DOI: 10.4274/tjcd.galenos.2021.2021-3-2
Turk J Colorectal Dis 2022;32:41-47

RESEARCH ARTICLE

Factors Affecting Morbidity in Appendectomy: A Single Center Experience

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ABSTRACT

Aim: To determine the factors affecting morbidity in acute appendicitis (AA) and to compare the results with previously published findings.
Method: After ethics committee approval, patients who underwent appendectomy in Iğdır State Hospital between January 2019 and July 2020 were retrospectively reviewed. Preoperative, intraoperative and postoperative data were collected and differences in morbidity were statistically evaluated. Factors associated with morbidity were investigated using logistic regression methodology.
Results: One hundred and fifty-eight patients were operated for AA, of whom 98 (62%) were male. The mean ± standard deviation age was 32.5±13.4 years, with a range of 18-93 years. The overall morbidity rate was 20.2% with no mortality. Preoperative fever [odds ratio (OR): 3,000 95% confidence interval (CI): 1,344-6,697; p=0.007)], late hospital admission (OR: 1,108, 95% CI: 1,026-1,196; p=0.009), preoperative diagnosis (OR: 4,130, 95% CI: 1,372-12,376; p=0.012), postoperative antibiotic type (OR: 4,387, 95% CI: 1,836-10,483; p<0.001), and length of stay (OR: 1,546, 95% CI: 1,280-1,866; p<0.001) affected morbidity. The rate of morbidity was significantly higher in the single antibiotic group compared to the combined antibiotic group (43.3% vs 14.8%; p<0.001). Patients suffering morbidity had significantly longer hospital stay (5.78 vs 3.3 days; p<0.001).
Conclusion: Preoperative fever, late hospital admission, complicated appendicitis, single antibiotic use and prolonged hospital stay increased morbidity. We recommend the use of combined antibiotics in the treatment of AA patients and discharge of patients as early as possible.
Keywords: Appendicitis, combine antibiotic, fever, morbidity, single antibiotic

Introduction

Acute appendicitis (AA) is the most common cause of acute abdomen in patients admitted to the emergency department in all age groups.[1,2] The clinical signs of AA begin with increased sensitivity of the visceral peritoneum. The clinical picture expands to include parietal peritoneum sensitivity with increased inflammation. Pain usually progresses to the right lower quadrant with increased parietal peritoneal inflammation, although initially there is no precise localization of the pain.

The symptoms and physical findings of the patients are diagnostic. Laboratory findings, such as white blood cell (WBC) count, leukocyte count, C-reactive protein (CRP) level, and screening methods such as ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging aim to support the diagnosis of AA. In addition, scoring systems such as the Alvarado score and Ohmann score,[1] are helpful for diagnosis. If the diagnosis has not been made despite these additional tests but AA is still suspected, diagnostic operations should be performed as a last resort.[3]

In the case of delay in either the diagnosis or surgery for AA, both morbidity and mortality increase. Morbidity rates of up to 10% and mortality rates of up to 5% for AA have been reported.[4] To reduce both morbidity and mortality, diagnosis should be made as soon as possible, and appropriate treatment should be initiated quickly.

The aim of this study was to determine the factors affecting morbidity in AA and to compare the results with previously published findings, thus expanding the evidence base.

Materials and Methods

A retrospective evaluation of patients who were operated on due to AA between January 2019 and July 2020 in Iğdır State Hospital was performed. Ethics committee approval

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Received: 22.03.2021 **Accepted:** 30.04.2021

was received from Non-invasive Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital (approval number: 2021/04-72). Subsequently, pre-, intra- and post-operative data were extracted from hospital records, consultation and operation notes, pathology reports and clinical charts of the patients. Exclusion criteria included: patients in the pediatric age group (0-18 years); pregnant patients; and patients treated at other centers and then admitted to our center. Patients were divided into two groups: morbidity positive (+) group and morbidity negative (-) group.

Preoperative Factors

Age and gender, admission symptoms and findings, and time from onset of symptoms to hospital admission were collected. Pre-operative hematological parameters, biochemical parameters, international normalized ratio value and CRP levels were collected from laboratory results. The Alvarado score was calculated for each patient. Imaging studies and reports thereof, including USG and CT scans, were used to record appendix diameter, presence or absence of fecalith and intra-abdominal fluid volumes.

