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Original Article

Splenectomy perspective for non-malignant hematological disorders: A cross-sectional study in the Eastern Province of KSA

Mortadah H. Alsalman, MD [a], Faisal A. Al Jabr [b,*], Samma T. Eraqe [c], Sayed I. Ali, PhD [d] and Abdallah Essa, MD [a,e]

[a] *Internal Medicine Department, College of Medicine, King Faisal University, Al-Ahsa, KSA*
[b] *College of Medicine, King Faisal University, Al-Ahsa, KSA*
[c] *Arabian Gulf University, Manama, Bahrain*
[d] *Family Medicine Department, College of Medicine, King Faisal University, Al-Ahsa, KSA*
[e] *Tropical Medicine Department, Faculty of Medicine, Menoufia University, Shebin-Elkom, Egypt*

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الملخص

أهداف البحث: يعتبر استئصال الطحال طريقة علاجية للعديد من أمراض الدم، على الرغم من احتمال حدوث المضاعفات. قيمت هذه الدراسة تأثير استئصال الطحال على اضطرابات الدم المختلفة ودور التدابير الوقائية على نتائج ما بعد الجراحة.

طرق البحث: أجريت هذه الدراسة المقطعية في المملكة العربية السعودية على مرضى بالغين يعانون من اضطرابات الدم غير الخبيثة وخضعوا لاستئصال الطحال.

النتائج: فحصت هذه الدراسة ١٧٩مريضا يعانون من اضطرابات الدم المختلفة، وخضع ٣٨ منهم (21.1٪) لاستئصال الطحال. من بين هؤلاء المرضى، أكثر من الثلثين (73.7%) خضعوا لعملية استئصال الطحال المفتوح. كان معدل الإقامة في المستشفى يومين إلى سبعة أيام، مع عدم وجود فرق كبير بين المنهجين المفتوح أو بالمنظار. لاحظ حوالي ٩٥٪ من المرضى تحسنا عاما في حالتهم بعد استئصال الطحال. ومع ذلك، أبلغ (٢٦,٣٪) من المرضى عن تكرار المرض أو الحاجة إلى المزيد من العلاج بعد عام أو أكثر من استئصال الطحال. حوالي ١٦٪ كان لديهم زيادة في حدوث المضاعفات المعدية بعد الجراحة، خاصة في مرض فقر الدم المنجلي ومرضى بيتا الثلاسيميا. أكثر من نصف الذين أصيبوا بمضاعفات لم يتلقوا التطعيم قبل الجراحة، بالمقارنة مع ٤٤,٤٪من المرضى الذين تم تطعيمهم والذين عانوا من مضاعفات.

الاستنتاجات: يعتبر استئصال الطحال خط علاج شامل لمعظم أمراض الدم غير الخبيثة. على الرغم من كونه علاجا فعالا، إلا أنه لا يزال غير واضح لماذا يمكن أن يكون لدى المرضى الذين يعانون من نفس المرض استجابات مختلفة. تعد العدوى من المضاعفات الشائعة بعد الجراحة، واللقاحات غير مستخدمة. تؤكد هذه الدراسة على دور تثقيف المريض، التطعيمات المجدولة، والاختيار الصحيح للمرضى في استخدام استئصال الطحال لعلاج أمراض الدم غير الخبيثة.

الكلمات المفتاحية: استئصال الطحال؛ أمراض الدم؛ النتائج؛ المنطقة الشرقية؛ المملكة العربية السعودية

Abstract

Objectives: Splenectomy is considered a therapeutic modality for several hematological diseases, although complications are possible. This study assessed the effects of splenectomy on various hematological disorders and the roles of prophylactic measures on postoperative outcomes.

Methods: This was a cross-sectional study performed in KSA on adult patients with underlying non-malignant hematological disorders who had undergone splenectomy.

