Research Article

Rafiye Ciftciler*, Aysel Pasayeva, Salih Aksu, Osman Ozcebe, Nilgun Sayınalp, Umit Yavuz Malkan, Yahya Buyukasık, Ibrahim C. Haznedaroglu

Indications and outcomes of splenectomy for hematological disorders

https://doi.org/10.1515/med-2019-0054
received February 24, 2019; accepted March 17, 2019

Abstract: Background and Aim: Splenectomy is a frequent component of the diagnosis and treatment of hematological disorders. The aim of this study was to define the indications and outcomes of splenectomy for benign and malign hematological disorders.

Materials and Methods: One hundred and two patients with hematological disease who had splenectomy at Hacettepe University Hospital between the years of 2010 and 2018 were evaluated.

Results: A total of one hundred and two patients were included in this study. The median age was 52 (20-82) years at the time of splenectomy. Most of the patients were female (57.9%). The median follow up time was 11.0 (0.03-87.9) months after splenectomy. Splenectomy was performed to diagnose thirty patients (29.4%). Seventy-two patients underwent splenectomy for the treatment of hematological disease (70.6%). Twenty-seven patients (90%) were diagnosed with various lymphomas. Two patients (6.7%) were diagnosed with hairy cell leukemia and one patient (3.3%) was diagnosed with large granular lymphocytic leukemia.

Conclusion: In conclusion, an improvement in medical therapy, especially with monoclonal antibodies, the indications and outcomes of splenectomy for hematologic disorders have changed extremely in last years. Nevertheless, splenectomy has an important role for diagnosis and treatment of benign and malign hematological disorders.

Keywords: Hematological disorders; splenectomy; idiopathic thrombocytopenic purpura

1 Introduction

Spleen is a lymphoid organ that has hematopoietic and immune functions. Splenectomy is a frequent component of the diagnosis and treatment of hematological disorders. Benign and malign hematological disorders compose the major indication for elective splenectomy [1]. Splenectomy is a standard and effective treatment modality for patients with recurrent, refractory, or chronic diseases for which drug treatment fails or is unable to cure [2]. After the failure of medical therapy, splenectomy is indicated for the red blood cells disorders and a variety of thrombocytopenic disorders. Splenectomy is also successful in reversing hypersplenism in myeloproliferative disorders. In the treatment of leukemia and lymphoma, indications and benefits of splenectomy are limited [3]. The aim of this study was to define the indications and outcomes of splenectomy for benign and malign hematological disorders. Herein we report a retrospective study of our experience with patients who underwent splenectomy for the diagnosis and/or treatment of benign and malign hematological disorders.

***Corresponding author: Rafiye Ciftciler,** Departments of Hematology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 06100.3Department of Adult Hematology, Hacettepe University Medical School, 06100 Ankara, Turkey, Telephone: +90-0312-3053050 +905055831798, Fax:+90-0312-3051614, E-mail: rafiyesarigul@gmail.com
Salih Aksu, Osman Ozcebe, Nilgun Sayınalp, Yahya Buyukasık, Ibrahim C. Haznedaroglu, Department of Hematology, Hacettepe University Faculty of Medicine, Ankara, Turkey
Aysel Pasayeva, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey
Umit Yavuz Malkan, Department of Hematology, Dıskapı Education and Research Hospital, Ankara, Turkey

2 Materials and methods

2.1 Study design and data collection

This study has been performed in a retrospective manner. Demographic data of the patients and treatment regimen were obtained from hospital database. As a result of application standards of the hospitals of Hacettepe Medical School, it has been recognized from the patient records that all of the studied patients had given informed consents at the time of hospitalization and before the administration of relevant diagnostic/therapeutic standards of care. Patients gave informed consent for the procedure.

Ethical approval: All of the ethical considerations had been strictly followed in accordance with the 1964 Helsinki declaration.

2.2 Patients and disease characteristics

One hundred and two patients with hematological disease who had splenectomy at Hacettepe University Hospital between the years of 2010 and 2018 were evaluated. The inclusion criteria were: patients ≥18 years of age with splenectomy for hematological benign or malign disorders. Our preparation protocol for elective splenectomy required all patients to have received polyvalent *pneumococcal* vaccine, *meningococcal* vaccine and *Haemophilus influenzae* vaccine, at least 3 weeks before splenectomy. All patients were covered prophylactically with oral penicillin after splenectomy.