Intraoperative Factors

Intra-operative data collected included operation time divided into day (08:00 a.m.-11:59 p.m.) or night (12:00-07:59 a.m.), type of surgery (laparoscopic or open), and type of incision (laparoscopic incision, McBurney incision or midline incision).

Postoperative Factors

The number and types of antibiotics used in the hospital after surgery, postoperative complications and treatment of these complications were evaluated. Pathological diagnosis of the resected specimen, appendix diameter, appendix length, omental tissue volume resected with the appendix, and the presence of perforation in the appendix sample were obtained from histopathology reports. Hospital stay was compared between the morbidity (+) and (-) groups.

Statistical Analysis

Statistical analyses were performed using SPSS, version 22.0 (IBM Inc., Armonk, NY, USA). Shapiro-Wilk test was used to assess the normality distribution of quantitative variables. Data are presented as mean and standard deviation (SD) or median and range, depending on normality of distribution. Independent samples t-test or Mann-Whitney U test was used to compare groups, as appropriate for the data set normality distributions. Chi-square tests (Fisher's exact test, Pearson chi-square and likelihood ratio test) were used to compare qualitative variables. Binary logistic regression was used to find factors affecting morbidity. A p-value below 0.05 was considered statistically significant.

The Process for Treatment of AA in Our Clinic from Presentation to Final Treatment

The presenting complaints and the duration of these complaints were questioned in all patients. A detailed physical examination was performed for each patient. Basic laboratory tests and screening imaging tools were used to confirm the diagnosis. Surgery was planned for patients definitely diagnosed with AA following clinical evaluation, laboratory and screening tests. Diagnostic operation was also performed in patients with suspected AA.

Laparoscopic surgery was the first choice for AA surgery. However, open surgery with McBurney incision was performed in septic patients, patients with intra-abdominal abscess or perforation. Laparoscopic surgery was performed with three trocars; a 10 or 12 mm trocar inserted supraumbilically, a 5 mm trocar inserted suprapubically, and a 10 or 12 mm trocar inserted from the left para-rectal area.

While open surgery was performed with McBurney incision in eight patients, midline incisions were used in converted surgery cases. The appendix was found and suspended after entering the abdominal cavity. The meso-appendix is sealed with energy devices and the appendix was released, two or, rarely, three Hem-o-lok clips were used to close the appendicial stump routinely. The appendix specimen was taken out of the abdomen with the help of a glove bag from the left para-rectal trocar opening. Depending on the amount of fluid present in the abdomen, an aspiration catheter was inserted into the pouch of Douglas.

Patients were followed up in the clinic postoperatively. Intravenous antibiotherapy was started for each patient. The antibiotics used were selected according to the findings determined during surgery and according to the antibiotic stock available in the hospital. Three different antibiotic groups were used: cephalosporin, 5-nitroimidazole, and carbapenem. While in the cephalosporin group, first generation cephalosporin (intravenous cefazolin sodium 1 g/every 12 hours) or third generation cephalosporin (intravenous ceftriaxone 1 g/every 12 hours) was used, in the 5-nitroimidazole group metronidazole (500 mg/100 mL) every 8 hours was used, and ertapenem 1 g/every 24 hours was used in carbapenem group. Simple analgesics, such as intravenous acetaminophen (500 mg/mL/every 12 hours) or intramuscular diclofenac sodium (2 x 25 mg/mL) were used for postoperative pain control.

Intravenous antibiotics were used during hospital stay. In general, combination therapy (cefazolin sodium plus metronidazole or ceftriaxone plus metronidazole) was preferred as the first choice antibiotherapy in most patients. The duration of both combined therapy and single therapy was adjusted according to the clinical improvement of the

patients. Postoperative carbapenem treatment was routinely started in patients with appendix perforation and intra-abdominal diffuse abscess. Carbapenem treatment was generally used for five days in patients, but treatment was extended to 7-10 days, if infection parameters suggested continuing infection.

Results

Between January 2019 and July 2020, 158 patients were operated for AA. Patients were divided into two groups: morbidity positive (+) group (n=32, 20.25%) and morbidity negative (-) group (n=126, 79.75%). Of the study cohort, 98 (62%) were male and the mean ± standard deviation age was 32.5±13.4 years, ranging from 18-93 years. Preoperative, intraoperative and postoperative data of the patients were compared between the groups. Neither gender distribution nor mean age differed between the morbidity groups (p=0.969 and p=0.638, respectively).