Results: This study examined 179 patients with various hematological disorders, 38 (21.1%) of whom had undergone a splenectomy. Of those 38 patients, more than two-thirds (73.7%) had an open splenectomy. The average hospital stay was 2–7 days, and no significant difference was observed between the open and laparoscopic approaches. Approximately 95% of the patients showed overall improvements in their condition after splenectomy. However, 26.3% of patients reported a

* Corresponding address: College of Medicine, King Faisal University, Al-Ahsa, Al Hafouf, 31982, KSA.
E-mail: Faisal-aj@hotmail.com (F.A. Al Jabr)

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recurrence or need for further treatment 1 year or more after splenectomy. Approximately 16% of patients had an increased incidence of postoperative infectious complications, particularly patients with sickle cell disease and beta thalassemia. More than half the patients who developed complications had not received vaccination preoperatively, whereas 44.4% of vaccinated patients experienced complications ($p = 0.04$).

Conclusion: Splenectomy is considered a universal line of treatment for most non-malignant hematological diseases. Although splenectomy is an effective treatment, the reasons why patients with the same disease can have different responses remains unclear. Infection is a common postoperative complication, and vaccinations are underused. This study emphasizes the roles of patient education, scheduled vaccinations and proper selection of patients in the use of splenectomy for the treatment of non-malignant hematological diseases.

Keywords: Eastern Province; Hematological diseases; KSA; Outcomes; Splenectomy

Introduction

The spleen, one of the largest lymphatic organs involved in the function of the hematopoietic system, is responsible for filtering the blood and controlling the quality of red blood cells. It also has a unique immunological role in the recognition of antigens to be filtered from the blood.[1]

Splenectomy is a therapeutic modality used to treat several non-malignant hematological diseases under certain circumstances.[2,3] For example, in chronic immune thrombocytopenic purpura (ITP), splenectomy is indicated clinically for refractory ITP resistant to the first line treatment of corticosteroids; this treatment supports long term remission, by decreasing the destruction of platelets in the spleen.[2] For sickle cell disease (SCD), splenic dysfunction occurs because of congestion of red blood cells in the red pulp, thereby increasing the risk of infection by encapsulated bacteria, acute splenic sequestration, splenomegaly and hypersplenism necessitating spleen removal.[3] Furthermore, warm autoimmune hemolytic anemia is a type of AHA for which splenectomy may be indicated.[4] Other diseases in which splenectomy is a therapeutic modality include hereditary spherocytosis and thalassemias.[4,5]

Splenectomy can be performed through different modalities, including open abdominal or minimally invasive laparoscopy, the latter of which is the gold standard modality in some circumstances.[4,5]

However, several complications can develop post-splenectomy, including increased vascular complications, particularly venous thromboembolisms, which frequently occur after splenectomy in patients with thalassemia intermedia.[6] Moreover, complications such as infections are seen more often in patients who have undergone splenectomy, with an estimated incidence of 0.23–0.42% per year and a lifetime risk of 5%, than in the general population. Among all hematological diseases, sickle cell anemia and beta thalassemia major are associated with the highest risk of infection. However, with optimal pre-splenectomy prophylactic strategies, life-threatening infectious episodes can be markedly decreased.[7]

This study assessed the effectiveness of prophylactic measures in patients with non-malignant hematological disorders who had undergone splenectomy, as well as the effects of these measures on complications among the Eastern Province population in KSA. This study also sought to determine the effects of splenectomy on the clinical courses of these disorders.

Materials and Methods

Study design and setting

This cross-sectional (descriptive) study involved male and female patients with certain non-malignant hematological diseases who had undergone splenectomy in Eastern Province, KSA. The participants were Saudi patients over the age of 16 years who had one of the following non-malignant hematological diseases: SCD, alpha thalassemia, beta thalassemia, ITP or autoimmune hemolytic anemia. Participants who had undergone splenectomy because of non-hematological disorders, malignant hematological disorders or trauma were excluded. Patients were grouped according to their diagnoses and then divided into splenectomized and non-splenectomized groups. The data collection sheet was formulated according to several sources from the literature.[8–11] Descriptive statistics include the number, percentage, mean and standard deviation as appropriate. For comparisons, chi-square test or Fisher's exact test were applied. Data analyses were performed in SPSS version 21, Armonk, New York, IBM Corporation.

