Predictive Factors for Success of Laparoscopic Splenectomy for ITP

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ABSTRACT

Background and Objectives: Therapy-resistant immune thrombocytopenia (ITP) is the most frequent indication of laparoscopic splenectomy (LS). It ensures the best results for this disease compared with possible second-line pharmacologic therapies. Therefore, learning about the safety of the surgical method and its long-term efficacy is important, as is selecting patients who respond to surgical treatment. Our purpose was to analyze the safety of LS and the short-and long-term prognostic significance of known perioperative parameters.

Methods: We performed 40 LSs for ITP from January 1, 2000, to January 1, 2015. We analyzed the roles of the perioperative parameters by using evidence-based guidelines.

Results: Complete response (CR; platelet count over 100×10^9/L) occurred in 28 cases (70%) and partial response (PR; platelet count between 30 and 100×10^9/L) in 5 cases (12.5%). Below the age of 50, 9% (2/22) of the patients had no response (NR; platelet count not increasing over 30×10^9/L), 28% (5/18) over the age of 50 ($P = $ .023) had no response. In the steroid-refractory group, 30% did not respond, whereas 100% of the steroid-dependent patients had a CR (NR: 7/23 steroid refractory vs 0/17 steroid dependent; $P = $ .027). The patients were followed up for a mean of 10.9 ± 6.9 years, and a long-term response (LTR) was detected in 21 of the responders (n = 33). Of the patients who originally had a CR, 71% also achieved LTR, whereas only 20% of the PR patients did.

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Conclusion: LS is safe and remains the most effective second-line treatment for ITP. In our study, younger age and response to preoperative steroids were predictive factors for the long-term success of splenectomy.

Key Words: Immune thrombocytopenia, Laparoscopic splenectomy, Response-predictive factors, Haematological outcome, Long-term results.

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune hematologic disorder accompanied by low platelet count and concomitant spontaneous bleeding. Low platelet count is partly related to accelerated degradation in the reticuloendothelial system and partly to decreased cell formation in the bone marrow. The prevalence of the disease is 2–3 times higher in women and develops primarily between the ages of 18 and 40. The disease is diagnosed by excluding other causes of thrombocytopenia by reviewing medical history, performing a physical examination, and studying blood count and a peripheral blood smear. Definitions of thrombocytopenia, criteria for starting treatment, response, and therapy-refractory disease have long remained nonstandardized. In 2009, an International Working Group (IWG) offered a unified terminology.[1] The term "immune thrombocytopenia" was suggested instead of idiopathic thrombocytopenic purpura, and the cutoff value for the platelet count was defined as 100×10^9/L. With regard to the immunologic mechanism of ITP, first-line standard therapy consisted of corticosteroids and intravenous immunoglobulins. If patients do not respond to the first treatment or if the disease responds to the treatment but continuous therapy is required, the disorder is called refractory ITP, and the administration of a second-line therapy is indicated. This treatment may consist of rituximab, thrombopoietin (TPO) receptor agonists, or splenectomy. Of these 3 treatment options, splenectomy provides the best and longest lasting results (an immediate response rate approximately 80% and the rate of permanent responders 60% for 5–10 years).[2]

The laparoscopic approach has been an acceptable surgical method in the treatment of ITP for decades because

of its numerous advantages. Hematologic outcomes of this method are similar to those of conventional splenectomy.[3] However, only limited publications are available on the long-term results of splenectomy according to standardized definitions and outcome criteria.[4,5] Furthermore, with regard to the fact that splenectomy is not effective immediately in 15–25% of the cases and that relapse occurs in one-third of the patients, it is important to determine predictive factors to avoid unnecessary surgeries and to plan the therapy. Several hypothetical factors have been examined in predicting the outcome of splenectomy. Data are available on the predictive value of age, response to steroid therapy, perioperative platelet count, and characteristics of platelet sequestration.[6] Our intention was to analyze the safety of splenectomy for ITP and to determine which perioperative parameters predict long-term results when using evidence-based guidelines.