2.3 Statistical analysis

Statistical analyses were performed using the SPSS software version 25. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorow-Simirnov/Shapiro-Wilk's test) to determine whether they are normally distributed or not. Statistical comparisons were made using Chi-square for categorical data. Student t-test (for two independent samples) was used for comparison of continuous numerical data. Values of $p < 0.05$ were considered statistically significant.

3 Results

3.1 Patient characteristics

A total of one hundred and two patients were included in this study. Median age was 52 (20-82) years at the time of splenectomy. Most of the patients were female (57.9%). Median follow up time was 11.0 (0.03-87.9) months after splenectomy. Splenectomy was performed to diagnose thirty patients (29.4%). Seventy-two patients received splenectomy for the treatment of hematological disease (70.6%) as shown in Figure 1. All patients who underwent diagnostic splenectomy were diagnosed (100%). Twenty-seven patients (90%) were diagnosed with various lymphomas as shown in Figure 2. Two patients (6.7%) were diagnosed with hairy cell leukemia (HCL) and one patient (3.3%) was diagnosed with large granular lymphocytic (LGL) leukemia. The baseline clinical and demographic characteristics of patients are listed in Table 1.

3.2 Response to splenectomy

Hemoglobin levels of the patients with autoimmune hemolytic anemia, thalassemia, sickle cell anemia and hereditary spherocytosis increased after splenectomy as shown in Figure 3. Of thirty-nine patients with idiopathic thrombocytopenic purpura (ITP) thirty-eight (97.4%) patients responded to splenectomy (PLT level >100x10^9/L) and only one patient (2.6%) did not respond to splenectomy. Thrombocyte levels before and after splenectomy are shown in Figure 4. Three patients with HCL, two patients with LGL leukemia, two patients with myelofibrosis (MF) had complete remission after splenectomy. Three patients had partial response after splenectomy and one patient died after splenectomy. Splenectomy was performed for the diagnosis in the majority of patients with lymphoma (69.2%). After splenectomy, six patients were diagnosed with follicular lymphoma (FL), two patients with diagnosed hepatosplenic T cell lymphoma (HSTCL), one patient with peripheral T cell lymphoma (PTCL), nine patients with diffuse large B cell lymphoma (DLBCL) and nine patients with splenic marginal zone lymphoma (SMZL). Twelve patients (30.8%) with lymphoma were submitted for splenectomy for the treatment of the disease. After splenectomy one patient with Hodgkin lymphoma, two patients with DLBCL and two patients with PTCL had complete remission. However, following splenectomy two patients with DLBCL and two patients with PTCL had progressive disease. One patient with FL had complete

Table 1. Baseline clinical and demographic characteristics of patients

Parameters	Splenectomy for diagnosis	Splenectomy for treatment
N (%)	30 (29.4%)	72 (70.6%)
Gender (male/female)	15/15 (50%/50%)	28/44 (38.9%/61.1%)
Age (range)	56 (27-82)	46 (20-80)
ECOG PS		
ECOG PS 0	23 (76.6%)	58 (80.5%)
ECOG PS 1	3 (10%)	3 (4.1%)
ECOG PS 2	4 (13.4%)	5 (6.9%)
ECOG PS 3	0	6 (8.3%)
Charlson comorbidity index		
0	6	34
1-2	14	22
3-4	9	13
≥5	1	3
Hematological disease (%)		
Lymphoma	27 (90%)	12 (16.6)
Hairy cell leukemia	2 (6.7%)	1 (1.4%)
Large granular lymphocytic leukemia	1 (3.3%)	1 (1.4%)
Hereditary spherocytosis	0	1 (1.4%)
Idiopathic thrombocytopenic purpura	0	39 (54.2%)
Autoimmune hemolytic anemia		9 (12.5%)
Sickle cell anemia	0	1 (1.4%)
Thalassemia	0	2 (2.8%)
Myelofibrosis	0	6 (8.3%)
Splenectomy related complications (%)		
Hematoma	0	1 (1.4%)
Infection	5 (16.7%)	10 (13.9%)
Thrombosis	0	3 (4.2%)
Splenectomy related mortality (%)	0	5 (6.9%)

Abbreviations: N: number of the patients; ECOG PS: ECOG PS: ECOG Performance Status

remission, and one patient with FL had partial response after splenectomy. One patient with FL died after splenectomy. In fifteen patients (14.7%) post-splenectomy infection developed. Hematoma was observed in one patient (0.9%) and thrombosis was observed in three patients (2.9%) after splenectomy. Five patients (4.9%) died due to complications within 2 months post-splenectomy and four patients died because of infectious complications. One patient died after splenectomy because of thrombosis.

