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Comparison of Splenectomy Indications According to Clinicopathological Variables

Splenektomi Endikasyonlarının Klinikopatolojik Değişkenlere Göre Karşılaştırılması

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ÖZET
Amaç: Bu çalışmanın amacı, benign ve malign hastalıklar nedeniyle splenektomi uygulanan olguların ameliyat öncesindeki, ameliyat sırasındaki ve ameliyat sonrasındaki farklılıklarını değerlendirmektir.
Materyal ve Metot: Ocak 2015-Ocak 2021 tarihleri arasında üçüncü basamak bir sağlık kuruluşunda splenektomi yapılan yetişkin hastalar (18 yaş ve üzeri) retrospektif olarak tarandı. Hastalar, benign hastalıklar nedeniyle splenektomi uygulanan hastalar (n=35) ve malignite cerrahisi sırasında splenektomi uygulanan hastalar (n=45) olmak üzere iki ana gruba ayrıldı. Ayrıca benign grup; travma nedeniyle, hematolojik hastalıklar nedeniyle ve kist nedeniyle cerrahi uygulanan olgular olmak üzere 3 alt gruba ayrıldı. Hastaların tıbbi kayıtlarından elde edilen klinikopatolojik değişkenler hem ana gruplarda hem de alt gruplar arasında karşılaştırıldı**.**
Bulgular: Çalışma kriterlerine uyan 80 hastanın yaş ortalaması 53.47±18.28 (18-86) olup; 44 hasta (%55) kadındı. Hastaların ortalama yaşı, laparoskopik cerrahi oranı, elektif cerrahi oranı, postoperatif komplikasyon oranı, eritrosit süspansiyonu ve taze donmuş plazma ihtiyacı, hastanede kalış süresi ve yoğun bakımda kalış süresi malignite grubunda daha yüksekti. Ayrıca son yıllarda malignite nedeniyle splenektomi olguları oransal olarak daha fazla idi. Çalışmanın bir diğer önemli sonucu da travmatik splenektomilerin daha uzun hastane yatışı gerektirmesi ve bu hastaların klinik yönetiminin diğer iyi huylu splenektomi nedenlerine göre daha zor olması idi.
Sonuç: Tüm splenektomi olguları arasında malign splenektomi olguları ve benign splenektomi olguları arasında travmatik splenektomi uygulanan olgular hastanede kalış süresinin daha uzun olması, kan ürünlerine daha fazla ihtiyaç duyulması ve morbidite oranlarının yüksek olması nedeniyle yönetimi zordur.

Anahtar Kelimeler: Malignite, Morbidite, Mortalite, Splenektomi, Travma.

ABSTRACT
Objective: The aim of this study is to evaluate the preoperative, intraoperative and postoperative differences in cases who underwent splenectomy for benign and malignant diseases.
Material and Method: Adult patients (18 years and older) who underwent splenectomy in a tertiary health center between January 2015 and January 2021 were searched retrospectively. The patients were divided into two main indication groups: patients who underwent splenectomy for benign diseases (n=35) and patients who underwent splenectomy during malignancy surgery (n=45). In addition, the benign group was divided into 3 subgroups as patients who underwent surgery due to trauma, hematological diseases and cysts. Clinicopathological variables obtained from the patients' medical records were compared between both main groups and subgroups.
Results: The mean age of 80 patients who met the study criteria was 53.47±18.28 (18-86), and 44 patients (55%) were female. The mean age of the patients, laparoscopic surgery rate, elective surgery rate, postoperative complication rate, need for erythrocyte suspension and fresh frozen plasma, length of hospital stay and length of stay in the intensive care unit were higher in the malignancy group. In addition, splenectomy cases due to malignancy were proportionally higher in recent years. Another important result of the study was that traumatic splenectomies require longer hospitalization, and the management of these patients' clinics is more difficult than other benign splenectomy causes.
Conclusion: Among all splenectomy cases, malignant splenectomy cases and benign splenectomy cases who underwent traumatic splenectomy are difficult to manage because of longer hospital stay, more need for blood products, and high morbidity rates.

Keywords: Malignancy, Morbidity, Mortality, Splenectomy, Trauma.

