients were rectal and 3 were resections due to endometriosis and rectal prolapse. Of the other patients in this group, one had a polyp located in the splenic flexure and three had diverticulosis located in the sigmoid colon.

Statistical Method

Nominal and ordinal data were analyzed using frequency analysis, while scale parameters were defined using means and standard deviations. Differences between nominal and ordinal parameters were analyzed using the Chi-square test and Chi-square similarity ratios. The Kolmogorov-Smirnov test was used for testing the normal distribution of scale parameters. Independent Samples T-test was utilized for normally distributed parameters, whereas the Mann-Whitney U test was used for non-normally distributed parameters. All analyses were conducted using SPSS 17.0 software with a significance level of 0.05 and a confidence interval of 95%. Software program used for statistical analysis was IBM Corp (2017). IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.).

RESULTS

Over a fourteen-month period, 45 patients were evaluated and 36 patients were involved in this study. Some demographic and clinical characteristics of the patient groups are shown in Table 1. The mean age was higher in the malignant group, but the BMI was higher in the benign group. The age difference was significant ($p<0.05$), whereas the difference in BMI values was not statistically significant ($p>0.05$). Gender and ASA class differences between patient groups

Table 1. Demographic and clinical characteristics of patient groups

	Malign (n=22)	Benign (n=14)	p
Age, mean±SD	60.86±9.28	53.00±13.17	0.043[a]
Gender, n (%)			
Female	9 (40.9)	13 (92.9)	0.002[b]
Male	13 (59.1)	1 (7.1)	
BMI, mean±SD	27.73±5.69	28.73±5.29	0.600[a]
ASA Score, n (%)			
1	2 (9.1)	1 (7.1)	0.032[c]
2	14 (63.6)	13 (92.9)	
3	6 (27.3)	-	
HT, n(%)	9 (40.9)	3 (21.4)	0.219[c]
DM, n(%)	8 (36.4)	2 (14.3)	0.137[c]
COPD, n(%)	1 (4.5)	-	0.317[c]
Other comorbidity, n (%)	2 (9.1)	3 (21.4)	0.303[c]
Abdominal Surgery, n (%)	6 (27.3)	8 (57.1)	0.073[b]

[a]Independent Samples T-test, [b]Chi-Square, [c]Chi-Square Likelihood Ratio. SD: Standard Deviation. BMI: Body Mass Index; ASA: American Society of Anesthesiologists; HT: Hypertension; DM: Diabetes Mellitus. COPD: Chronic Obstructive Pulmonary Disease.

Table 2. Analysis results and comparison between patient groups in terms of specimen and operative technical parameter differences

	Malign (n=22)	Benign (n=14)	p
Lesion localization, n (%)			
Sigmoid colon	9 (40.9)	3 (21.4)	0.000[a]
Rectum	1 (4.5)	10 (71.4)	
Rectosigmoid	11 (50.0)	-	
Right colon	1 (4.5)	-	
Splenic flexure case	-	1 (7.1)	
Max specimen dimension, mean±SD	14.67±14.10	12.21±5.07	0.860[b]
Max lesion dimension, mean±SD	3.05±1.51	6.67±3.78	0.005[c]
Number of trocars, mean±SD	4.14±0.35	4.28±0.47	0.470[b]
Mesentery dissection, n (%)	22 (100.0)	4 (28.6)	0.000[a]
Organ resection, n (%)			
No	20 (90.9)	10 (71.4)	0.131[a]
Yes	2 (9.1)	4 (28.6)	
Specimen extraction, n (%)			
Transanal	20 (90.9)	6 (42.9)	0.002[a]
Transvaginal	2 (9.1)	8 (57.1)	
Anastomosis type, n (%)			
Circular staplers	20 (91.0)	13 (92.9)	0.580[a]
Linear staplers	1 (4.5)	1 (7.1)	
Coloanal	1 (4.5)	-	
Anvil localization, n (%)			
Extracorporeal	12 (54.5)	3 (21.4)	0.049[d]

[a]Chi-Square Likelihood Ratio, [b]Mann Whitney U Test, [c]Independent Samples T-Test, [d]Chi-Square. SD: Standard Deviation.

were also found to be statistically significant ($p<0.05$). The difference in comorbidity distribution between patient groups was not statistically significant ($p>0.05$). Differences in specimen and operative technical parameters between patient groups and the analysis results are shown in Table 2. Lesion localization was predominantly in the rectosigmoid in the malignant group and in the rectum due to endometriosis in the benign group, and the difference

Table 3. Perioperative and postoperative characteristics of patients and difference analysis results