The mean ages of the patients who underwent splenectomy showed statistically significant difference according to the diagnosis ($p<0.001$). The gender of the patients who underwent splenectomy was similar according to the diagnosis ($p=0.77$). Pre ($p<0.001$) and post-splenectomy ($p<0.001$) hemoglobin (HB) levels, pre-splenectomy white blood cells levels (WBC) ($p=0.003$), pre ($p<0.001$) and post-splenectomy platelet (PLT) ($p=0.001$) levels were statistically significant different according to the diagnosis as shown in Table 2. Only post-splenectomy WBC levels were not statistically significant different in all patients with various hematological disorders ($p=0.15$).

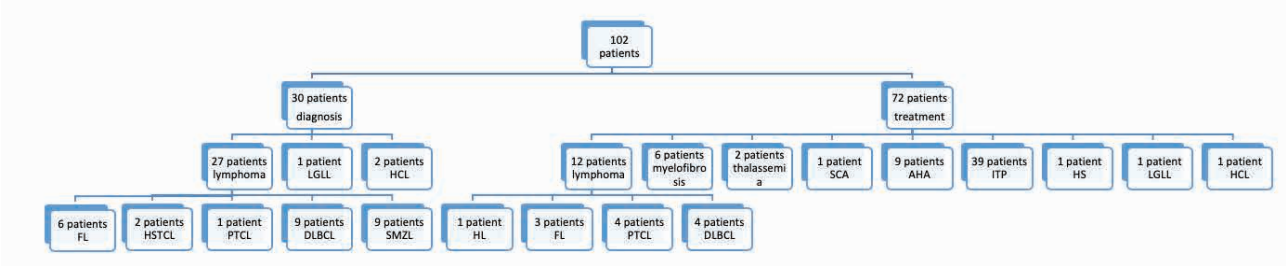

Figure 1. Diagnosis of patients undergoing splenectomy

Abbreviations: AHA: Autoimmune hemolytic anemia; DLBCL: Diffuse large B cell lymphoma; FL: Follicular lymphoma; HSTCL: Hepatosplenic T cell lymphoma; HS: Hereditary spherocytosis; HL: Hodgkin lymphoma; LGLL: Large granular lymphocytic leukemia; HCL: Hairy cell leukemia; PTCL: Peripheral T cell lymphoma; SCA: Sickle cell anemia; SMZL: Splenic marginal zone lymphoma; ITP: Idiopathic thrombocytopenic purpura

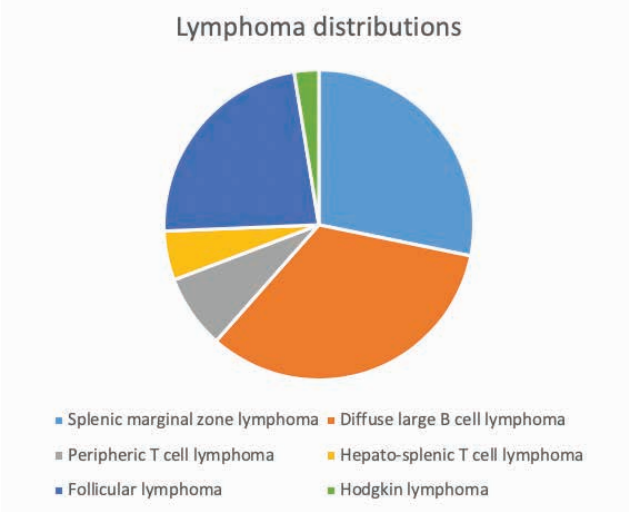

Figure 2. The distribution of lymphomas (splenectomy for diagnosis and treatment)

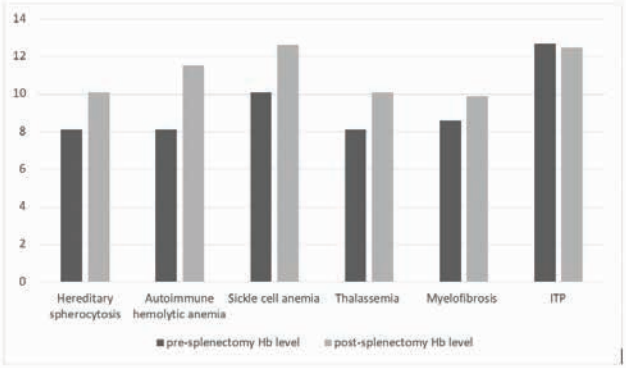

Figure 3. Pre- and post-splenectomy hemoglobin levels of the patients (gr/dL)