While 138 (87.3%) patients had abdominal pain on admission, 121 (76.6%) patients had migrative pain, 82 (51.9%) patients had vomiting and nausea, and 104 (65.8%) had lack of appetite. In addition, 154 (97.5%) patients had right iliac fossa tenderness, 152 (96.2%) had rebound on physical examination and 65 (41.1%) had fever. When the pre-operative signs and symptoms were compared between the groups, patients with morbidity were significantly more likely to present with fever (p=0.006) and to have a longer duration of symptoms before attending hospital (p=0.03). The demographic characteristics, and patients' symptoms and signs are shown in Table 1.

While 134 (84.8%) patients had leukocytosis, 96 (60.8%) had neutrophilia. Neither leukocytosis nor neutrophilia had an association with morbidity, (p=0.582 and p=0.821, respectively). There was no difference in the parameters evaluated in comparison.

USG was used as first-line radiological tool for the diagnosis of AA in 108 (68.3%) patients. While 78 (49.4%) patients had clear findings of AA (mean appendix diameter: 9.01±1.74 mm), the appendix could not be detected on ultrasound in 20 (12.7%) patients. AA continued to be considered in 10 (6.3%) patients with secondary findings, such as edema, heterogeneity, perforated appendicitis or plastron appendicitis, and CT investigation was recommended by the radiologist. In 13 (8.2%) cases, there was fluid located in the right lower quadrant and pelvic simultaneously. In addition, a fecalith was identified in six patients on USG.

CT scan was used in 89 (56.3%) in total, either as a second step radiological technique or in cases where appendicitis could not be diagnosed on ultrasound. While 74 (46.8%) patients had clear evidence of AA (mean appendix diameter: 10.8±2.8 mm), in 10 (6.3%) patients the appendix could not be detected on CT. In five (3.2%) cases, a diagnosis of AA was suspicious on CT scan. In 16 (10.1%) cases, there was fluid located in the right lower quadrant and pelvic simultaneously. In addition, a fecalith was identified in 19 (12%) patients on CT.

Table 1. Comparison of demographic data, and symptoms and signs at admission between patients with and without morbidity

Parameters	Morbidity (+) (n=32)	Morbidity (-) (n=126)	p-value
Gender, n (%)			0.638*
- Male	11 (18.3)	49 (81.7)	-
- Female	21 (21.4)	77 (78.6)	-
Age (mean rank)	79.78	79.43	0.969**
Symptoms and signs on admission			
Migrative abdominal pain, n (%)			0.817*
- Yes	25 (20.7)	96 (79.3)	-
- No	7 (18.9)	30 (81.1)	-
Vomiting and nausea, n (%)			0.082*
- Yes	21 (25.6)	61 (74.4)	-
- No	11 (14.4)	65 (85.6)	-
Lack of appetite, n (%)			0.696*
- Yes	22 (21.1)	82 (78.9)	-
- No	10 (18.5)	44 (81.5)	-
Right iliac fossa tenderness, n (%)			0.583*
- Yes	32 (20.8)	122 (79.2)	-
- No	0 (0)	4 (100)	-
Rebound, n (%)			0.349*
- Yes	32 (21)	120 (79)	-
- No	0 (0)	6 (100)	-
Fever, n (%)			**0.006***
- Yes	20 (30.8)	45 (69.2)	-
- No	12 (12.9)	81 (87.1)	-
Alvarado score, n (%)			0.072***
- 5-6	4 (12.9)	27 (87.1)	-
- 7-8	16 (17.6)	75 (82.4)	-
- >8	12 (33.3)	24 (66.7)	-
Time home to hospital (mean rank)	100.84	74.08	**0.003****

*Chi-square test, **Mann-Whitney U test, ***Likelihood ratio test

There was no difference between the morbidity groups in terms of appendix diameter, presence of AA findings, presence of intra-abdominal fluid and presence of fecaliths, both by USG and CT (p>0.05). Preoperative laboratory parameters and results of imaging tools are shown in Table 2.

