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Insights from 151 Consecutive Pancreaticoduodenectomies at a High-Volume Tertiary Center: A Cross-Sectional Observational Study

Yüksek Hacimli Bir Tersiyer Merkezde 151 Ardışık Pankreatikoduodenektomi: Kesitsel Gözlemsel Bir Çalışma

Ali Emre ATICI, Ayşegül Bahar ÖZOCAK, Mümin COŞKUN, Şevket Cumhur YEĞEN

Marmara University Faculty of Medicine, Department of General Surgery, İstanbul, Türkiye

ABSTRACT

Aim: Pancreaticoduodenectomy (PD) is a complex and essential procedure in the treatment of localized periampullary neoplasms. Due to its comlexity, postoperative morbidity and mortality remain significant concerns. The aim of this study was to evaluate our short-term outcomes, categorize them according to international standards, and compare our findings with those reported in the existing literature.

Materials and Methods: One hundred and fifty-one patients underwent classical PD for pancreatic tumors between February 2019 and May 2023 at the Department of General Surgery, Marmara University Faculty of Medicine, Department of General Surgery. Patients meeting the inclusion criteria were enrolled in the study. Clinical, operative, pathological, and short-term outcome data, prospectively recorded, were retrospectively analyzed.

Results: The mean age of the patients was 63.6 years, with 87 (57.6%) being male. The median operative time was 227.4±48.5 minutes. Clavien-Dindo grade 3 or higher complications were observed in 38 patients (25.2%). Intraabdominal abscesses were noted in 9 patients, chylous fistula in 9 patients, and postoperative bleeding in 6 patients. Postoperative pancreatic fistula was diagnosed in 54 patients (35.8%), of which 38 (70.3%) were classified as grade A and 16 (29.7%) as grade B. No grade C pancreatic fistulas were observed. The overall incidence of delayed gastric emptying was 26.5% (n=40). Two patients required reoperation: one for postoperative bleeding and the other for gastroenterostomy leakage. In the early postoperative period, five patients died.

Conclusion: Effective management of complications following complex surgeries plays a critical role in improving postoperative outcomes. The morbidity and mortality rates in our series were relatively lower compared to those reported in the literature.

Keywords: Pancreaticoduodenectomy, periampullary tumor, postoperative complications

ÖZ

Amaç: Pankreatikoduodenektomi (PD), lokalize periampüller neoplazmların tedavisinde karmaşık ve hayati bir cerrahi prosedür olmakla birlikte postoperatif morbidite ve mortalite oranları hala en önemli endişe konusu olmaya devam etmektedir. Bu çalışmanın amacı, postoperatif kısa dönem sonuçlarımızı değerlendirmek, uluslararası standartlara göre sınıflandırmak ve elde edilen bulguları mevcut literatürle karşılaştırmaktır.

Gereç ve Yöntem: 2019 Şubat ile 2023 Mayıs tarihleri arasında, Marmara Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalında periampuller tümör tanısı ile 151 hastaya klasik PD operasyonu yapıldı. Dahil edilme kriterlerini karşılayan hastaların prospektif olarak kaydedilen klinik verileri ve kısa dönem postoperatif sonuçları retrospektif olarak analiz edildi.

Bulgular: Hastaların ortalama yaşı 63,6 yıl olup, 87 hasta (%57,6) erkekti. Ortanca operasyon süresi 227,4±48,5 dakika olarak bulundu. Clavien-Dindo sınıflamasına göre derece 3 ve üzeri daha yüksek komplikasyonlar 38 hastada (%25,2) izlendi. Dokuz hastada intraabdominal apse, 9 hastada

Address for Correspondence: Ali Emre ATICI MD, Marmara University Faculty of Medicine, Department of General Surgery, İstanbul, Türkiye
E-mail: ali.emre@marmara.edu.tr **ORCID ID:** orcid.org/0000-0001-5094-0461
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şilöz fistül ve 6 hastada postoperatif kanama saptandı. Elli dört hastada (%35,8) postoperatif pankreatik fistül gelişirken, 38'i (%70,3) derece A, 16'sı (%29,7) derece B fistül ile uyumlu idi. Derece C pankreatik fistül hiçbir hastamızda izlenmedi. 40 (%26,5) hastada geçikmiş mide boşalımı gözlendi. Bir hasta postoperatif kanama diğer bir hastada gastroenterostomi kaçağı nedeniyle postoperatif erken dönemde yeniden opere edildi. Toplam 5 (%3) hasta ise erken postoperatif dönemde hayatını kaybetti.