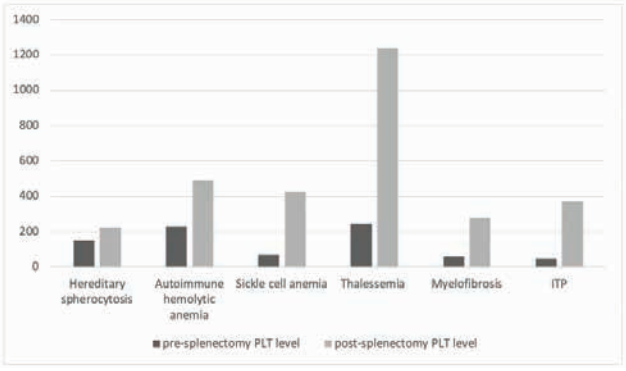

Figure 4. Pre- and post-splenectomy thrombocyte levels of the patients (10^9/L)

4 Discussion

Splenectomy plays a role in the diagnosis and treatment of many hematological diseases. With the improving of the advent of monoclonal antibody treatment, the indications and outcomes of splenectomy for benign and malign hematological diseases have changed in recent years [1]. Nevertheless, splenectomy has its place in hemoglobinopathies and hemolytic diseases. It improves thrombocytopenia in refractory ITP, can reverse symptoms linked to splenomegaly secondary to MF, and can be used for diagnostic and treatment purposes in lymphoproliferative diseases [1].

In this study, we retrospectively evaluated patients who underwent splenectomy for hematological diseases. Most patients had splenectomy for the treatment of hematological disease. Fewer patients had splenectomy for diagnosis of hematological disease. All patients who underwent diagnostic splenectomy were diagnosed. Post-operative complications such as hematoma, thrombosis and infection were observed in nineteen patients. Post-operative mortality was observed in five patients who underwent splenectomy for the treatment.

Cases of splenectomy for various hematological diseases have been analyzed in the past literature. Kojouri et al. reported a 66% complete response rate after splenectomy. A complete response was defined as the achieve-

Table 2. Demographic characteristics and laboratory results of 102 patients with hematological disorders who underwent splenectomy

Parameters	Lymphoma	HCL	LGLL	HS	ITP	AIHA	SCA	Thalassemia	Myelofibrosis	P
N	39 (38.2%)	3 (2.9%)	2 (2%)	1 (1%)	39	9 (8.8%)	1 (1%)	2 (2%)	6 (5.9%)	
Age±SD	57±15	53±8	33±6	61	40±14	59±15	31	36±10	63±11	**<0.001**
Sex (M/F)	18/21	2/1	0/2	0/1	15/24	4/5	1/0	1/1	2/4	0.77
Pre-splenectomy HB (g/dL)±SD	10±1.9	11.1±1.7	9.8±1.7	8.9	12.7±2.1	8.1±2.2	10.1	8.1±1.5	8.6±1.0	**<0.001**
Post-splenectomy HB (g/dL)±SD	10.3±1.9	10.8±2	12.3±0.2	9.9	12.5±1.9	11.5±1.5	12.6	10.1±1.8	9.9±2.1	**<0.001**
Pre-splenectomy WBC (10^9/L)±SD	5.7±1.2	7.5±9.1	1.3±0.6	6.3	10.6±4.0	6.8±2.8	11.4	9.3±4.3	6.9±6.6	**0.003**
Post-splenectomy WBC (10^9/L)±SD	11.4±6.3	5.9±4.3	13.1±10.3	18.7	14.3±6.8	11.7±3.6	9.2	22.4±2.1	15.8±14.2	0.15
Pre-splenectomy PLT (10^9/L)±SD	140±143	85±19	166±48	150	47.4±44.4	229±109	67	246±65	61.6±47.5	**<0.001**
Post-splenectomy PLT (10^9/L)±SD	470±291	438±71	556±123	226	372±178	491±302	425	1270±217	278±417	**0.001**
Splenectomy related mortality (%)	4 (3.9%)	0	0	0	0	0	0	0	1 (0.9%)	0.12