Complicated appendicitis was considered preoperatively in 15 (9.5%) patients, including perforated or plastron appendicitis and diffuse intra-abdominal or right lower quadrant abscess. While the morbidity rate in complicated group was 46.7%, the morbidity rate in non-complicated group was 17.5% (p=0.014).

In terms of surgical technique, 145 (91.8%) patients were operated with laparoscopic surgery, and only five (3.2%) patients were operated with open surgery. In the remaining 7 of 8 patients, because of difficulty at dissection, laparoscopic surgery was switched to open surgery. In one patient, the operation was completed via open surgery because of mesenteric vascular bleeding due to iatrogenic trocar injury. We found that open surgery did not increase the morbidity rate, which was 30.8% in the open surgery arm and 19.3% in the laparoscopic surgery arm (p=0.301). Similarly, the incision type did not affect the morbidity rate (p=0.510). There was no correlation between timing of the operation (day vs night) and morbidity (p=0.664). Table 3 shows operative and postoperative factors of the patients.

Postoperative antibiotherapy use was classified as single antibiotherapy use or combined antibiotherapy use. Single antibiotics were cephalosporins (cefazolin sodium or ceftriaxone), 5-nitroimidazole group (metronidazole) and carbapenem group (ertapenem). In the combined antibiotic group there were two combinations: cefazolin with metronidazole or ceftriaxone with metronidazole.

In the single antibiotic group there was a significant difference (p=0.010) in morbidity rates: 0% in the cefazolin arm, 11.1% in ceftriaxone arm, 78.6% in ertapenem arm, and 100% in metronidazole arm. Total morbidity rate in the single antibiotic group was 43.3%. In the combined antibiotic group, there was no difference in morbidity rate between the two arms (p=0.22) However, the morbidity associated with single antibiotic usage was significantly higher at 43.3% compared to the same rate for combined antibiotic use which was 14.8% (p<0.001).

There were five histopathological diagnoses reported: AA (11.4%); AA with peri-appendicitis (16.5%); AA with serositis (4.4%); AA with localized peritonitis (66.4%); and perforated appendicitis (1.3%). No correlation was found between appendix length, diameter, simultaneously resected omental volume, presence of perforation at appendix specimen and morbidity (p>0.05).

Table 2. Comparison of groups according to laboratory and screening tools parameters

Parameters	Morbidity (+) (n=32)	Morbidity (-) (n=126)	p-value
Laboratory values on admission (mean)			
- WBC (10^3/mm^3)	14.8	14.5	0.770*
- Hb (g/dL)	14.5	14.6	0.839**
- Platelet (10^3/mm^3)	268.0	257.3	0.523*
- Neutrophil (%)	76.4	76.7	0.746*
- Lymphocyte (%)	16.4	16.5	0.552*
- ALT (U/L)	31.9	22.2	0.082*
- AST (U/L)	24.7	21.8	0.119*
- Creatine (mg/dL)	0.82	0.78	0.243*
- CRP (mg/L)	11.31	7.73	0.879*
- INR	1.35	1	0.495*
USG criterias (n=108)			
Appendix diameter (n=78) (mean, mm)	9.2	8.95	0.619*
Acute appendicitis, n (%)			0.068***
- Positive or suspicious	21 (24.1)	66 (75.9)	-
- Negative	1 (4.8)	20 (95.2)	-
Fecalith, n (%)			0.600***
- Yes	2 (33.3)	4 (66.7)	-
- No	20 (19.6)	82 (80.4)	-
Abdominal fluid, n (%)			0.461***
- Yes	4 (30.8)	9 (69.2)	-
- No	18 (19)	77 (81)	-
CT criteria (n=89)			
Mean appendix diameter (n=74), (mm)	11.54	10.63	0.252*
Acute appendicitis, n (%)			>0.999***
- Positive or suspicious	14 (18)	64 (82)	-
- Negative	2 (18.1)	9 (81.9)	-
Fecalith, n (%)			>0.999***
- Yes	3 (5)	57 (95)	-
- No	13 (44.9)	16 (55.1)	-
Abdominal fluid, n (%)			>0.999***
- Yes	3 (18.75)	13 (81.25)	-
- No	13 (17.8)	60 (82.2)	-
Diagnosis before surgery, n (%)			**0.014*****
- Non-complicated AA	25 (17.5)	118 (82.5)	-
- Complicated AA	7 (46.7)	8 (53.3)	-