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INTRODUCTION

Splenectomy is the surgical procedure to remove the spleen for various indications. Indications for splenectomy can be evaluated in two main categories: benign splenectomy and malignant splenectomy. Benign splenectomy is applied for penetrating trauma, blunt trauma, indirect trauma, spleen cyst, and hematological diseases. On the other hand, malignant splenectomy is performed to treat or stage primary splenic malignancy, metastatic splenic malignancy and intra-abdominal organ malignancies (Ahmad et al., 2017).

As the immunological functions of the spleen became clear, splenectomy was not performed as often as before. Because of its important role, the spleen-sparing approach was developed, and more conservative treatments was started to prefer (Buffet et al., 2006). However, inevitable surgical indications remain up to date. One of the inevitable indications for splenectomy is malignancy especially in proximal gastric cancers and distal pancreatic tumors. Besides, hematological diseases unresponsive to medical treatments still required splenectomy such as immune thrombocytopenic purpura, hereditary spherocytosis and thrombotic thrombocytopenic purpura. One of the other inevitable splenectomy indications is spleen trauma. Although spleen-preserving approaches are dominant in the early stages of spleen trauma, splenectomy is needed in advanced traumas because it will cause vital losses (Mufti et al., 2007).

The prevalence of overall morbidity associated with splenectomy ranges between 21.8% and 52% (Balague et al., 2004; Arshed et al., 2011). On the other hand, according to a large cohort study using a nationwide trauma database, the overall mortality was 6.1% (Hamlet et al., 2012).

Since the subject of splenectomy has started to take an important place in cancer surgery more than benign indications, it is aimed to compare the cases of splenectomy performed during malignancy and splenectomy performed during benign diseases and to emphasize what will be encountered in which cases. Therefore, in this study, it is aimed to compare splenectomy cases performed for benign and malignant diseases according to clinicopathological features.

MATERIAL and METHOD

Patients who were operated for splenectomy between January 2015 and January 2020 in Erzurum City Hospital were searched retrospectively. The study excluded the patients in the pediatric age group (0–18 years) and those who were diagnosed and treated at external centers and then referred to our clinic. A total of 80 patients were enrolled in the study after fulfilling the desired inclusion criteria via purposive sampling technique. 80 patients were divided into two main groups according to splenectomy indications: patients operated due to benign diseases and patients operated due to malignant diseases. In addition, patients operated due to benign diseases divided into three subgroups as trauma, hematological diseases and splenic cyst.

Data Collection

Age, gender, primary indication for splenectomy, surgical emergency, type of surgery, year of splenectomy, amount of erythrocyte suspension replacement and fresh frozen plasma replacement during hospitalization, and postoperative morbidity and mortality were searched. Additionally, length of hospital stay (at intensive care unit and total) were evaluated. Main groups and subgroups were compared with suitable statistical tests.

Statistical Analysis

Statistical evaluation was made with SPSS v22.0 (IBM, Armonk, NY, USA). The normality distribution of quantitative variables was checked with Shapiro-Wilk test, histograms, Q-Q plot, and box plot charts. Mann-Whitney U test and Independent Sample T test were used according to the results of the normality tests. In addition, Chi-Square test and Likelihood Ratio Test were used to compare qualitative variables. In addition, Kruskal Wallis Test was

used for multi-group statistical comparison because data did not meet the parametric test assumptions. A p-value below 0.05 was considered statistically significant.

This retrospective study was conducted after the local ethical committee's approval (Decision: 2021/11-179).

RESULTS

Between January 2015 and January 2021, 80 patients underwent splenectomy. The mean age of all patients was 53.47±18.28 (18-86), and 44 (55%) patients were female. Splenectomy was performed in 45 (56.3%) patients due to malignancy and in 35 (43.8%) patients due to benign diseases. There was no case of splenectomy due to primary spleen malignancy or metastatic spleen malignancy, and all malignant splenectomy cases were performed during intra-abdominal cancer surgery. On the other hand, benign diseases were divided into 3 subgroups: trauma in 16 patients (20%), hematological diseases in 13 patients (16.3%), and splenic cyst in 6 patients (7.5%). No additional organ resection was performed in splenectomy performed for benign diseases. The clinical variables of the patients and comparison of these variables according to benign splenectomy and malign splenectomy are shown in Table 1.