METHODS

The study was approved by the ethics committee of the University of Szeged (No. WHO3932). From January 1, 2000, to January 1, 2015, 40 splenectomies were performed for ITP. The patients had been treated in the Hematology Department, and the surgical indication was made on the basis of the hematology specialist's report. All the patients received corticosteroid therapy before surgery, and splenectomy was performed in steroid-refractory or steroid-dependent cases. Azathioprine or intravenous immunoglobulin (IVIG) therapy was administered to 10 patients before surgery, as well.

All the patients received vaccines against *Streptococcus pneumoniae*, *Neisseria meningitides*, and *Haemophilus influenzae*. Surgeries were done with antibiotic prophylaxis, with close control of hemostatus. The patients received prophylactic low-molecular-weight heparin (LMWH) in the peri- and postoperative period (for 30 days after discharge).

Surgical Technique

LS was performed with the patient lying in the lateral decubitus position at 30° with the "anterolateral hanging spleen" technique, according to Delaitre et al.[7] During the learning period, an Endo GIA stapler (Medtronic, Minneapolis, Minnesota, USA) was used to ligate the hilar vessels, followed by individual vessel dissection and Hem-o-lok clip (Teleflex, Morrisville, North Carolina, USA) ligation. The specimen was placed in an EndoBag (Medtronic) with morcellation via the lateral port (**Figure 1**). A drain was left in the abdominal
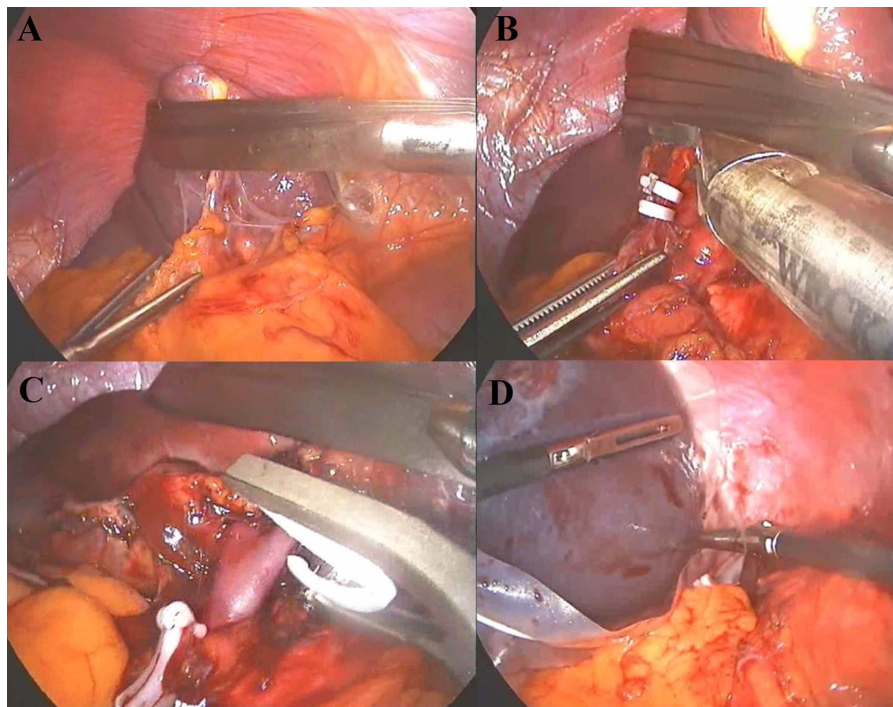
Figure 1. Steps in the laparoscopic splenectomy: (**A**) Exploration of the splenic hilum, (**B**) clipping of the splenic artery, (**C**) clipping of the splenic vein, and (**D**) removal of the specimen in a specimen retrieval container.

cavity after surgery in all cases, and the drain was removed on the second postoperative day.

Follow-up and Hematological Response

Perioperative data were examined, such as preoperative platelet count, duration of surgery, use of the laparoscopic technique or conversion to open, mortality and morbidity, and the weight of the specimen removed.

Average duration of long-term patient follow-up was 10.9 ± 6.9 years. In accordance with the 2009 guidelines issued by the IWG[1] and the evidence-based guidelines issued by the American Society of Hematology in 2011,[8] response categories were complete response (CR; platelet count over 100×10^9/L); partial response (PR), defined as at least a 2-fold increase compared to the baseline value (a platelet count between 30 and 100×10^9/L); and nonresponse (NR), defined as not reaching a 2-fold increase compared to the baseline value (platelet count not increasing over 30×10^9/L); and whether these changes occurred within 30 days.