Results

This study examined 179 patients with various hematological disorders who were treated at hematology units in public hospitals and medical centers in the Eastern Province of KSA. As shown in Table 1, the most common age group was 18–29 years (31.3%). More than half the patients were women (51.4%), and 58.1% lived in Al Ahsa. More than half (53.6%) the patients had a high school education level or below. Furthermore, approximately half the participants had a normal BMI (47.4%), whereas the others were either overweight (29.3%) or obese (13.8%). In 36.8% of the patients, a diagnosis of hematological disease had been made before the age of 18 years. Most patients had SCD (75.4%) and had been diagnosed before the age of 18 years (82.1%). Socio-demographic variables, such as age group, sex, area of residence, educational level, marital status, BMI, associated blood diseases and age at diagnosis, did not significantly influence the splenectomy procedure (all P-values > 0.05).

Table 1: Socio-demographic characteristics of patients according to splenectomy status.

Study variables	Overall N (%) (n = 179)	Splenectomy		χ^2	P-value[a]
		Yes N (%) (n = 38)	No N (%) (n = 141)		
Age group					
• <18 years	23 (12.8%)	14 (36.8%)	07 (4.9%)	6.448	0.168
• 18–29 years	56 (31.3%)	11 (28.9%)	45 (31.9%)		
• 30–39 years	54 (30.2%)	11 (28.9%)	43 (30.4%)		
• 40–49 years	33 (18.4%)	02 (05.2%)	31 (21.9%)		
• ≥50 years	13 (07.3%)	00 (00.0%)	13 (09.2%)		
Sex					
• Male	87 (48.6%)	21 (55.3%)	66 (46.8%)	0.857	0.355
• Female	92 (51.4%)	17 (44.7%)	75 (53.2%)		
Residence area					
• Inside Al Ahsa	104 (58.1%)	18 (47.4%)	86 (61.0%)	2.282	0.131
• Outside Al Ahsa	75 (41.9%)	20 (52.6%)	55 (39.0%)		
Educational level					
• High school or below	96 (53.6%)	18 (47.4%)	78 (55.3%)	0.761	0.383
• Bachelor's degree or above	83 (46.4%)	20 (52.6%)	63 (44.7%)		
Marital status					
• Unmarried	72 (40.2%)	15 (39.5%)	57 (40.4%)	0.011	0.915
• Married	107 (59.8%)	23 (60.5%)	84 (59.6%)		
BMI (n = 116)					
• Underweight (<18.5)	11 (09.5%)	02 (05.4%)	09 (11.4%)	4.989	0.173
• Normal (18.5–24.9)	55 (47.4%)	21 (56.8%)	34 (43.0%)		
• Overweight (25–29.9)	34 (29.3%)	07 (18.9%)	27 (34.2%)		
• Obese (≥30)	16 (13.8%)	07 (18.9%)	09 (11.4%)		
Associated blood diseases					
• Sickle cell anemia	135 (75.4%)	29 (76.3%)	106 (75.2%)	5.909	0.315
• Alpha thalassemia	10 (05.6%)	03 (07.9%)	07 (05.0%)		
• Beta thalassemia	06 (03.4%)	03 (07.9%)	03 (02.1%)		
• Immune thrombocytopenic purpura	06 (03.4%)	01 (02.6%)	05 (03.5%)		
• Autoimmune hemolytic anemia	05 (02.8%)	01 (02.6%)	04 (02.8%)		
• Other	17 (09.5%)	01 (02.6%)	16 (11.3%)		
Age at diagnosis					
• <18 years	147 (82.1%)	34 (89.5%)	113 (80.1%)	1.776	0.183
• ≥18 years	32 (17.9%)	04 (10.5%)	28 (19.9%)		

[a] P-value calculated with chi-square test.