Sonuç: Karmaşık cerrahiler sonrasında komplikasyonların etkin yönetimi, postoperatif sonuçları iyileştirmede kritik bir rol oynamaktadır. Morbidite ve mortalite oranlarımız literatürde bildirilen verilere kıyasla nispeten daha düşük bulunmuştur.

Anahtar Kelimeler: Pankreatikoduodenektomi, periampüller tümör, postoperatif komplikasyonlar

INTRODUCTION

Pancreaticoduodenectomy (PD) is one of the most complex abdominal surgeries performed for malignant lesions of the pancreatic head and periampullary region[1]. German surgeon Kausch performed the first successful PD for periampullary tumors in 1909, but it was later popularized by Allen Whipple[2]. In the early years, due to high morbidity and mortality rates, only a limited number of procedures were performed. However, since the 1980s, with advancements in surgical techniques and perioperative patient care, mortality rates have significantly decreased and have now fallen below 5%. In contrast, morbidity rates have not decreased at the same rate and continue to range between 22% and 57%[1,2]. Postoperative morbidity, by causing prolonged hospital stay, increased treatment costs, and delays in adjuvant therapy, negatively impacts prognosis and survival[3]. Therefore, although it may not be possible to eliminate postoperative morbidity, identifying its causes, determining predictive factors, and taking preventive measures will significantly reduce morbidity rates, such as mortality rates.

Currently, the most frequently observed causes of morbidity after PD are post-operative pancreatic fistula (POPF), delayed gastric emptying (DGE), and post-pancreatectomy hemorrhage (PPH)[1]. To standardize the definition of these complications and enable inter-center comparisons, internationally recognized classification systems have been developed considering the severity of complications. After that, most efforts have focused on reducing them[3]. This study aimed to assess the short-term outcomes, classify our probable complications according to international definitions, and compare our results with the current literature.

MATERIALS AND METHODS

One hundred and eleven patients underwent classical PD (with 20-40 percent antrectomy) due to tumoral mass in the periampullary region at the Department of General Surgery, Marmara University Faculty of Medicine, from February 2019 to May 2023, and those who met the inclusion criteria were enrolled. Prospectively recorded patients' clinical, operative, pathologic, and short-term outcomes were analyzed retrospectively. The study protocol was approved by the Ethics Committee of Marmara University Faculty of Medicine, and was conducted by the principles of the Declaration of Helsinki (desicion no: 09.2023.892, date: 14.07.2023).

Study Population

Eligibility criteria included being over 18 years of age, having a tumor confined to the pancreatic head, and meeting the definition of resectable disease. Resectability was defined based on the criteria established by Isaji et al.[4] Patients who had received neoadjuvant chemotherapy, had distant metastasis, had synchronous or metachronous tumors, and in addition, to minimize variability related to postoperative outcomes, patients who had undergone complex procedures such as vascular or multiorgan resections (such as gastric or colonic) were excluded. Patient age, sex, body mass index (BMI), American Society of Anesthesiologists classification, Eastern Cooperative Oncology Group performance status, co-morbidities, surgical parameters, and early postoperative complications were recorded.

Surgery

All surgical procedures were carried out by two experienced hepatobiliary surgeons. The patients underwent resection with curative intent, including standard open-technique PD and lymphadenectomy[5]. Pyloric preservation was not performed on any patients. Anastomoses were constructed on a single jejunal loop repositioned upwards through transverse mesocolon into a subhepatic resection field in the reconstruction phase. Pancreaticojejunostomy was performed using either the modified Blumgart or Heidelberg technique[6,7]. Surgical team also performed a subjective assessment of the pancreatic tissue texture intraoperatively. Hepaticojejunostomy was performed with absorbable interrupted sutures. Then, a hand-sewn or linear stapler performed gastrojejunostomy to the same jejunal loop.

Postoperative Care

The nasogastric tube was removed within 24 hours after surgery and reinserted if nausea and vomiting occurred. Oral intake was initiated on the first postoperative day and increased based on tolerance. Prophylaxis for deep vein thrombosis was

started with low-molecular-weight heparin 12 hours before anesthesia induction. Antibiotic prophylaxis was administered to patients for 24 hours. No patient received a prophylactic somatostatin analog to prevent POPF. In the decision to remove the abdominal drains, the character of the drainage content and amylase levels were considered.