WBC: White blood cell count, Hb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CRP: C-reactive protein, INR: International normalized ratio, USG: Ultrasonography, CT: Computed tomography, AA: Acute appendicitis, *: Mann-Whitney U test result, **: Independent t-test result, ***chi-square test

Table 3. Comparison of the groups with (+) and without (-) morbidity in terms of intraoperative and postoperative factors

Parameters	Morbidity (+) (n=32)	Morbidity (-) (n=126)	p-value
Operation time, n (%)			0.664*
- 08:00 a.m. - 11:59 p.m.	30 (20)	120 (80)	-
- 12:00 a.m. - 07:59 a.m.	2 (25)	6 (75)	-
Operation type, n (%)			0.301*
- Laparoscopic	28 (19.3)	117 (80.7)	-
- Open	4 (30.8)	9 (69.2)	-
Type of incision, n (%)			0.510**
- 3 trocar	28 (19.3)	117 (80.7)	-
- McBurney	3 (37.5)	5 (625)	-
- UMI + LMI	1 (20)	4 (80)	-
Type of antibiotics after surgery (single vs combine)			**<0.001***
Single antibiotherapy, n (%)			**0.010****
- Cefazolin IV	0 (0)	6 (100)	-
- Ceftriaxone IV	1 (11.1)	8 (88.9)	-
- Metronidazole IV	1 (100)	0 (0)	-
- Ertapenem IV	11 (78.6)	3 (21.4)	-
Combine antibiotherapy, n (%)			0.218**
- Ceftriaxone IV with metronidazole IV	13 (12.7)	89 (87.3)	-
- Cefazolin IV with metronidazole IV	6 (23)	20 (77)	-
Pathological specimen evaluation			
Mean appendix length (cm)	4.48	4.94	0.612***
Mean appendix diameter (cm)	0.99	1.05	0.615***
Mean resected omental volume (cm^3)	13.8	12.41	0.096***
Presence of appendix perforation, n (%)			0.204*
- Yes	3 (37.5)	5 (625)	-
- No	29 (19.3)	121 (80.7)	-
Pathological diagnosis			0.580**
- AA with peri appendicitis	2 (7.7)	24 (92.3)	-
- AA with localized peritonitis	25 (23.8)	80 (76.2)	-
- AA with serositis	1 (14.3)	6 (85.7)	-
- AA	4 (22.2)	14 (77.8)	-
- Congested appendix	0 (0)	2 (100)	-
Mean hospital stay (days)	5.8	3.3	**<0.001*****

UMI: Upper midline incision, LMI: Lower midline incision, IV: Intravenous, AA: Acute appendicitis, *chi-square test, **Likelihood ratio test, ***Mann-Whitney U test result

Postoperative complications after appendectomy are shown in Table 4. In this study, the most common complications were trocar site infection (10.1%) and intra-abdominal infection (3.8%). In the morbidity (+) group, there was a longer hospital stay (5.78 days) compared to 3.3 days in the morbidity (-) group (p<0.001). Notably, the mortality rate during the study period for AA was 0%.

Regression analysis showed that preoperative fever (OR: 3,000, 95% CI: 1,344-6,697; p=0.007), time between onset of symptoms and presentation at hospital (OR: 1,108, 95% CI: 1,026-1,196; p=0.009), preoperative diagnosis (OR: 4,130, 95% CI: 1,372-12,376; p=0.012), postoperative antibiotic type (OR: 4,387, 95% CI: 1,836-10,483; p<0.001) and length of hospital stay (OR: 1,546, 95% CI: 1,280-1,866; p<0.001) were associated with morbidity.

Table 4. Postoperative complications and treatments methods

Complication	Treatment	n (%)
SSI (trocar)	Drainage and daily cleaning	16 (10.1)
Intra-abdominal abscess		6 (3.8)
- Localized at RLQ	Spontaneous regression (antibiotherapy)	5 (3.2)
- Localized right flank	Surgical drainage	1 (0.6)
Ileus	Medical	4 (2.5)
Seroma (trocar)	Drainage and daily cleaning	3 (1.9)
Port hernia (umbilical)	Hernia repair	1 (0.6)
Hematoma (intra-abdominal)	Spontaneous regression	1 (0.6)
Hematoma (trocar)	Re-suturation	1 (0.6)
Total	-	32 (20.2)

SSI: Surgical site infection, RLQ: Right lower quadrant

Discussion

AA is an emergency surgical problem affecting all age groups of patients. Most of the patients present to emergency clinics with a typical history and physical examination findings. While laboratory tests and imaging investigations help the diagnosis in most patients, AA cannot be diagnosed in a small number of patients, despite all examinations.