Characteristics of 38 patients (21.1%) who underwent splenectomy are described in Table 2.

The most common reason for not undergoing splenectomy was that the procedure had not been discussed by the treating physicians, which was followed by a fear of postoperative complications and the patients' believing that the procedure was not needed, as shown in Figure 1.

An open splenectomy was performed in more than two-thirds (73.7%) of patients in whom the entire spleen was removed. Moreover, splenectomy was performed electively in 73.7% of patients, and 63.2% of patients remained in the hospital for 2–7 days after the procedures. No significant difference was observed between the open and laparoscopic approaches, as shown in Table 3.

Furthermore, 81.6% of patients who underwent splenectomy required preoperative blood transfusion, compared with 50% who continued to have transfusions postoperatively. Additionally, 94.7% of patients showed an overall improvement in their condition after splenectomy. Eventually, 26.3% of patients relapsed after splenectomy and required further therapy. However, the duration of this interval was not significantly correlated with the underlying hematological disease (P-value >0.05), as shown in Table 4.

A total of 47.4% of patients were offered vaccines preoperatively, whereas 55.3% were offered vaccines postoperatively. Of note, more than half the patients (55.6%) who developed complications did not receive vaccination preoperatively, whereas 44.4% of patients received vaccination preoperatively (P-value 0.04), as shown in Table 5.

Additionally, 55.3% of patients were instructed to seek care at a nearby facility if they experienced fever symptoms in the postoperative period. Similarly, 81.6% of patients were offered antibiotics postoperatively, and 15.8% of patients had an increased incidence of infections, particularly pneumonia and surgical site infections. However, no significant relationship was observed between age group and the provision of antibiotics postoperatively ($\chi^2 = 4.791$; $p = 0.396$), as shown in Table 6.

In nine patients, complications developed after the procedure. Three patients developed surgical site infections, three developed pneumonia, and three had venous thrombosis. Approximately 88.9% of patients with complications received

Table 2: Characteristics of patients before and after the splenectomy procedure (n = 38).

Variables	N (%)
Age at diagnosis	
• <18 years	14 (36.8%)
• 18–29 years	11 (28.9%)
• 30–39 years	11 (28.9%)
• 40–49 years	02 (05.3%)
Type of splenectomy procedure	
• Laparoscopic splenectomy	10 (26.3%)
• Open splenectomy	28 (73.7%)
Type of procedure	
• Elective and discussed with patient	28 (73.7%)
• Emergency	10 (26.3%)
Duration of postoperative hospital stay	
• 2–7 days	24 (63.2%)
• 8 days or more	14 (36.8%)
Preoperative vaccination	
• Yes	18 (47.4%)
• No	20 (52.6%)
Postoperative regular vaccination	
• Yes	21 (55.3%)
• No	17 (44.7%)
Postoperative warning to visit doctor immediately for fever	
• Yes	21 (55.3%)
• No	17 (44.7%)
Number of preoperative blood transfusions	
• Never	07 (18.4%)
• Once per week	12 (31.6%)
• Once in 2 weeks	0
• Once in 3 weeks	04 (10.5%)
• Once in 4 weeks	11 (28.9%)
• More than once in 4 weeks	04 (10.5%)
Number of postoperative blood transfusions	
• Never	19 (50.0%)
• Once per week	08 (21.1%)
• Once in 2 weeks	01 (02.6%)
• Once in 3 weeks	03 (07.9%)
• Once in 4 weeks	03 (07.9%)
• More than once in 4 weeks	04 (10.5%)
Postoperative antibiotic administration	
• Yes	31 (81.6%)
• No	07 (18.4%)
Postoperative complications	
• No	29 (76.3%)
• Infections (pneumonia/surgical site infections)	06 (15.8%)
• Venous thrombosis	03 (07.9%)