Table 1. Clinicopathologic, Treatment, and Outcome Variables of 80 Patients with Splenectomy and Comparison of Main Indication Groups.

Clinical Parameters	All Cases n=80 (mean±sd)(Min-max) or n (%)	Main Indication Groups		p value
		Benign n=35 Mean rank or n (%)	Malignant n=45 Mean rank or n (%)	
Age	53.47±18.28 (18-86)	25.60	52.09	**<0.001***
Gender				0.571**
Male	36 (45%)	17 (47.2%)	19 (52.8%)	
Female	44 (55%)	18 (40.9%)	26 (59.1%)	
Surgical Emergency				**<0.001****
Elective	62 (77.5%)	19 (30.6%)	43 (69.4%)	
Urgent	18 (22.5%)	16 (88.9%)	2 (11.1%)	
Type of Surgery				**<0.001****
Open	66 (82.5%)	21 (31.8%)	45 (68.2%)	
Laparoscopy	14 (17.5%)	14 (100%)	0 (0%)	
Years				**<0.001*****
2015-2016	8 (10%)	6 (75%)	2 (25%)	
2016-2017	8 (10%)	5 (62.5%)	3 (37.5%)	
2017-2018	7 (8.8%)	7 (100%)	0 (0%)	
2018-2019	14 (17.5%)	11 (78.6%)	3 (21.4%)	
2019-2020	26 (32.5%)	5 (19.2%)	21 (80.8%)	
2020-2021	17 (21.3%)	1 (5.9%)	16 (94.1%)	
ES replacement (units)	5.26±5.23 (0-29)	26.27	51.57	**<0.001***
FFP replacement (units)	20.98±21.83 (0-122)	20.84	55.79	**<0.001***
Overall Morbidity				**0.028****
Yes	29 (36.3%)	8 (27.6%)	21 (72.4%)	

No	51 (63.7%)	27 (52.9%)	24 (47.1%)	
Overall Mortality				0.455**
Yes	8 (10%)	2 (25%)	6 (75%)	
No	72 (90%)	33 (45.8%)	39 (54.2%)	
LOS (days)	14.66±9.99 (1-48)	26.00	51.78	**<0.001***
ICU stay (days)	6.67±7.68 (0-48)	24.70	52.79	**<0.001***

ES: Erythrocyte Suspension, FFP: Fresh Frozen Plasma, LOS: Length of Stay, ICU: Intensive Care Unit. *Mann Whit-ney U test, **Chi-square test,***Likelihood Ratio test

43 patients (53.8%) were operated under elective conditions, while only 14 splenectomy cases (17.5%) were done via laparoscopy. While the number of splenectomies did not exceed 10 before 2018, the number of splenectomies increased after 2018. Malignancy operations have been identified as the main factor in this increase.

Postoperative complications after splenectomy were seen in 29 patients (36.5%). Pulmonary complications, the most commonly seen complications, were seen in 13 patients (16.25%) in this study. Postoperative complications are seen in Table 2. Postoperative mortality was seen in 8 patients (10%). 2 patients died from gastrointestinal bleeding, 2 from enterocutaneous fistula, one from sepsis, one from early postoperative period cardiac arrest, one from hepatorenal syndrome, one from multi-trauma, and one from cerebrovascular disease.

Table 2. Postoperative Complications.

Postoperative Complications	**n (%)**
Atelectasis	6 (7.5%)
Pleural effusion	5 (6.3%)
Surgical site infection	4 (5%)
Pneumonia	2 (2.5%)
Enterocutaneous fistula	2 (2.5%)
Cerebrovascular disease	2 (2.5%)
Intra-abdominal hematoma	2 (2.5%)
Ileus	2 (2.5%)
Atrial fibrillation	1 (1.3%)
Deep vein thrombosis	1 (1.3%)
Gastrointestinal hemorrhage	1 (1.3%)
Pneumothorax	1 (1.3%)
Total	29 (36.3%)

Comparison of splenectomy main groups and subgroups

The mean age of the patients (p<0.001), laparoscopic surgery rate (p<0.001), elective surgery rate (p<0.001), postoperative complication rate (p=0.028), need for erythrocyte suspension (p<0.001) and fresh frozen plasma (p<0.001), hospital stay (p<0.001), and length of intensive care unit stay (p<0.001) were higher in the malignancy group. In addition, splenectomy due to malignancy have been performed more frequently in recent years (p<0.001). While the rate of malignant splenectomy has increased in the last 2 years of the study, the rate of splenectomies due to the other indications has decreased. Comparison of main groups is shown in Table 1.