	Malign (n=22)	Benign (n=14)	p
Operation duration (min), mean±SD	171.59±42.85	190.00±33.97	0.184[a]
Blood loss (ml), mean±SD	49.54±26.99	39.28±19.40	0.311[b]
Oral intake (day), mean±SD	1.86±0.56	1.43±0.65	0.049[b]
Postop VAS, mean±SD	2.18±1.62	2.14±1.23	0.835[b]
Drain duration (day), mean±SD	4.73±0.88	4.57±1.02	0.629[a]
Hospitalization duration (day), mean±SD	4.86±0.94	5.21±1.19	0.511[b]
Perop complications, n (%)			
None	19 (86.4)	14 (100.0)	0.209[c]
Trocar site bleeding	1 (4.5)	-	
Colon injury	2 (9.1)	-	
Post complications, n (%)			
None	17 (77.3)	12 (85.7)	0.186[c]
Trocar site hernia	1 (4.5)	-	
Bleeding	2 (9.1)	-	
Atelectasis	1 (4.5)	-	
Rectovaginal fistula	1 (4.5)	-	
Ileus	-	1 (7.1)	
Bleeding + Trocar site hernia + Rectovaginal fistula	-	1 (7.1)	

[a]Independent Samples T-test, [b]Mann Whitney U Test, [c]Chi-Square Likelihood Ratio. SD: Standard Deviation; VAS: Visual Analogue Scale.

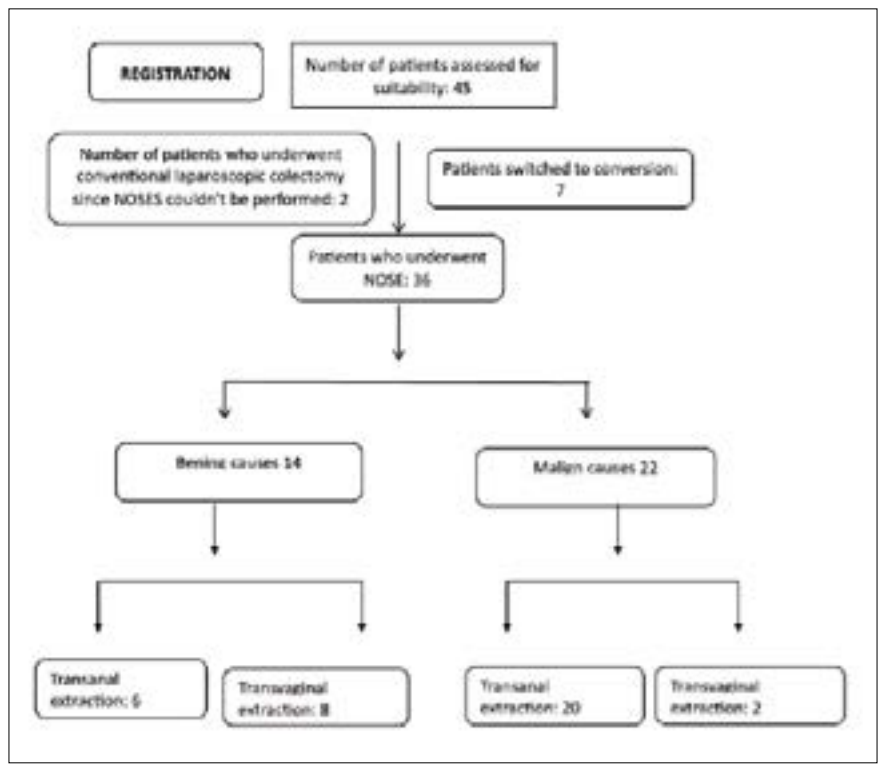

Figure 1. Flow Chart.

in lesion localization between groups was statistically significant (p<0.05). The maximum specimen size was larger in the malignant group (p>0.05), and the maximum lesion size was higher in the benign group (p<0.05). Mesenteric dissection distribution was higher in the malignant group (p<0.05). The distribution of sample extraction site and

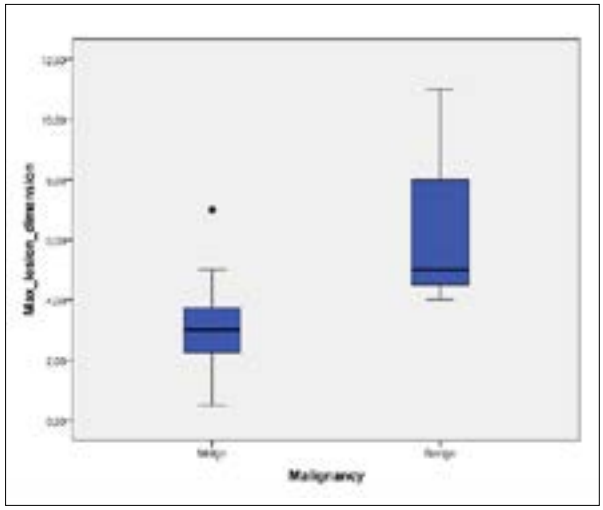

Figure 2. Evaluation of malignant and benign lesions by lesion diameter.