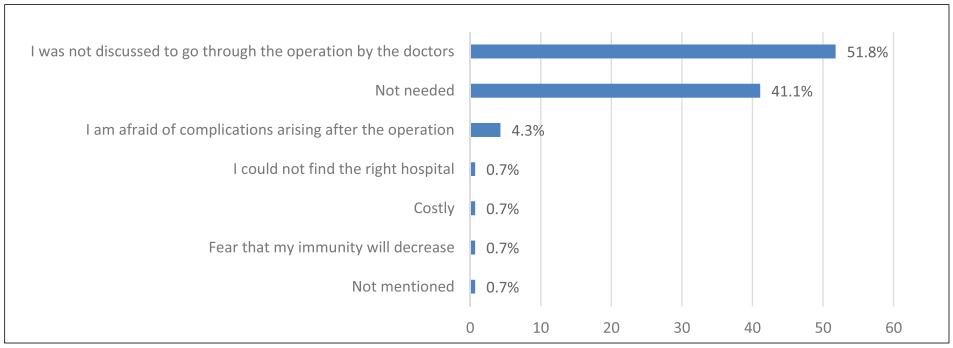

Figure 1: Reasons for not undergoing splenectomy.

Table 3: Relationships between procedure type and patient characteristics pre- and postoperatively (n = 38).

Factor	Type of procedure		χ^2	P-value[a]
	Laparoscopy N (%) (n = 10)	Laparotomy N (%) (n = 28)		
Associated blood diseases				
• Sickle cell anemia	09 (90.0%)	20 (71.4%)	2.552	0.918
• Alpha thalassemia	0	03 (10.7%)		
• Beta thalassemia	01 (10.0%)	03 (10.7%)		
• Immune thrombocytopenic purpura	0	01 (03.6%)		
• Autoimmune hemolytic anemia	0	01 (03.6%)		
Complications				
• Yes	04 (40.0%)	05 (17.9%)	1.999	0.205
• No	06 (60.0%)	23 (82.1%)		
Preoperative blood transfusion				
• Yes	08 (80.0%)	23 (82.1%)	0.023	1.000
• No	02 (20.0%)	05 (17.9%)		
Postoperative blood transfusion				
• Yes	07 (70.0%)	12 (42.9%)	2.171	0.269
• No	03 (30.0%)	16 (57.1%)		
Postoperative antibiotics				
• Yes	09 (90.0%)	22 (78.6%)	0.640	0.650
• No/do not know	01 (10.0%)	06 (21.4%)		
Postoperative improvement of condition				
• Yes	10 (100%)	26 (92.9%)	0.754	1.000
• No	0	02 (07.1%)		
Length of hospital stay				
• 2–7 days	06 (60.0%)	18 (64.3%)	0.058	1.000
• 8 days or more	04 (40.0%)	10 (35.7%)		

[a] P-value calculated with Fisher's exact test.

Table 4: Patterns of improvement in patients with blood disorders after surgery (n = 38).

Factor	Improvement		χ^2	P-value[a]
	Yes N (%) (n = 36)	No N (%) (n = 2)		
Associated blood diseases				
• Sickle cell anemia	27 (75.0%)	02 (100%)	0.655	1.000
• Alpha thalassemia	03 (08.3%)	0		
• Beta thalassemia	04 (11.1%)	0		
• Immune thrombocytopenic purpura	01 (02.8%)	0		
• Autoimmune hemolytic anemia	01 (02.8%)	0		
Interval between splenectomy and recurrence				
• <1 month	01 (02.8%)	0	19.950	0.078
• 1–3 months	03 (08.3%)	0		
• 4–6 months	02 (05.6%)	0		
• 7–12 months	07 (19.4%)	0		
• >12 months	09 (25.0%)	01 (50.0%)		
• Other	0	01 (50.0%)		
• No symptoms	14 (38.9%)	0		

[a] P-value calculated with Fisher's exact test.