Patients were considered to be stable responders if the response was maintained during the follow-up, no additional therapy was required, and there was no bleeding requiring hospitalization after splenectomy. The case was determined to be refractory ITP or loss of response if any thrombocytopenic event occurred with platelet count lower than 100×10^9/L in a previous responder patient (CR), if the platelet count was below 30×10^9/L, or if the platelet count was lower than twice the baseline value (PR). Spontaneous bleeding or restarting medical therapy was regarded as a loss of response, as well.

Finally, the predictive value of pre- and perioperative parameters was analyzed for long-term results (CR, PR, NR and loss of response).

Statistics

The t test and one-way ANOVA were used to compare the mean values, as well as the Mann-Whitney and Kruskal-Wallis tests in cases of non-normality. Categorical data were analyzed using χ^2 and Fisher's exact tests. The normal distribution of samples was assessed with the Kolmogorov-Smirnov test. SPSS version 15.0 (IBM, Armonk, New York, USA) was used for the statistical analyses.

RESULTS

The female-to-male ratio was 28:12. The average age of the patients was 46.62 ± 17.48 years, ITP was diagnosed at an average age of 43 years, and the surgery was performed an average of 25.1 ± 5.73 months after the diagnosis. In all cases, the first-line treatment for ITP was steroid therapy. Twenty-three cases (57.5%) were steroid refractory, and 17 (42.5%) were steroid dependent. After steroid treatment, 30 patients underwent splenectomy as the second-line therapy. In 7 cases, azathioprine was administered, and 3 patients received IVIG therapy as a second-line therapy, followed by splenectomy.

Results of Surgery

In 4 of the 40 cases (10%), conversion to open surgery was required. Three of the 4 conversions were required before 2004 during the learning curve (LS was introduced at our clinic in 2000).There was no perioperative mortality. Two patients (5%) required reoperation for bleeding. The average duration of the surgery was 113.5 ± 62.71 minutes; The literature defines the learning curve as 20 surgeries for laparoscopic splenectomy,[9] which was exceeded in 2006, taking into account LS performed with other indications. After this, the average duration of the surgeries decreased significantly from 132 to 104 minutes ($P = .032$). The average weight of the specimens removed was 174 ± 89.6 g. The average duration of postoperative care was 5.44 ± 2.84 days. Perioperative morbidity occurred in 4 cases: 1 patient had pneumothorax, 1 experienced superficial thrombophlebitis, and 2 had recurring fever.

Short- and Long-Term Hematological Results of Splenectomy for ITP

The average preoperative platelet count was $66.7 \pm 47.84 \times 10^9$/L. In cases requiring a platelet suspension (n = 27), it was administered during surgery after the vessels of the spleen were clipped. On the third postoperative day, the average platelet count was $148.4 \pm 93.7 \times 10^9$/L. Based on the postoperative platelet counts, CR occurred in 28 (70%) cases and PR in 5 (12.5%). A total of 82.5% of the patients responded to splenectomy in accordance with the guidelines. Seven (17.5%) patients showed no response.

Follow-up lasted an average of 10.9 ± 6.9 years. During this time, 2 patients died, 5 and 7 years after the splenectomy. Cause of death was a cardiac event in an 84-year-old patient and neoplasm was the cause of death in a 56-year-old patient. During the follow-up, 21 (63.6%) of the responders (CR + PR = 33) had a long-term response. Patients with a CR experienced a long-term response in 20/28 cases (71%), whereas a long-term response was achieved in 1 of 5 cases (20%) among the PR patients.

Relapse (restarting medical therapy, spontaneous bleeding, platelet count $< 30 \times 10^9$/L) occurred 12.5 ± 7.3 months on average after the splenectomy. The relapse rate was significantly higher in the PR group compared with the CR patients (80% vs 28.6%). PR cases experienced relapse sooner compared with the CR patients (9.7 vs 18.6 months; $P < .001$).

The 12 patients with relapse and the 7 nonresponder patients underwent steroid, TPO receptor agonist (romiplostim and eltrombopag), azathioprine, or IVIG therapy as further treatment.

The general results of the patients are summarized in **Table 1**.