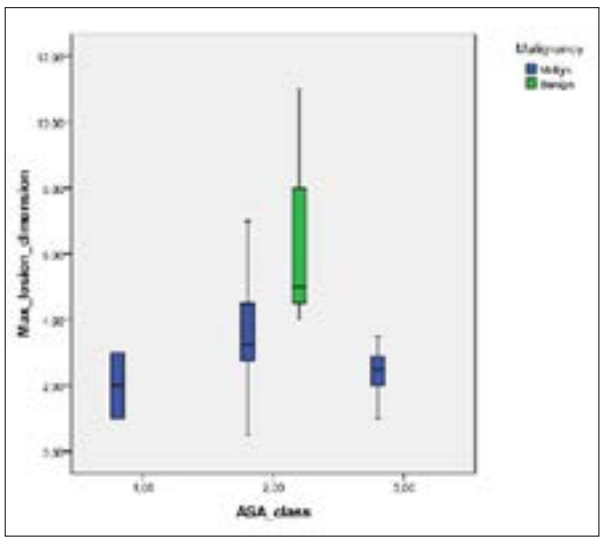

Figure 3. Comparison of maximum lesion diameter with ASA class.

anvil localization was also significantly different between patient groups ($p<0.05$). The transanal and extracorporeal regions were more common in the malignant group, while the transvaginal and intracorporeal regions were more common in the benign group. The preoperative and postoperative characteristics of patients and the results of the difference analysis are provided in Table 3. As seen in Table 3, only the oral fluid intake time was significantly higher in the malignant patient group ($p<0.05$). On the other hand, the operation time, level of blood loss, postoperative VAS, drainage removal, hospital stay, perioperative, and postoperative complications did not show statistically significant differences between groups ($p>0.05$). The average lesion was lower in the malignant group and higher in the benign group, and the range of variation was higher in the benign group (Fig. 2). The largest lesion size was observed in benign cases with the ASA score of 2, and the range of variation was also higher in ASA 2 when compared to other classes, indicating more diverse values (Figs 3, 4).

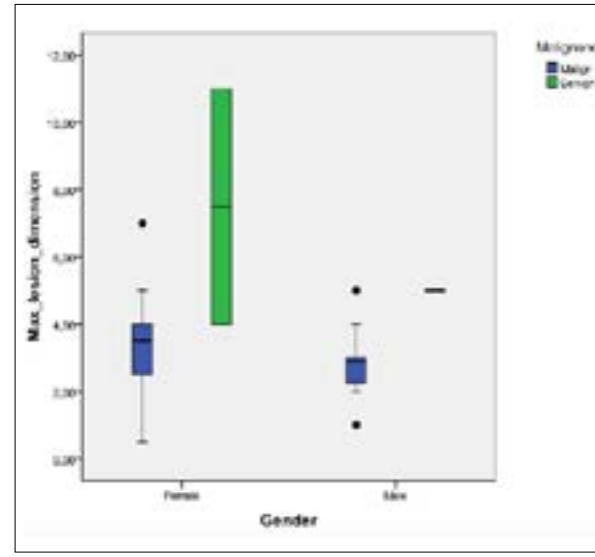

Figure 4. Comparison of maximum lesion diameter with gender.

DISCUSSION

The rate of colorectal diseases treated with laparoscopic surgery is increasing.[14] Laparoscopic colorectal surgery is undoubtedly superior to open surgery.[15] Upon determining the advantages of laparoscopic colorectal surgery, minimally invasive surgery came to the forefront to take these advantages further. Natural orifice specimen extraction surgery was developed to minimize surgical trauma and enhance recovery after laparoscopic surgery. Many studies confirmed that the anus is the most ideal orifice, particularly in left-sided colorectal surgery, in line with minimally invasive surgery.[16] In colorectal surgery, natural orifice specimen extraction can be categorized into two categories: transanal and transvaginal routes.[17,18] The vagina may be an ideal alternative to transanal extraction due to reasons such as sufficient flexibility and blood flow, healing capacity, and easy access.[19,20] Transvaginal specimen extraction was first used in gallbladder removal and later in the extraction of colon, kidney, and spleen samples.[21] After Franklin et al.[13] published the NOSES study, many studies were published in the last 20 years on this subject. However, there is no study comparing benign and malignant colorectal lesions. Differing from the other studies, the present study was carried out to evaluate the transanal and transvaginal extraction of colorectal benign and malignant lesions. Transvaginal extraction is less common today than transanal extraction due to the need for incision for specimen extraction from this healthy organ, and it is only applicable to female patients.[11] Transcolonic specimen extraction is performed through colonoscopy, mostly after right-sided or proximal segmental colon resections, and there are two studies in the literature on this subject.[22,23] Its practical applicability is debated. In-