Definitions

Postoperative complications were classified from grade I to grade V according to the Clavien-Dindo (C-D) classification[8]. DGE and POPF were categorized according to the criteria of the International Study Group of Pancreatic Surgery[9,10]. Deaths related to postoperative complications were recorded.

Statistical Analysis

Descriptive statistical analysis was performed using the SPPS Software Program Version 26.0 (SPSS, Inc., Chicago, IL, USA). Continuous variables are expressed as mean ± standard deviation (SD). Categorical variables are described as frequency and percentage. Categorical variables were analyzed using the chi-square test or the Fisher's exact test, as appropriate, to assess associations between groups. Results were considered statistically significant at a p-value<0.05.

RESULTS

Mean ± SD age was 63.6 (11.9) years, and 87 patients (57.6%) were male. Mean ± SD BMI of the patients was 26.2 (4.4) kg/m^2. Diabetes mellitus was the most common co-morbidity present in 57 (37.7%) patients. Of the 151 patients, 107 required preoperative biliary drainage, of which 72 (47.7%) had endoscopic retrograde cholangiopancreatography (ERCP)-plastic biliary stent, and 35 (23.2%) had percutaneous biliary catheter placement. Eighty-eight (58.3%) had normal bilirubin levels pre-operatively. Baseline patient characteristics are shown in Table 1.

Intraoperative Findings

Median operative time was 227.4±48.5 minutes. All pancreaticojejenostomy anastomoses were performed duct-to-mucosa using either the modified Blumgart (n=125, 82%) or the Heidelberg technique (n=26, 17%). Out of these, stents were used in 71 (47.3%) cases, while stents were not applied in 79 (52.7%) cases. 69 (45.7%) patients were observed to have a soft pancreatic texture, while 76 (56.3%) patients had a firm pancreatic texture (as decided by the surgeon who performed the surgery). The pancreatic duct size was measured by a sterile plastic ruler intraoperatively. 43 (28.5%) had a duct size of less than 3 mm, while 96 (63.6%) had a duct size of more than 3 mm (Table 2).

Postoperative Results

The total rate of POPF was 35.8% (n=54). Out of 54 patients, 38 (70.3%) patients had grade A and 16 (29.7%) had grade B pancreatic fistula. Grade C pancreatic fistula was not observed. The incidence of DGE was 26.5% (n=40). Of 40 patients, 23 (57.5%) had grade A, 1 (37.5%) had grade B, and 2 (5%) had grade C (Table 3). Intra-abdominal abscess (n=9), chylous

Table 1. Demographic data

All cases n=151 (%)	
Age mean (SD)	63.6±11.9
Sex	
Female	64 (42.4)
Male	87 (57.6)
BMI mean (SD), kg/m^2	26.2±4.4
ASA score	
1	15 (9.9)
2	66 (43.7)
3	70 (46.3)
ECOG score	
0	51 (33.7)
1	80 (52.9)
2	20 (13.2)
Diabetes mellitus	
No	94 (62.3)
Yes	57 (37.7)
Total bilirubin mean (SD), mg/dL	
0-1.99	88 (58.3)
2-6	33 (21.9)
6<	27 (17.9)
Pre-operative biliary drainage	
No drainage	43 (28.5)
ERCP	72 (47.7)
PTBD	35 (23.2)
no data (missing)	1 (0.7)
Tumor location	
Pancreatic head	76 (50.3)
Papillary tumor	23 (15.2)
Uncinate process	19 (12.6)
Periampullary tumor	31 (20.5)

SD: Standard deviation, BMI: Body-mass index, ASA: American Society of Anesthesiologists, ECOG: Eastern Cooperative Oncology Group, ERCP: Endoscopic retrograde cholangiopancreatography, PTBD: Percutaneous transhepatic biliary drainage

fistula (n=9), and postoperative bleeding (n=6) were the most common complications. Two patients were re-operated due to bleeding and anastomotic leakage, respectively. In the early postoperative period, a total of 5 patients died. Three of these patients died due to sepsis, while the other two succumbed to postoperative bleeding. Mean postoperative hospital stay was 8.7±4.3 days (Table 4). When postoperative complications were evaluated in general rather than specifically, 38 (25.2%) had C-D grade 3 or above complications. No significant association was identified between pancreatic texture, Wirsung's duct diameter, anastomosis type, or intraoperative blood loss and the occurrence of complications (Table 5).