Table 5: Relationships among postoperative complications and pre- or postoperative blood transfusion, vaccination and associated hematological diseases in patients (n = 38).

Factor	Complications		χ^2	P-value[a]
	Yes N (%) (n = 9)	No N (%) (n = 29)		
Associated blood diseases				
• Sickle cell anemia	07 (77.8%)	22 (75.9%)	4.932	0.694
• Alpha thalassemia	0	03 (10.3%)		
• Beta thalassemia	02 (22.2%)	02 (06.8%)		
• Immune thrombocytopenic purpura	0	01 (03.4%)		
• Autoimmune hemolytic anemia	0	01 (03.4%)		
Preoperative blood transfusion				
• Yes	08 (88.9%)	23 (79.3%)	0.419	1.000
• No	01 (11.1%)	06 (20.7%)		
Postoperative blood transfusion				
• Yes	06 (66.7%)	13 (44.8%)	1.310	0.447
• No	03 (33.3%)	16 (55.2%)		
Preoperative vaccination				
• Yes	04 (44.4%)	14 (48.3%)	0.040	1.000
• No	05 (55.6%)	15 (51.7%)		
Postoperative vaccination				
• Yes	04 (44.4%)	17 (58.6%)	0.558	0.703
• No	05 (55.6%)	12 (41.4%)		

[a] P-value calculated with Fisher's exact test.

Table 6: Pattern of antibiotics provided by age group undergoing splenectomy (n = 38).

Age group	Antibiotics		χ^2	P-value[a]
	Yes N (%) (n = 31)	No N (%) (n = 7)		
• <18 years	13 (41.9%)	01 (14.2%)	4.791	0.396
• 18–29 years	06 (19.3%)	05 (71.4%)		
• 30–39 years	10 (32.2%)	01 (14.2%)		
• 40–49 years	02 (6.4%)	0		

[a] P-value calculated with Fisher's exact test.

blood transfusions preoperatively, whereas 11.1% did not. Moreover, no significant relationships in terms of the pre- and postoperative blood transfusions were observed among the studied hematological diseases. Furthermore, 77.8% of complications were found in patients with SCD, and the remainder were found in patients with beta thalassemia.

Discussion

Splenectomy can be the modality of choice for the treatment of different hematological diseases.[8,9] In our study, splenectomy was performed in 21.2% of patients with underlying hematological disease. Patients with SCD, followed by patients with beta thalassemia, constituted a large proportion of those who underwent splenectomy. These findings are concordant with those from a previous study in Oman indicating that patients with SCD and beta thalassemia are more likely to have splenectomy than other hematological disorders.[10] This finding may be explained by the relatively high prevalence of SCD in the Mediterranean Basin the Middle East.[11,12] Moreover, we found that most patients with SCD underwent splenectomy at less than 18 years of age or between 30 and 39 years of age, unlike those with beta and alpha thalassemia, who underwent the procedure before the age of 30. These findings might be explained by a relatively high risk of splenic sequestration crisis in younger patients with SCD before splenectomy.

Susceptibility to infection post-splenectomy is relatively high, as clearly demonstrated in a prospective cohort study in Los Angeles and another study conducted in Olmsted County. Both studies have found that splenectomy can have infection complications in 50% and 40% of patients.[13,14] However, despite the increased risk of infection post-splenectomy,[13] only half the patients who underwent splenectomy were instructed to visit a health care facility if they experienced fever symptoms in the postoperative period. Nevertheless, we observed that only 15.8% of participants developed post-splenectomy infection—a percentage significantly lower than that previously reported.[13,14]

The British Committee for Standards in Hematology has set guidelines for preventing infections in patients post-splenectomy, on the basis of three components:

vaccination, prophylaxis with antibiotics and patient education.[15] These components have an essential role, particularly within the first 3 years after the operation, because of infection susceptibility.[15,16] The findings from our study support this association: patients with underlying SCD who underwent splenectomy and patients who were not offered vaccination, particularly preoperatively, were more likely to have infection complications. Antibiotics have been recommended to be prescribed post-splenectomy for children under the age of 5 years.[4,5] However, we observed that prescribing antibiotics to patients up to the age of 40 remains a common practice among physicians.