deed, no transcolonic extraction was performed in this study. Transrectal NOSES can be applied in both sexes. It is a suitable option for the extraction of specimens in benign and left-sided malignant tumors such as diverticulitis, adenoma, and endometriosis, and for colorectal anastomosis.[1] In this study, transanal extraction was applied to 6 patients and transvaginal extraction to 8 patients for benign reasons, whereas transanal extraction was applied to 20 patients and transvaginal extraction to 2 patients for malignant reasons. Transvaginal extraction was more common for benign reasons due to gynecological lesions, while transanal extraction was more common for malignant lesions. The advantage of transvaginal NOSES is that it allows the extraction of larger lesions that cannot be extracted transanally in both right and left colon resections. However, this approach can only be applied to female patients. In the present study, the first choice for colorectal specimen extraction was transanal extraction. However, in cases where this was not possible, the second choice was transvaginal extraction. The size of benign lesions is one of the challenging situations for the NOSES method. Especially, the length of the segment resected in rectal prolapse and diverticular disease pose difficulties in creating a safe anastomosis. However, one of the advantages of benign cases is that the specimen can be divided without oncological concerns during the extraction of a large specimen. Nevertheless, in malignant cases, specimen division may pose risks of oncological consequences. Studies have shown that lesions smaller than 3 cm can be easily removed transanally, while those larger than 3 cm present challenges. Tumor size is a significant factor affecting the success of transanal NOSES procedures. Specimens up to 5 cm in size can be easily removed transvaginally,[9] but this technique is applicable only in female patients. In this study, the mean lesion size for benign tumors was 6.67 cm, while it was 3.05 cm for malignant tumors. As expected, the maximum specimen size was larger in the malignant group, but the maximum lesion size was higher in the benign group. Another concern in malignant diseases treated with the NOSES technique is whether oncological principles are compromised. Protective devices are placed in the orifices before specimen extraction in both transanal and transvaginal methods to prevent tissue and tumor contact. If the lesion size or specimen size is not suitable for extraction through the orifices, or if there is a risk of tumor perforation, then the conventional laparoscopic method is switched to, and specimen extraction is achieved through a suprapubic mini-incision. Gynecologists may have difficulty closing posterior colpotomy wounds.[24] If difficulties are encountered during the procedure, the vaginal incision may be left open. However, all posterior colpotomy incisions were closed in this study. In cases where closure was challenging, intracorporeal suturing was performed.

The average operation time was reported to be 229 minutes by Awad et al.[25] and 212 minutes by McKenzie et al.[26] Park et al.[27] reported the operation time to be 171 minutes and Franklin et al.[13] reported it to be 159 minutes. In this study, the mean duration was 171 minutes for malignant lesions and 190 minutes for benign lesions. NOSES surgery is performed after a long learning curve, and the operation time in this study was comparable to those reported by other authors. Transanal NOSES colectomy was significantly associated with shorter operation times when compared to conventional laparoscopic colectomy.[28] The major limitation of this study is that transvaginal extraction can only be performed in female patients, resulting in heterogeneous extraction sites for both benign and malignant lesions. Another limitation is the difficulty in removing large malignant tumors. Other findings may vary relative to these limitations. Additionally, we plan to publish the long-term oncological outcomes of our study with larger series in the future.

Conclusion

NOSES, which has a long learning curve, can be safely performed following a suitable malignant and benign colorectal surgery. Benign lesions are more advantageous than malignant lesions due to both ease of manipulation and specimen size. Numerous prospective studies are needed to compare the differences.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 28.01.2020, Decision No: 2019/514/146/2).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Y.E.A., İ.E.; Design: Y.E.A., O.A.; Supervision: Y.E.A., İ.E.; Fundings: O.A., İ.E.; Materials: Y.E.A., O.A.; Data collection &/or processing: İ.E., O.A.; Analysis and/or interpretation: O.A.; Literature search: Y.E.A.; Writing: İ.E.; Critical review: Y.E.A., İ.E.

Conflict of Interest

None declared.

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Laparoskopik Kolorektal Cerrahi Sonrası NOSES'de Benign ve Malign Lezyonların Karşılaştırılması; Bir Prospektif Çalışma

Amaç: Laparoskopik kolorektal cerrahi sonrası spesmenin doğal deliklerden çıkarılması natürel orifis spesmen ekstraksiyonu cerrahisi (NOSES) olarak adlandırılmakta olup, bu işlem minimal invaziv cerrahinin önemli bileşenidir. Çalışma, laparoskopik kolorektal cerrahi sonrası rezeke edilen malign ve benign lezyonların doğal deliklerden çıkarılmasını karşılaştırma amacı ile yapılmıştır.

Gereç ve Yöntem: Ocak 2019 ile Mart 2020 tarihleri arasında kliniğimizde laparoskopik kolorektal rezeksiyon sonrası NOSES planlanan 45 hastadan 36 hastaya NOSES yapıldı. Laparoskopik rezeksiyondan sonra ekstraksiyon için jinekolojik kaynaklı değilse öncelikle transanal yol denendi. Jinekolojik kaynaklı ve histerektomi yapılmışsa öncelikle transvajinal yol denendi. Hastalar, çıkarılan materyallerin benign ve malign lezyonlar olmasına göre iki gruba ayrıldı. Hastaların demografik bulgularına, peroperatif ve postoperatif bulgularına, patoloji ve spesmen boyutlarına bakıldı.