In the subgroup analysis of the patients who underwent splenectomy due to benign diseases, open surgery rate (p<0.001), emergency surgery rate (p<0.001), postoperative complication rate (p=0.012), need for erythrocyte suspension (p<0.001) and fresh frozen plasma (p<0.001), hospital stay (p=0.032), and length of intensive care unit stay (p=0.002) were higher in the traumatic splenectomy group. However, no difference was observed in terms of age, gender and mortality. Comparison of subgroups is shown in Table 3.

Table 3. Comparison of Benign Indication Subgroups.

Clinical Parameters	Benign Indication Subgroups			p value
	Trauma (n=16)	Hematological (n=13)	Splenic Cyst (n=6)	
Age (mean rank)	20.41	13.38	21.58	0.119*
Gender				0.307**
Male	10 (58.8%)	5 (29.4%)	2 (11.8%)	
Female	6 (33.3%)	8 (44.4%)	4 (22.2%)	
Surgical Emergency				**<0.001****
Elective	0 (0%)	13 (68.4%)	6 (31.6%)	
Urgent	16 (100%)	0 (0%)	0 (0%)	
Type of Surgery				**<0.001****
Open	16 (76.2%)	1 (4.8%)	4 (19%)	
Laparoscopy	0 (0%)	12 (85.7%)	2 (14.3%)	
Year				**0.002****
2015-2016	6 (100%)	0 (0%)	0 (0%)	
2016-2017	1 (20%)	1 (20%)	3 (60%)	
2017-2018	3 (42.9%)	2 (28.6%)	2 (28.6%)	
2018-2019	2 (18.2%)	9 (81.8%)	0 (0%)	
2019-2020	3 (60%)	1 (20%)	1 (20%)	
2020-2021	1 (100%)	0 (0%)	0 (0%)	
ES replacement (mean rank)	25.72	10.62	13.42	**<0.001***
FFP replacement (mean rank)	24.81	11.31	14.33	**<0.001***
LOS (mean rank)	22.31	12.35	18.75	**0.032***
ICU stay (mean rank)	24.41	12.12	13.67	**0.002***
Overall Morbidity				**0.012****
Yes	6 (75%)	0 (0%)	2 (25%)	
No	10 (37%)	13 (48.1%)	4 (14.8%)	
Overall Mortality				0.194**
Yes	2 (100%)	0 (0%)	0 (0%)	
No	14 (42.4%)	13 (39.4%)	6 (18.2%)	

ES: Erythrocyte Suspension, FFP: Fresh Frozen Plasma, LOS: Length of Stay, ICU: Intensive Care Unit. * Kruskal Wallis test, **Chi-square test.

DISCUSSION

Splenectomy is a commonly performed operation for various conditions, including trauma, hematological diseases, and malignant diseases (Kristinsson et al., 2014; Ahmad et al., 2017). Penetrating trauma such as gunshot wounds, blunt trauma such as a direct blow to the left upper quadrant, and indirect trauma such as a tear in the splenic capsule during colonoscopy or traction on the spleno-colic ligament are mechanisms of injury. Many hematological diseases such as hemolytic anemia and idiopathic thrombocytopenic purpura are treated with splenectomy due to medical treatment resistance (Hill et al., 2004).

Malignancies involving the spleen can be grouped into lymphoproliferative diseases, myeloproliferative diseases, metastatic diseases, and primary (non-lymphoma) malignancies. Hematological malignant diseases are the leading indication for splenectomy among the malignancy cases. Primary cancers that metastasize to the spleen include colonic, gastric, ovarian, endometrial, lung, breast, prostatic, melanoma, and esophageal (Ahmad et al., 2017). Hydatid splenic cyst is also a rare cause for splenectomy.

Past studies indicate that traumatic splenic injury is the most common indication for splenectomy (Cadeddu et al., 2006; Beuran et al., 2012). In the present study, different from the literature, we found that the number of cases who underwent splenectomy due to malignancy increased over the years. However, among the benign diseases, trauma was found to be the main indication for splenectomy.