Table 6 summarizes the distribution of the histopathologic phenotype. The most common histopathological finding was adenocarcinoma, specifically the pancreaticobiliary subtype. Among the other histopathological findings, neuroendocrine carcinoma (n=8), chronic pancreatitis (n=4), autoimmune pancreatitis (n=3), serous cystadenoma (n=2), and mucinous cystadenoma (n=1) were observed, respectively.

Table 2. Intraoperative and perioperative parameters

All cases n=151 (%)	
Pancreatic texture	
Soft	69 (45.7)
Firm	76 (50.3)
No data (missing)	6 (4.0)
Pancreatic duct diameter, mm	
<3	43 (28.5)
3<	96 (63.6)
no data (missing)	12 (7.9)
Stent	
No	79 (52.3)
Yes	71 (47.0)
no data (missing)	1 (0.7)
Type of pancreaticojejunostomy	
Blumgart	125 (82.0)
Heidelberg	26 (17.0)
Operative time, mean ± SD	227.4±48.5
Blood loss, mL	
0-299	19 (12.6)
300-750	71 (47.0)
750<	21 (13.9)
SD: Standard deviation	

DISCUSSION

In the presented study, the rate of severe postoperative complications was 25.2%. Overall pancreatic fistula rate was 35.8%, and the DGE incidence was 26.5%. Two patients were re-operated, one due to postoperative bleeding and the other due to gastroenterostomy leakage. Mortality rate was 3.3%. As a result, morbidity and mortality rates were found to be comparable to the literature data and even relatively better.

Although the complexity of surgery and the challenges in managing postoperative complications led to a reluctance toward PD, the increase in surgical experience over time and advances in postoperative patient care have reduced mortality rates to below 5%[1,2]. However, morbidity rates remain relatively high, ranging from 30% to 50%[2].

POPF after PD is the most common cause of postoperative mortality. Additionally, it contributes directly or indirectly to other morbidities such as DGE, bleeding, and sepsis[1]. Factors such as pancreatic texture, pancreatic duct diameter,

Table 3. The rates of POPF and DGE

All cases n=151 (%)	
POPF	
No	97 (64.2)
Yes	54 (35.8)
POPF grade	
Grade A	38/54 (70.3)
Grade B	16/54 (29.7)
Grade C	0
DGE	
No	111 (73.5)
Yes	40 (26.5)
DGE grade	
Grade A	23/40 (57.5)
Grade B	15/40 (37.5)
Grade C	2/40 (5)
PPH	
No	145 (96.1)
Yes	6 (3.9)
PPH grade	
Grade A	4 (2.6)
Grade B	1 (0.6)
Grade C	1 (0.6)
POPF: Post-operative pancreatic fistula, DGE: Delayed gastric emptying, PPH: Post-pancreatectomy hemorrhage	

intraoperative blood loss, and pancreaticojejunal anastomosis technique are considered predictive for POPF. Its incidence remains between 3 and 45 % at high-volume centers[11]. In the current study, the POPF rate was 35.8%. Although it may appear to be a relatively high rate, most of these fistulas were biochemical leaks not classified as clinically relevant fistulas (70.3%). The incidence of biochemical fistula in our study was consistent with, and even slightly lower than, the rates reported in the literature[10]. The rate of clinically relevant POPF with intra-abdominal collection detected on postoperative control computed tomography scans was 29.7%. Of these patients, 56.3% (n=9) underwent placement of a drainage catheter by interventional radiology. No grade C fistulas were detected in any patient. The use of standard surgical techniques by the same surgical team and a relatively short average operative time are the major factors contributing to low clinically relevant fistula rates. Additionally, the pancreatic duct size greater than 3 millimeters in 63.6% of the cases may be another important reason for this.