Bulgular: Lezyon lokalizasyonu malign grupta rektosigmoid, benign grupta rektum çoğunluktaydı ve lezyon lokalizasyonu gruplar arasında istatistiksel olarak anlamlı derecede farklıydı ($p<0.05$). Maksimum spesmen boyutu malign grupta daha yüksekti ($p>0.05$) ve maksimum lezyon boyutu benign grupta daha yüksekti ($p<0.05$). Mezenter diseksiyonu dağılımı malign grupta daha yüksekti ($p<0.05$). Spesmen ekstraksiyon yeri dağılımı ve anvil lokalizasyonuna göre de gruplar arasında anlamlı farklılık vardı ($p<0.05$). Transanal ekstraksiyon ve ekstrakorporeal anastomoz malign grupta, transvajinal ekstraksiyon ve intrakorporeal anastomoz benign grupta daha yaygındı.

Sonuç: Uygun olan malign ve benign kolorektal lezyonlarda NOSES güvenle yapılabilir. Benign lezyonlar her ne kadar lezyon boyutu bakımından malign lezyonlardan büyük olsa da spesmen boyutu olarak malign lezyonlardan daha küçüktür. Bu nedenle laparoskopik rezeksiyon sonrası doğal deliklerden çıkarılmaları daha kolaydır. Ayrıca benign lezyonlar, malign lezyonların aksine daha küçük boyutlara bölünerek çıkarılabilir.

Anahtar Sözcükler: Benign kolorektal tümörler; laparoskopik kolorektal cerrahi; malign kolorektal tümörler; minimal invaziv cerrahi; doğal orifis yoluyla örnek çıkarma cerrahisi.

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Original Article

Evaluating Long-Term Survival Determinants in Bronchopulmonary Carcinoids Following Anatomical Resection: A Retrospective Analysis

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Keywords: Carcinoid Tumor; Lobectomy; Thoracic Surgery; Video-Assisted.

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ABSTRACT

Objective: Bronchopulmonary carcinoid tumors (BCTs) are a rare type of lung cancer (1–2%). They are divided into two subtypes: typical (TK) and atypical (AK). Prognosis depends on various factors such as tumor type, size, spread, and Ki-67 (cell proliferation marker). This study aimed to identify these prognostic factors to improve treatment and survival rates in BCT patients. The main objective of this research was to retrospectively investigate the factors associated with long-term survival in patients with bronchopulmonary carcinoid tumors.

Methods: The data of 56 patients who underwent surgery at our center between February 2008 and March 2021 and were histopathologically diagnosed with bronchopulmonary carcinoid tumor were retrospectively analyzed.

Results: Most of the patients were female (60.7%) with a median age of 43. Lobectomy was the most common surgical procedure (60.7%). Prolonged air leak was the most common complication. Typical carcinoids were more common than atypical ones (69.6%–30.4%). Mediastinal lymph node metastasis was more common in atypical tumors. The findings of the study showed that tumor stage, lymph node metastasis, and Ki-67 index were prognostic factors associated with long-term prognosis in patients with bronchopulmonary carcinoid tumors. The 5-year survival rate was higher in typical carcinoids than in atypical ones (82.1%–64.7%). The recurrence rate was higher in atypical tumors (25%–2.4%).

Conclusion: These findings highlight the critical role of tumor characteristics in determining long-term outcomes in patients with bronchopulmonary carcinoid tumors. Considering factors such as tumor type, lymph node involvement, stage, and Ki-67 index, more personalized treatment strategies can be developed. Further research involving larger, multicenter patient groups may provide more robust data to improve prognostic models for this patient population and guide treatment decisions.

INTRODUCTION

Bronchopulmonary carcinoid neoplasms (BCNs) are a distinct category of lung cancers characterized by neuroendocrine features. While uncommon, they represent approximately 1% to 2% of all diagnosed lung carcinomas.[1,2] The initial histological description of a carcinoid tumor is credited to Theodor Langhans in 1867.[3] However, the first clinical cases documented were two patients with ileal carcinoid tumors discovered during autopsy by Otto Lubarsch in 1888.[4,5]

The incidence of BCNs has exhibited a significant rise over the past three decades.[6,7] This increase might not necessarily reflect a true surge in their prevalence but could be attributed to advancements in diagnostic techniques. The use of low-dose CT (Computerized Tomography) scans for lung cancer screening programs has likely played a role in identifying more incidental BCNs at an earlier stage.[8]

The 2015 IASLC classification system, established by Lee et al.,[9] categorizes BCNs into two main subtypes: typical carcinoid (TC) and atypical carcinoid (AC). TCs, constituting roughly 90% of all lung carcinoids, are generally indolent tumors with a slow growth rate and a favorable

prognosis.[10] They are typically associated with lower rates of metastasis and longer disease-free survival compared to Acs.[11] ACs, on the other hand, demonstrate a more aggressive biological behavior, exhibiting a higher propensity for local recurrence and distant metastasis.[12]

The cornerstone of treatment for patients with operable BCNs remains surgical resection.[13] Anatomical surgical resection, which aims to remove the entire tumor along with surrounding lymph nodes, offers the best chance for cure, particularly for patients with TC.[14] However, the prognosis for BCNs can vary depending on several factors. These factors can be broadly categorized into tumor-related characteristics, patient-related characteristics, and treatment-related factors. Tumor-related characteristics include histological subtype (TC vs. AC), tumor size, presence of lymph node involvement (stage), and markers of cell proliferation (Ki-67 index). Patient-related characteristics encompass age, gender, and underlying comorbidities. Treatment-related factors primarily focus on the extent of surgical resection (complete vs. incomplete) and the use of adjuvant therapies such as somatostatin analogs for patients with advanced or metastatic disease.