Predictive Factors for Short- and Long-Term Response

Based on the results above, we examined which known perioperative factors and parameters predicted short- and long-term success (**Table 2**).

All the patients operated on as steroid dependent (n = 17) were CR, whereas patients operated on because they were steroid refractory were classified as CR (n = 11), PR (n = 5), and NR (n = 7). From a different perspective, all PR and NR patients fell into the preoperative steroid-refractory group. Significantly more NR patients were in the steroid-refractory group (0/17 vs 7/23; $P = .027$).

Long-term results suggest that, among the steroid-dependent patients (n = 17), 12 had a persistent response (70.6%), whereas 9 of 16 patients (56.3%) in the steroid-refractory group were persistent NRs.

The average age of the CR group was 42.79 ± 13.24, that of the PR group was 49.2 ± 18.32, and that of the NR group was 60.14 ± 24.21 years. Among the patients below the age of 50 years (n = 22), 17 were CR, 3 were PR, and 2 were NR. Among the patients over the age of 50 years (n = 18), 11 were CR, 2 were PR, and 5 were NR. Therefore, in the younger group, 9% of the patients were NR; this rate was 28% among the patients in the older group (2/22 vs. 5/18; $P = .023$).

Long-term follow-up showed that the average age of persistent responders was 42.6 ± 16.5, and that of patients with relapse was 45.75 ± 21.3 years. Among the patients below the age of 50 years, 14 of 20 were persistent responders (70%), whereas this rate was 7 of 13 among older patients (53.8%) (nonsignificant [NS]).

Of the patients whose preoperative platelet count was below 30×10^9/L (n = 16), 7 were in the CR group (43.75%), 5 were in the PR group (31.25%), and 4 were in the NR group (25%). Among the patients with a platelet count over 30×10^9/L (n = 24), 21 were in the CR group (87.5%), and 3 were in the NR group (12.5%) (NS).

Of the 10 patients who had undergone splenectomy as a third- and not a second-line therapy (after azathioprine or IVIG therapy), the surgery was performed after an average of 17.75 ± 3.43 months after the diagnosis, which was unexpectedly shorter compared with the average value of all the patients. Of these 10 patients, 6 were CR, 2 were PR, and 2 were NR (NS).

In summary, response to first-line steroid therapy (dependency) ($P = .027$) and younger age ($P = .023$) proved to be more effective in predicting short-term efficacy of splenectomy based on logistic regression analysis (**Table 3**).

Table 1.
General Results of Splenectomy in Patients With ITP

	CR (Plt $>100 \times 10^9$/L)	PR (Plt 30–100 $\times 10^9$/L)	NR (Plt $<30 \times 10^9$/L)
Patients, n (%)	28 (70%)	5 (12.5%)	7 (17.5%)
Age (years)	42.79 ± 13.24	49.2 ± 18.32	60.14 ± 24.21
Gender (F/M)	18/10	5/0	5/2
Splenic weight (g)	160.13 ± 12.47	206.25 ± 10.21	229 ± 9.62
Postoperative increase in thrombocyte count ($10^3/\mu$L)	122.5 ± 34.2	50.8 ± 11.5	8 ± 9.62
Relapse rate, n (%)	8/28 (28.6%)	4/5 (80%)	
Median time to relapse (months)	18.6	9.7	

N = 40.

Table 2.
Possible Predictive Factors

	CR (Plt >100 × 10⁹/L) (n = 28)	PR (Plt 30–100 × 10⁹/L) (n = 5)	NR (Plt <30 × 10⁹/L (n = 7)
Preoperative steroids, n (%)			
Dependent (n = 17)	17 (100%)	0	0
Refractory (n = 23)	11 (47.8)	5 (21.7)	7 (30.4)
Age			
<50 years (n = 22)	17 (77.3)	3 (13.6)	2 (9)
>50 years (n = 18)	11 (61)	2 (11)	5 (27.8)
Preoperative platelet count			
<30 × 10⁹/L (n = 16)	7 (43.75)	5 (31.25)	4 (25)
>30 × 10⁹/L (n = 24)	21 (87.5)	0	3 (12.5)
Surgery indication			
Second-line therapy (n = 30)	22 (73.3)	3 (10)	5 (16.7)
Third-line therapy (n = 10)	6 (60)	2 (20)	2 (20)

Data are number of patients (percentage of total group).