Abbreviations: N: number of the patients; HB: hemoglobin; WBC: white blood cell; PLT: platelet

ment and maintenance of a normal platelet count (at least 100×10^9/L) without additional ITP treatment [4]. Patel et al. reported the effect of splenectomy in patients with ITP refractory to medical treatment and AHA. In the ITP group (n=45), 91% of the patients had complete response within a median period of 51 days and in the AHA group (n=15), 93% of the patients had complete response within a median period of 172 days after splenectomy [5]. Two other studies showed that splenectomy is a potent treatment modality for symptomatic patients with SMZL [6, 7]. Subbiah et al. showed that all patients with LGL in their analyses had hematologic response and achieved transfusion independence after splenectomy [8]. Another study showed that a significant continuous fall in annual blood transfusion requirement and a rise in platelet counts occurred post-splenectomy in thalassemia patients [9].

Infection is a common complication of splenectomy, as the spleen has a major role in eradicating infections from the body. Bisharat et al. reported that the incidence of infection after splenectomy was 3.2% with a mortality rate of 1.4% [10]. In this study, the post-splenectomy infection rate was 14.7% and the splenectomy related mortality rate was 6.9%. The hypercoagulable state predisposes patients with splenectomy to an increased risk of thrombotic complications [11]. Thrombosis was observed in this study after splenectomy with a rate of 4.2%. In one patient (0.9%), hematoma developed after splenectomy.

Our study had a few limitations. Firstly, the study was retrospective and secondly the diagnosis of the patients were heterogeneous. Additionally, the sample size was small. In conclusion, an improvement in medical therapy, especially with monoclonal antibodies, the indications and the outcomes of splenectomy for hematologic disorders have changed extremely in last years. Nevertheless, splenectomy has an important role in hemoglobinopathies and hemolytic diseases, as it improves thrombocytopenia in refractory ITP, can reverse cytopenia and symptoms related to splenomegaly secondary to MF, or can be used for diagnostic purposes or for splenomegaly in lymphoproliferative diseases.

Role of the funding source: None.

Conflict of Interest: The authors of this paper have no conflict of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

References

[1] Bonnet S, Guedon A, Ribeil J-A, Suarez F, Tamburini J, Gaujoux S. Indications and outcome of splenectomy in hematologic disease. Journal of visceral surgery. 2017;154(6):421-429

[2] George JN, Woolf SH, Raskob GE, Wasser J, Aledort L, Ballem P, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996;88(1):3-40

[3] Schwartz SI. Role of splenectomy in hematologic disorders. World journal of surgery. 1996;20(9):1156-1159

[4] Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. Blood. 2004;104(9):2623-2634

[5] Patel NY, Chilsen AM, Mathiason MA, Kallies KJ, Bottner WA. Outcomes and complications after splenectomy for hematologic disorders. The American Journal of Surgery. 2012;204(6):1014-1020

[6] Lenglet J, Traullé C, Mounier N, Benet C, Munoz-Bongrand N, Amorin S, et al. Long-term follow-up analysis of 100 patients with splenic marginal zone lymphoma treated with splenectomy as first-line treatment. Leukemia & lymphoma. 2014;55(8):1854-1860

[7] Xing KH, Kahlon A, Skinnider BF, Connors JM, Gascoyne RD, Sehn LH, et al. Outcomes in splenic marginal zone lymphoma: analysis of 107 patients treated in British Columbia. British journal of haematology. 2015;169(4):520-527

[8] Subbiah V, Viny AD, Rosenblatt S, Pohlman B, Lichtin A, Maciejewski JP. Outcomes of splenectomy in T-cell large granular lymphocyte leukemia with splenomegaly and cytopenia. Experimental hematology. 2008;36(9):1078-1083

[9] Merchant RH, Shah AR, Ahmad J, Karnik A, Rai N. Post splenectomy outcome in β-thalassemia. The Indian Journal of Pediatrics. 2015;82(12):1097-100

[10] Bisharat N, Omari H, Lavi I, Raz R. Risk of infection and death among post-splenectomy patients. Journal of Infection. 2001;43(3):182-186

[11] Hassan MN, Tahereb GM, Ahmad T, Asghar DA, Reza EDM, Ali B, et al. Correlation of splenectomy with portal vein thrombosis in β thalassemia major. JPMA-Journal of the Pakistan Medical Association. 2011;61(8):760