This study aims to investigate the prognostic factors that influence outcomes in patients undergoing anatomical lung resection for bronchial carcinoid tumors. By identifying these factors, we can potentially refine treatment strategies and improve patient survival rates. Understanding the interplay between these various factors will allow for a more personalized approach to BCN management, optimizing treatment efficacy and maximizing patient outcomes.

MATERIALS AND METHODS

The study included all patients with histologically confirmed typical and atypical carcinoid tumors who underwent anatomical surgical resection at the Department of Istanbul University Istanbul School of Medicine Thoracic Surgery from February 2008 to March 2021. Patient informed consent was not required due to retrospective data analysis. This study was conducted in accordance with the Declaration of Helsinki and approved by the Istanbul University Istanbul School of Medicine Clinical Trials Ethical Board (2023/707).

It is based on demographic data (such as age at diagnosis, gender, race, marital status, life expectancy, and duration), tumor characteristics (site of onset, laterality, histological grade, histological type, primary tumor size, T, N, and M stage), Ki-67 index, and clinical data (surgery, radiology, and chemotherapy). Additional evaluations included medical history review, physical examination, blood hematology and biochemistry, respiratory function test, chest x-ray, and contrast-enhanced tomography (CT) of the chest and abdomen. Further evaluation of the disease included 2-deoxy-2-(18F) fluoro-D-glucose (FDG) positron emission tomography (PET)/CT and fiberoptic bronchoscopy (requires biopsy).

The main outcomes of this study were cancer-specific survival (CSS), time to cancer diagnosis, and incidence of cancer death. The Cox proportional hazards regression model was used to identify independent predictors of survival by calculating relative hazards and associated 95% confidence intervals. Variables found to be significant ($p<0.05$) in univariate Cox regression analysis were included in multivariate Cox regression analysis. Kaplan-Meier curves and logistic regression were used to compare and contrast the CSS of patients in different groups. The accuracy of survival prediction was also evaluated using the area under the receiver operating characteristic (ROC) curve. Two-sided $p<0.05$ indicates statistical significance.

This study was conducted with the ethical approval of the Istanbul University Istanbul School of Medicine Ethics Committee (approval number: 1737659, date: April 28, 2023). This ensures that the research adhered to ethical guidelines and participant safety was prioritized throughout the study. This approval process included the review and participant consent for all procedures involved in the study.

RESULTS

A total of 56 patients were included in the study, with a median age of 43 (range 15–57) years. There were 34 (60.7%) females and 22 (39.3%) males. Among them, lobectomy was performed in 34 (60.7%) patients, sleeve lobectomy in 10 (17.9%) patients, segmentectomy in 5 (8.9%) patients, and bi-lobectomy in 6 (10.7%) patients. The median hospital stay for all patients was 7±1.3 days. The most common complication affecting all patients was prolonged air leak, diagnosed in 8 patients. One patient who underwent sleeve right upper lobectomy required pneumonectomy afterward due to total atelectasis in the early postoperative period. Patients with any type of complications had a significantly longer duration of hospital stay, with a median of 18 days compared to 6.3 days for patients without complications ($p=0.001$). No 90-day mortality was observed.

Of the cases included in the study, 39 (69.6%) were typical carcinoid tumors and 17 (30.4%) were atypical carcinoid tumors. Although females tended to have typical carcinoid tumors more frequently, this difference was not statistically significant ($p=0.68$). Similarly, patients with atypical carcinoids tended to be younger, but this was also not significant ($p=0.06$). Among the typical carcinoid tumors, 3 (7.7%) had nodal invasion, while among the atypical carcinoid tumors, 3 (17.7%) had nodal invasion. One patient with an atypical carcinoid presented with subcarinal lymph node metastasis.

In terms of TNM 8 staging, 35 (62.5%) patients were staged for T stage as T1a, 7 (12.5%) as T1b, 5 (8.9%) as T2a, 4 (7.1%) as T2b, and 5 (8.9%) as T3a. The median Ki-67 index was 3.23% for typical carcinoids and 7.76% for atypical carcinoids ($p=0.002$). Compared to other patients, stage IA patients had lower Ki-67 values ($p=0.033$),

less necrosis (p=0.016), a significantly lower rate of mitosis (p=0.004), and were more likely to have typical carcinoid tumors (p=0.007).

The median follow-up period was 87 months. Median follow-up for typical and atypical carcinoid tumors was 102 and 70 months, respectively. Table 1 summarizes patient characteristics and prognostic factors. The 5-year survival rates for typical and atypical carcinoid tumors were 82.1% and 64.7% (p=0.02). Also, early postoperative complications (p=0.905), tumor necrosis (p=0.9), significant mitosis presence (p=0.981), and gender (p=0.206) showed no survival difference. The 5-year survival rates were significantly different for tumor status (T) (p=0.001), lymph node status (N) (p=0.005), and pathologic tumor-node-metastasis (TNM) stage (p=0.0001). Overall survival rates according to T stage, based on the TNM 8 classification, are detailed in Figure 1.