DGE is another common cause of morbidity after PD. Its incidence rate ranges between 10% and 60%[12]. In the presented study, the postoperative DGE rate was 26.5%, with grade B and C DGE observed in 15 and 2 patients, respectively. Of the patients with clinically relevant DGE, 38.3% underwent gastroscopy, while 14.9% required percutaneous drainage and total parenteral nutrition due to intra-abdominal

Table 4. Overall postoperative complications

All cases n=151 (%)	
Intra-abdominal abscess/collection	9 (6.0)
Chylous fistula	9 (6.0)
Bleeding	6 (4.0)
Surgical site infection	4 (2.0)
Liver failure	4 (2.0)
Biliary leakage	3 (2.0)
Sepsis	3 (2.0)
Pneumonia	1 (0.6)
Anastomotic stenosis (GJ)	1 (0.6)
Renal failure	1 (0.6)
Pulmonary embolism	1 (0.6)
Hospital stay, day, mean ± SD	8.7±4.3
Re-operation	2 (1.3)
Mortality	5 (3.3)

GJ: Gastrojejunostomy, SD: Standard deviation

Table 5. Complication rates according to intraoperative parameters

	C-D <3	3≤ C-D**	p-value
	n (%)	n (%)	
	113 (74.8)	38 (25.2)	
Pancreatic texture			0.960
Soft	52 (75.4)	17 (24.6)	
Firm	57 (75)	19 (25)	
Wirsung diameter, mm			0.71
<3	31 (72.1)	12 (27.9)	
3<	72 (75.0)	24 (25.0)	
Stent			0.261
No	56 (70.9)	23 (29.1)	
Yes	56 (78.9)	15 (21.1)	
Type of pancreaticojejunostomy			0.21
Blumgart	92 (74.8)	31 (25.2)	
Heidelberg	21 (77.8)	6 (22.2)	
Blood loss, mL			0.15
0-299	17 (89.5)	2 (10.5)	
300-750	48 (67.6)	23 (32.4)	
750<	16 (76.2)	5 (23.8)	

**C-D 3a; n=27, C-D 3b; n=2, C-D 4a; n=2 , C-D 4b; n=2, C-D 5; n=5, C-D: Clavien-Dindo classification, p: Probability

collection. Many factors are blamed among the causes of etiopathogenesis, but the exact reason remains unclear[13,14]. Previous studies have shown a significant correlation between DGE and complications such as postoperative pancreatitis, pancreatic fistula, biliary fistula, and enteric leaks. It has been suggested that the developing local or abdominal inflammation is the underlying physiopathological mechanism[14]. Considering this possible relationship, the low rates of clinically relevant pancreatic fistulas suggest a positive impact on our low-grade B and C DGE rates.

PPH is a rare but one of the serious complications after pancreatic resection. In most case series, its incidence varies between 3% and 10%[15]. It has been categorized (grades A, B, and C) by the International Study Group based on the timing (early or late), severity (mild or severe), and location of the bleeding (intraluminal or extraluminal)[16]. Potentially life-threatening bleeding is defined as grade C. Bleeding occurring within the first 24 hours after the operation is classified as early hemorrhage, usually resulting from technical issues related to the hemostasis of the vascular-rich area or due to anticoagulant medications and an underlying coagulopathy[15]. Hemorrhages occurring in the late period are typically due to erosion of vascular structures caused by POPF, most commonly arising from the stump of the gastroduodenal artery[16]. In our case series, we encountered postoperative hemorrhage in six patients, one of which required reoperation. The remaining five patients were managed conservatively. Four of them were grade A, and one was grade B. In six patients, the bleeding occurred in the early postoperative period. Therefore, secondary causes such as pancreatic fistula could be excluded. Unfortunately, one patient who was re-operated due to PPH died in the postoperative period due to disseminated intravascular coagulation.

Table 6. Histopathologic findings

All cases n=151 (%)	
Adenocarcinoma	120 (79.4)
Pancreatobiliary	71
Ductal	21
Biliary	12
Undifferentiated	4
Intestinal	2
Mucinous	3
Adenosquamous	2
Mixt	4
Tubular	1
Neuroendocrine tumor/carcinoma	8 (5.3)
Chronic pancreatitis	4 (2.6)
Autoimmune pancreatitis	3 (2.0)
GIST	2 (1.3)
IPMN	2 (1.3)
Serous cystadenoma	2 (1.3)
Mucinous cyst	1 (0.7)
*Other	9 (6.0)

*Undif sarcoma 2, carcinosarcoma 1, squamous carcinoma 1, cohesive carcinoma 1, gastric cancer 1, gastric peptic ulcus 2, acinar cell carcinoma 1