Splenectomy is frequently performed via laparoscopy; however, some patients still undergo open splenectomy depending on patient-specific factors and surgeon experience (Ardestani and Tavakkoli, 2013). While splenectomy was performed with open surgery in the past, surgical techniques gained a new dimension with the introduction of laparoscopic splenectomy in 1991. Nowadays, minimal invasive surgery has played an important role in splenectomy with the increase in laparoscopic facilities and the increase in surgical experience. Although spleen size is considered a barrier to laparoscopic surgery, Park et al. recommended open splenectomy for spleen sizes over 25 cm in their studies (Park et al., 1999). In some other studies, it has been reported that massive splenomegaly is not a contraindication for laparoscopic splenectomy (Erözgen et al., 2013).

There are several prospective studies comparing open surgery and laparoscopic surgery. Laparoscopic surgery results in less morbidity and mortality (Bulus et al., 2013; Bonnet et al., 2017). In addition, retrospective studies have shown that laparoscopic surgery is advantageous in postoperative complications (Park et al., 1999). In our study, morbidity was higher in the open surgery group, but no difference was found between open and laparoscopic surgery in terms of mortality. While laparoscopic surgery was applied in 85.7% of hematological diseases, the use of laparoscopic surgery in spleen cysts was 14.3%. Laparoscopic splenectomy was not performed in either trauma patients or patients with malignancies. However, open surgery was used in all splenectomy indications, but mostly performed in malignancy cases ($p<0.001$).

Splenectomy has been shown to cause pulmonary, hemorrhagic, infection, pancreatic, and thromboembolic complications (Santos et al., 2014; Wang et al., 2013). Of these, left lower lobe pneumonia and atelectasis are the most commonly reported complications (Misiakos et al., 2017). In another study, the perioperative morbidity was increased only by blood loss and intra-operative adverse effects (Wysocki et al., 2018). In the study of Moorjani et al., blood loss is the most important prognostic factor for postoperative complications after non-traumatic splenectomies. Pneumonia is the main prognosis factor for perioperative mortality (Moorjani et al., 2014). Similar to the literature, postoperative pulmonary complications were the most common complications. In addition, morbidity after splenectomy was more common in advanced age, patients operated for malignancy, and patients operated with open surgery. Patients with morbidity required more erythrocyte

suspension and fresh frozen plasma, and the development of morbidity extended both the length of hospital stay and the duration of intensive care follow-up.

In the study of Ugur et al., mortality after splenectomy was only affected from emergency surgery (Ugur et al.). A previous study comparing laparoscopic with open splenectomy among 1781 patients demonstrated that laparoscopic splenectomy was associated with fewer complications, less blood transfusion, and lower operative mortality (Musallam et al., 2013). Also, in studies, the indication of splenectomy is the most predictive risk factor for the development of post-splenectomy mortality (Weledji, 2014; Leone and Pizzigallo, 2015). However, in our study, emergency splenectomy, splenectomy indication, and type of surgery did not affect mortality. Also, patients with mortality needed more erythrocytes and fresh frozen plasma.

Due to the immune functions of the spleen, its immunological importance has increased in recent years. However, surgical treatment is the curative treatment in severe traumas, hematological diseases resistant to medical treatment, and large cysts. In addition, since the positive effect of adding splenectomy to malignancy surgeries on survival has been proven in recent years, adding splenectomy to malignancy cases has become a surgical option. Therefore, splenectomy has started to be applied in malignant cases and the main splenectomy indication has been malignancy. In the present study, it was found that morbidity rate, need for erythrocyte suspension, need for fresh frozen plasma, and hospital stay were increased in malignant splenectomy cases. Hence, both the case management is difficult and the length of stay in the hospital is prolonged. In addition, splenectomy due to traumas are more difficult to manage among the benign splenectomy cases. We attribute all these results to extensive organ resections during malignancy surgery and to massive intra-abdominal bleeding in traumatic splenectomies.

Patient's Consent

Informed consent was obtained from the patient regarding publication of data.

Ethical Approval

Ethical approval was obtained from the local Ethical Committee's approval (Decision: 2021/11-179).

Conflict of Interest

The authors declared no conflict of interest.

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