Table 1. Clinicopathologic features of the patients with broncopulmonary carcinoid tumors

Feature	Mean±SD	Percentage (%)
Age	43.25±14.6	
Sex		
Female	33	60.7
Male	22	39.4
Smoking history (pack-year)	18±22.3	
Tumor localization		
Right upper lobe	7	12.5
Right middle lobe	8	14.3
Right lower lobe	15	26.8
Left upper lobe	12	21.4
Left lower lobe	14	25
Resection Type		
Lobectomy	34	60.7
Bi-lobectomy	6	10.7
Sleeve Resection	10	17.9
Segmentectomy	5	8.9
Pneumonectomy	1	1.8
Operation Preference		
Minimaly Invasive	29	51.8
Open thoracotomy	27	48.2
Complications		
Cardiovascular Complications	1	1.8
Chylothorax	1	1.8
Prolonged Air Leak	8	14.3
Pneumonia	3	5.4
Hystopathological Features		
Typical Carcinoid Type	39	69.6
Atipical Carcinoid Type	17	30.4
Staging		
Ia	35	62.5
Ib	7	12.5
2a	5	8.9
2b	4	7.1
3a	5	8.9
Pathological Structural Invasion		
Lymphovascular	16	28.1
Spread through air spaces	1	1.8
Perineural	1	1.8
Vascular	1	1.8

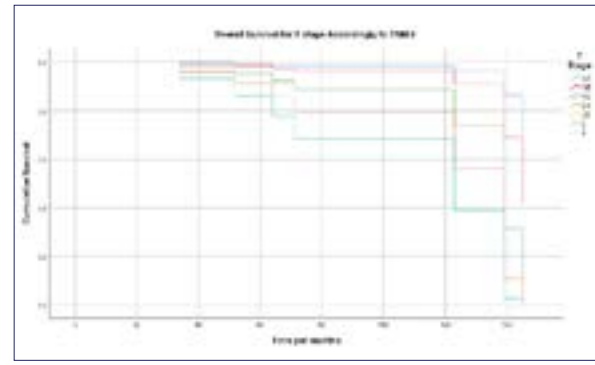

Figure 1. Stage-Specific Overall Survival Based on TNM 8 Classification.

A Ki-67 index greater than 3 was associated with a worse overall prognosis (p=0.03). During this time, 5 (2.4%) patients with typical carcinoid tumors and 7 (25%) patients with atypical carcinoid tumors experienced recurrences. Among the typical carcinoid tumors, 2 recurrences resulted in locoregional metastases, all occurring in N0 patients. Among the atypical carcinoid tumors, 5 recurrences were locoregional and 2 were distant metastases. Four of the locoregional recurrences were in N0 patients, while three were in N1/N2 patients, with one case of distant metastasis in each group. All recurrences were diagnosed during follow-up SRI PET/CT (somatostatin receptor positron emission tomography) or SPECT (Single-photon emission computed tomography) scans in asymptomatic patients.

DISCUSSION

Carcinoid tumors exhibit features similar to large cell neuroendocrine tumors and small cell carcinomas in terms of structure, morphology, and immunohistochemistry. However, their biological behavior differs considerably.[7] Studies suggest a relatively favorable prognosis for carcinoid tumors following surgery compared to other non-small-cell lung carcinomas (NSCLCs), even with tissue-sparing resection.[8]

While Lee et al.[9] reported no significant sex disparity, Soldath et al.[10] observed a female predominance in their cohort of 171 patients (71.3%). Conversely, larger studies have shown a male majority ranging from 54% to 63%.[11,12]

Our findings on five-year survival rates are consistent with previous literature. Kasprzyk et al.[13] reported a 65% rate in their study of 65 patients, while Rea et al.[14] observed a significantly higher 98% rate over the same period for

210 patients with typical carcinoids. Additionally, several studies, including ours, have identified the Ki-67 proliferation index as another significant prognostic factor in pulmonary carcinoid tumors,[14-16] which was also consistent with our research.