The postoperative hospital stay after a splenectomy procedure can vary, with an average length between 3 and 9 days.[18–20] However, a study has reported that laparoscopic splenectomy for benign hematological disorders is significantly associated with prolonged postoperative hospital stays and greater blood loss.[17] In our study, most patients had a hospital stay period between 2 and 7 days. This time period is similar to that in the general population and less than that previously reported in patients with hematological diseases who underwent splenectomy.[18–20]

Previous studies suggest better outcomes and improvements after the procedure for several hematological diseases, although no studies have addressed the duration of improvement before the need for another line of treatment.[21,22] We defined improvement as a decrease in blood component requirements, the frequency of hospitalization and the need for additional lines of treatment. We found that splenectomy resulted in 30% less blood component transfusion than that before splenectomy, and this finding was observed in patients with SCD, as previously reported.[19,23] However, blood transfusion requirements in patients with beta thalassemia did not differ pre- and postoperatively, in contrast to findings in previous studies.[24,25] Furthermore, preoperative selective blood transfusions in patients with SCD can help minimize postoperative complications.[26] Additionally, most patients showed an overall improvement in their condition after the procedure. Approximately one-third of patients had an average period of 1 year without a need for an additional line of treatment. However, no significant difference was observed in terms of improvement across diseases. The splenectomy procedure remains often performed in patients with SCD and beta thalassemia.[19] Vaccines are mandatory and aid in preventing overwhelming post-splenectomy infections,[25,27] although vaccination in this study did not alter the infection frequency.

This study addresses several essential points indicating the role of splenectomy in treating various hematological diseases and its influence on the clinical course. Furthermore, our findings emphasize that specific measures might minimize perioperative complications.

Limitations

Several limitations might have influenced the results of this study. First, the sample size is not sufficient to represent the effects of splenectomy on various hematological diseases. Moreover, a comparison to the population that did not undergo splenectomy is highly warranted.

Conclusion

Although many treatment paradigms for non-malignant hematological diseases have emerged, splenectomy is considered an important line of treatment for most of these diseases. However, the variable nature of the diseases and immunological weakness have led to controversy regarding whether splenectomy is a suitable treatment option.

Additionally, although splenectomy is an effective treatment for certain non-malignant hematological diseases, why one group of patients in the same disease population may benefit while others do not remains unclear. Nonetheless, preoperative vaccination and elective surgery clearly result in better outcomes. Therefore, a combination of elective splenectomy, scheduled vaccinations and proper selection of patients who would benefit from splenectomy would result in optimal outcomes.

Recommendations

Because spleen removal can result in several complications in patients with non-hematological diseases, we recommend pre- and postoperative education of patients by treating physicians to avoid these unwanted and preventable complications. Furthermore, regular vaccines should be administered to patients pre- and postoperatively. In addition, further studies should be performed in a broader cohort of patients to obtain more reliable and valid results.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

Ethical approval for the study was obtained from the Institutional Review Board and the Research Ethics Committee of King Faisal University in Al Hasa, KSA. Research Number: 04/01/2019, date: 27/10/2019. For this type of study, written informed consent was required to be obtained from participants before they completed questionnaires.

Authors contributions

MS: conceptualization; supervision; data curation; writing original draft; writing review and editing. FJ: data curation; writing original draft; investigation; methods. SE: data curation; writing original draft; investigation; methods. SI: formal analysis; methods; software. AE: conceptualization; supervision; writing original draft; writing review and editing. All authors have critically reviewed and approved

the final draft and are responsible for the content and similarity index of the manuscript.

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