Table 3.
Results of Logistic Regression Analysis in the NR Subgroups

Factor	OR	95% CI	P
Preoperative steroids	1.265	1.063–1.496	0.027
Age	1.359	1.0370–1.771	0.023

None of the parameters examined and listed in **Table 2** predicted long-term hematologic outcomes, although we confirmed that the extent of the immediate response was a good predictor of long-term results, which is often described in the literature as well: 71% long-term response for CR and 20% for PR ($P <$ .001).

DISCUSSION

Splenectomy in the Treatment of ITP

In steroid-refractory and steroid-dependent ITP, splenectomy provides the best and most permanent results as a second-line therapy compared with medicinal therapy (TPO mimetics and rituximab).[6,10]

A splenectomy exerts its effect by removing the primary site of platelet destruction and partly by removing an important site of antiplatelet antibody production, with the response rate reported at an average of 80% and the rate of permanent responders ~60%.[4,6]

In a systematic review of 135 cases published in 2004, the response rate was 88%, and a complete response was found in 66% of the patients, with a median follow-up duration of 28 months.[3] In a systematic review of laparoscopic splenectomies published in 2009, the conversion rate of the 1223 patients examined was 5.6%, and the success rate was 72%.[11]

In our study, CR was found in 70% (n = 28) and PR occurred in 12.5% (n = 5) of the cases; that is, a total of 82.5% of the patients responded to splenectomy performed in accordance with the guidelines. This rate was not influenced by whether the splenectomy was performed as a second- or third-line therapy. In patients treated with azathioprine or IVIG after steroid treatment, CR was achieved in 60% after splenectomy, PR occurred in 20% after the surgery, and NR in 20%. These rates are consistent with the results found after examining all the patients; therefore, previous treatment did not influence the efficacy of the splenectomy.

After a follow-up of an average of 9.92 years, 63.6% of the responder patients (CR + PR = 33) had a long-term response (n = 21), which correlates with the known rate of one-third of patients showing a response initially and developing a relapse later.[3,10]

If relapse occurs after splenectomy, based on data in the literature, it takes place at 12–48 months. After this time, it occurs only sporadically.[10] Our study confirmed this re-

sult. In our patients, relapse developed after an average of 12.5 months, and no relapse was detected after 47 months.

Alternative options for second-line therapy are medications such as rituximab or TPO-RAs. The long-term efficacy of these treatments is less than that of splenectomy. Rituximab (a chimeric monoclonal antibody against CD20) has an immediate efficacy of 50–65%, although relapse occurs frequently; therefore, the long-term response after 12 and 24 months is only between 20 and 30%. In 2015, a multicenter randomized, double-blind, placebo-controlled study was published, describing a long-term response rate for rituximab similar to that for the placebo.[12]

A study published in 2016 comparing the results for splenectomy, and rituximab therapy found splenectomy to be more effective (the 30-month primary outcome–free survival rate was 84–86% for splenectomy vs 47% for rituximab; $P =$ .0002).[5]

TPO agonists exert their effect by enhancing platelet production, not by modulating the immune system. TPO agonists stimulate platelet production of megakaryocytes. A response rate of 59–80% can be achieved with these medications; however, a great disadvantage of these products is that they are expensive and that permanent treatment is required, because withdrawal of therapy leads to the recurrence of thrombocytopenia.[13]

With regard to the splenectomy technique, several publications are available comparing LS and open splenectomy (OS). It can be concluded that LS and OS are similarly effective from a hematologic point of view.[8] Qu et al[4] performed OS and LS, and found no significant difference for relapse-free survival during a 36-month follow-up (86% for OS vs 91% for LS; $P =$ .792). Chater et al[5] reached similar results for 30-month event-free survival, with no difference found between LS and OS (86% vs 84%). In a systematic review conducted on 47 case series in 2004, a lower mortality rate (1% vs 0.2%) and fewer complications (12.9% vs 9.6%) were observed for LS vs OS.[3] The main limitation of the laparoscopic technique is splenomegaly (a spleen weighing over 500 g), although our previous results showed that laparoscopic splenectomy was not contraindicated, even in the case of extreme splenomegaly (a spleen weighing over 2000 g).[14] Splenomegaly causing technical difficulties is not characteristic of ITP; therefore, this limiting factor is not common either.