Morbidity due to AA has been evaluated by many studies. While most authors showed that complications were higher in elderly patients,[5,6,7,8] Bos et al.[9] showed that younger patients were susceptible to morbidity. In addition, complications are more common in males.[7,10,11] However, in this study, the gender and age of the patients did not affect morbidity.

Preoperative symptoms and signs are the main predictors at diagnosis of AA. Abdominal migratory pain, lack of appetite, and vomiting and nausea are the main complaints, and these complaints should be investigated carefully. Right lower quadrant tenderness, rebound, and fever are present in most patients. While tenderness and rebound can be seen in each period of the AA, preoperative fever has been reported to indicate complicated AA. Thus, fever has previously been reported as a predictive factor for morbidity, and our results are consistent with this.[7,12]

Early diagnosis of AA is important because the possibility of appendix perforation increases as diagnosis delay increases. Delay in appendectomy affects both the possibility of intra-abdominal abscess and postoperative complications.[13] However, there are studies indicating that delayed appendectomy does not affect morbidity.[14,15] Other studies have shown that early appendectomy reduces the risk of perforation and surgical site infections.[16,17] Our findings support the reports of delayed hospital admission increasing morbidity.

Complicated appendicitis is defined as perforated appendicitis, peri-appendicular abscess or peritonitis, which is defined as acute inflammation of the peritoneum secondary to appendiceal infection. These diagnoses are investigated, but may not be identified, by imaging tools such as USG and CT.[18] In the present study, the morbidity rate of the complicated group was 46.7% but only 17.5% in the non-complicated group which is in keeping with earlier reports of complicated appendicitis being related to morbidity.[5,9,19]

Laboratory parameters are useful to confirm diagnosis. The main laboratory findings are increased WBC count, presence of leukocytosis, WBC shift to the left, and increased CRP levels. Leukocytosis and shift of WBC to the left are also Alvarado score parameters. Increased WBC count was a predictor of morbidity in the study of Andert et al.[5] and shift of WBC to the left was a predictor in the study of Sheu et al.[7], while increased CRP levels was associated with morbidity in several studies.[5,8] In contrast, in the present study, no relationship was found between laboratory parameters and morbidity.

There is no definite consensus that operative factors affect morbidity. However, many studies have shown that operative factors play a role in morbidity. Open surgery,[20,21,22,23,24] conversion to open surgery,[5] operation at night,[5] and adverse events[19] were reported to have a negative effect on morbidity. However, in contrast to this, no operative factor was associated with increased morbidity in this study.

Postoperative factors also play a major role on the occurrence of morbidity. Longer hospital stay,[6,8] unsuitable or longer antibiotics usage,[6] and severity of pathological findings had a negative effect on morbidity. In our study longer hospital stay was associated with higher morbidity while single antibiotic use had a significant effect on the likelihood of morbidity.

Conclusion

The aim of this study was to analyze risk factors associated with postoperative complications after appendectomy. The overall morbidity rate was 20.2% with no mortality. Preoperative fever, delayed hospital admission, complicated appendicitis, and single antibiotic use all increased morbidity while prolonged hospital stay was associated with morbidity. Although there is no factor increasing the likelihood of morbidity that is amenable to alteration, we recommend the use of combined antibiotics in the treatment of AA patients to reduce morbidity and to discharge the patients as early as possible.

Ethics

Ethics Committee Approval: Ethics committee approval was received from Non-invasive Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital (approval number: 2021/04-72).

Informed Consent: As the study was designed retrospectively, anonymized data was collected from clinical archives and no individual patient consent was required.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.K., S.B., Concept: T.K., S.B., Design: T.K., Data Collection or Processing: T.K., S.B., Analysis or Interpretation: T.K., S.B., Literature Search: T.K., S.B., Writing: T.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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