GIST: Gastrointestinal stromal tumor, IPMN: Intraductal papillary neoplasm

Obstructive jaundice is the most common symptom in patients with periampullary mass[17]. However, it is increasingly acknowledged that routine preoperative biliary drainage cannot be recommended in patients with obstructive jaundice due to the increased rate of infectious complications associated with drainage procedures in these patients. Recent studies have indicated that biliary drainage before PD should be reserved only for patients with severe and long-standing jaundice, cholangitis, renal failure, or malnourishment or with indications for neoadjuvant therapy[18,19]. In our case series, ERCP and percutaneous transhepatic cholangiography were performed pre-operatively in 47.7% and 23.2% of the patients, respectively, and the remaining underwent direct surgery without preoperative biliary drainage. In subgroup analysis, the postoperative complication rate was higher in patients who underwent ERCP compared to those who underwent percutaneous transhepatic biliary drainage (PTBD) (44.4% vs. 28.6%), and this difference did not reach statistical significance (p=0.115). We believe that the development of symptomatic or asymptomatic ascending cholangitis in patients who underwent ERCP increases the risk of postoperative infectious complications[13]. Therefore, PTBD should be considered the preferred drainage method for patients requiring preoperative biliary drainage. The lack of a statistically significant difference may be due to the limited sample size in our study.

The need for reoperation occurred in only two patients, one for previously mentioned postoperative bleeding and the other for a gastrojejunostomy anastomotic leak. Five patients died in the postoperative early period. Three of these patients died due to sepsis. In all three cases, the clinical signs of sepsis developed on the first postoperative day, and the patients died due to septic shock and multiorgan failure. The common feature of these three patients was that they had undergone preoperative endoscopic biliary drainage and had a plastic biliary stent placed in the bile duct. Another shared characteristic was that they were all elderly patients. Due to these cases, we revised our antibiotic prophylaxis protocol in the clinic. Specifically, for patients who had undergone preoperative biliary drainage, we started using broad-spectrum antibiotics covering gram-negative bacteria one day before surgery. We continued this

treatment in the postoperative period until the results of intraoperative bile cultures were available. Following the protocol change regarding the use of prophylactic antibiotics in patients undergoing preoperative biliary drainage, no cases of clinical sepsis were observed on postoperative first day. One of the other two patients died in the early postoperative period due to respiratory failure caused by pneumonia, while the other died due to bleeding.

Finally, it was found that approximately one in every four patients required intervention during the postoperative period. Therefore, it would be appropriate to recommend that this surgery be performed in reference centers with level three intensive care units and with interventional radiology to perform percutaneous drainage for postoperative abdominal collections[20].

Study Limitations

The study's limitations include selection bias because of the study design, even if we have a prospectively recorded database. Second, excluding patients with borderline and locally advanced disease who received neoadjuvant treatment, even though their numbers were relatively low, might have had a relatively positive impact on our results. Third, it was conducted at a single center, which may limit the generalizability of the findings. Institutional practices, patient populations, and perioperative management protocols may differ across centers, potentially influencing outcomes. Therefore, multicenter studies are warranted to validate these results in broader clinical settings. Fourth, the lack of long-term follow-up data precludes assessment of delayed complications, recurrence rates, and long-term efficacy of the intervention.

CONCLUSION

As a result, the conclusions drawn primarily reflect short-term outcomes. Another limitation is that this study's cross-sectional nature may reflect the relatively good results of our team after gaining some experience in this complex surgery. This study allowed us to document and report our PD results in a standardized manner and compare them with the literature. Morbidity and mortality rates were relatively better compared to the literature data. Managing complications after complex surgeries is the most important factor affecting postoperative outcomes. In addition, using the same type of surgical technique by the same surgical team and the relatively short average operative time were the primary positive contributing factors to our results.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Marmara University Faculty of Medicine, and was conducted by the principles of the Declaration of Helsinki (desicion no: 09.2023.892, date: 14.07.2023).

Informed Consent: Prospectively recorded patients' clinical, operative, pathologic, and short-term outcomes were analyzed retrospectively.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.E.A., M.C., Ş.C.Y., Concept: A.E.A., A.B.Ö., M.C., Ş.C.Y., Design: A.E.A., Data Collection or Processing: A.B.Ö., Analysis or Interpretation: A.E.A., M.C., Ş.C.Y., Literature Search: A.B.Ö., Writing: A.E.A., A.B.Ö.

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