Anatomical resection is often chosen for bronchopulmonary carcinoids due to its effectiveness in achieving complete tumor removal and addressing potential lymphatic spread. Studies suggest that non-anatomical resections may leave behind microscopic disease or miss lymphatic involvement, which can increase recurrence risk. Anatomical resection also includes removal of regional lymph nodes, which is important in cases of atypical carcinoids that have higher rates of lymph node involvement.[16] This approach addresses possible spread through lymphovascular or perineural invasion, thereby helping to reduce locoregional recurrence. For typical carcinoids, anatomical resection supports long-term disease-free survival by ensuring thorough removal of the tumor and surrounding structures. Overall, anatomical resection remains a preferred approach for bronchopulmonary carcinoids, particularly in addressing lymphatic involvement and tumor spread. Even though small, centrally located tumors often have a favorable prognosis and positive long-term outcomes, their location can necessitate more extensive surgical resections. Therefore, close and frequent follow-up is essential during the monitoring period to ensure timely detection of any potential recurrence. A center specializing in thoracic oncology, staffed by experienced pulmonary oncologists, chest physicians, and thoracic surgeons, is critical for optimal follow-up care. Our study reaffirms the importance of the Ki-67 proliferation index as a significant prognostic factor, aligning with previous literature. Despite the generally positive prognosis for small, centrally located tumors, the necessity for extensive surgical resections and the risk of recurrence underscore the importance of meticulous, ongoing follow-up. Optimal patient outcomes are best achieved through comprehensive care provided by specialized thoracic oncology centers equipped with experienced multidisciplinary teams.

Conclusion

Anatomical resections remain the preferred surgical approach, ensuring complete tumor removal and addressing lymphatic spread, particularly in atypical carcinoids. Despite the favorable prognosis for small, centrally located tumors, the potential for recurrence necessitates vigilant long-term follow-up.

Ultimately, the integration of precise surgical techniques, close postoperative monitoring, and multidisciplinary collaboration in specialized thoracic oncology centers is essential for optimizing patient outcomes and minimizing recurrence risk. Future research focusing on long-term survival and advanced imaging techniques may further refine treatment strategies for bronchopulmonary carcinoid tumors.

Ethics Committee Approval

The study was approved by the Istanbul University Istanbul School of Medicine Clinical Trials Ethics Committee (Date: 28.04.2023, Decision No: 1737659).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: S.D., B.Ö.; Design: S.D., M.K.; Supervision: B.Ö., A.D., M.K., S.A.T.; Fundings: M.K., S.A.T.; Materials: S.D., A.S.; Data collection &/or processing: S.D., A.S.; Analysis and/or interpretation: A.S.; Literature search: B.Ö., S.A.T.; Writing: S.D., A.S.; Critical review: B.Ö., A.D., M.K., S.A.T.

Conflict of Interest

None declared.

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Bronkopulmoner Karsinoidlerde Anatomik Rezeksiyon Sonrası Uzun Dönem Sağkalım Belirleyicilerinin Değerlendirilmesi: Retrospektif Veri Analizi

Amaç: Bronkopulmoner karsinoid tümörler (BKT), akciğer kanserinin nadir bir türüdür (%1-2). Tipik (TK) ve atipik (AK) olmak üzere iki alt tipe ayrılırlar. Prognoz; tümör tipi, boyutu, yayılımı ve Ki-67 (hücre proliferasyon belirteci) gibi çeşitli faktörlere bağlıdır. Bu çalışma, BKT hastalarında tedavi ve sağkalım oranlarını iyileştirmek amacıyla bu prognostik faktörlerin belirlenmesini amaçlamıştır. Bu araştırmanın ana hedefi, bronkopulmoner karsinoid tümörlü hastalarda uzun dönem sağkalım ile ilişkili faktörlerin retrospektif olarak incelenmesidir.

Gereç ve Yöntem: Şubat 2008 ile Mart 2021 tarihleri arasında merkezimizde ameliyat edilen, histopatolojik olarak bronkopulmoner karsinoid tümör tanısı almış 56 hastanın verileri retrospektif olarak analiz edildi.

Bulgular: Hastaların çoğu kadın (%60.7) olup ortanca yaşları 43 idi. Lobektomi en sık yapılan cerrahi olarak saptandı (%60.7). Uzamış hava kaçağı en sık komplikasyon olarak izlendi. Tipik karsinoidler atipik olanlardan daha yaygındı (%69.6-%30.4). Atipik tümörlerde mediastinal lenf metastazı daha sık saptandı. Çalışmanın bulguları, bronkopulmoner karsinoid tümörlü hastalarda uzun dönem prognozu ile ilişkili prognostik faktörlerin tümör evresi, lenf nodu metastazı ve Ki-67 indeksi olduğunu göstermiştir. Tipik karsinoidlerde 5 yıllık sağkalım oranı atipik olanlara göre daha yüksekti (%82.1-%64.7). Atipik tümörlerde nüks oranı daha yüksek olarak saptandı (%25-%2.4).

Sonuç: Bu bulgular, bronkopulmoner karsinoid tümörlü hastalarda uzun dönem sonuçların belirlenmesinde tümör özelliklerinin kritik rolünü vurgulamaktadır. Tümör tipi, lenf nodu tutulumu, evre ve Ki-67 indeksi gibi faktörleri göz önünde bulundurarak daha kişiselleştirilmiş tedavi stratejileri geliştirilebilir. Daha büyük, çok merkezli hasta gruplarını içeren ileri araştırmalar, bu hasta popülasyonu için prognoz modellerini iyileştirmek ve tedavi kararlarına rehberlik etmek için daha sağlam veriler sağlayabilir.

Anahtar Sözcükler: Göğüs cerrahisi; karsinoid tümörler; lobektomi; video-yardımlı cerrahi.