Potential Complications of Splenectomy

With second-line medicinal therapy, the possibility of peri- or postoperative or late complications of splenec-

tomy is often emphasized.[10] In our study, complications were observed after splenectomy in only 2 cases, with the patients experiencing bleeding that required reoperation. No complication occurred besides reoperation due to bleeding in 5% of the patients, although surgery was performed with a platelet count of 5000/mL in 3 of them. Several publications analyzed the safety of surgeries performed in patients with a low platelet count. Cai et al[15] compared the results of LS in patients with a platelet count below 10×10^9/L (grade 1) with those of patients operated on with a higher platelet count (grade 2: $10–30 \times 10^9$/L, and grade 3: $>30 \times 10^9$/L). Our results showed that blood loss and the number of complications was not significantly increased, and hospital stay was not significantly prolonged in patients operated on with a lower platelet count. Wu et al[16] examined surgical patients with a platelet count below 20×10^9/L and found no difference with regard to the outcome in patients who did not receive preoperative platelet transfusion compared with those who did. In our case, reoperation was performed in 2 patients with platelet counts of 36 and 42×10^9/L.

No pancreatitis, perioperative infection, or suppuration occurred in our series. Patients who have splenectomy are more susceptible to infections and vascular complications in the long term. Increased risk of infections is confirmed in patients who undergo splenectomy. In a Danish cohort study, susceptibility to infections among 3,812 patients who had splenectomy was compared with that of 8,310 matched nonsplenectomized patients and that of 38,120 control patients. The risk rate for sepsis increased 14-fold during the first year in patients who had splenectomy compared with the general population; after 1 year, the risk rate decreased to 4-fold. Comparing the results with those of nonsplenectomized patients with ITP, an increased risk rate of sepsis was found only during the first 90 days.[17] Perioperative vaccination, patient education on the risk of overwhelming sepsis, and use of antibiotic prophylaxis greatly aid in preventing septic complications. For instance, Vianelli et al[18] examined 402 patients in their study and did not report sepsis-related mortality. In our study, no sepsis-related mortality occurred.

In addition to the risk of infection, there is potential for vascular complications. The thrombocytopenia in ITP makes patients susceptible to thromboembolization, according to data in the literature,[19] and splenectomy increases the risk of venous thromboembolization.[20] In our study, with prophylactic LMWH administered permanently (35–40 days), no deep venous thrombosis was confirmed; only one superficial thrombophlebitis was identified.

In our investigation, surgery-related morbidity was not significant, and because of potential risks, estimation of response is very useful in considering surgery based on predictive parameters.

Predictive Factors of the Efficacy of Splenectomy

There are several publications about predictive factors that may be determined before splenectomy and that may be used to predict long-term results of surgery, as well. The most widely accepted predictive factors are younger age, steroid dependency, nonrefractory status, higher platelet count before surgery, and splenic sequestration. In our study, no data were available for splenic sequestration, so the other factors were analyzed for predictive value.

Our study confirmed the predictive value of younger age described in the literature.[21–22]

The average age of the CR group was 42.79 ± 13.24 years, that of the PR group was 49.2 ± 18.32 years, and that of the NR group was 60.14 ± 24.21 years. Long-term follow-up for persistent responders showed an average age of 42.6 ± 16.5 years, and patients developing a relapse were 45.75 ± 21.3 years of age on average. The response rate for patients below the age of 50 years (n = 22) was 90.1% (77.3% CR and 13.6% PR), whereas this rate was 72.2% (61.1% CR and 11.1% PR) in patients over the age of 50 (n = 18). There were significantly more NR patients in the older group (P = .023). In addition, 70% of the patients below the age of 50 showing an immediate response also had a long-term response, whereas this rate was only 53.8% in older patients. Shojaiefard et al[21] obtained results similar to ours; in their study, patients below the age of 52 responded to splenectomy more positively compared to elderly patients (P < .01). Fabris et al[22] confirmed age below 40 years to be the only major predictive factor in a similar investigation. Opposite results have been reported in the literature, as well: Vianelli et al[10] studied 233 patients for more than 10 years and found no link between age and response to splenectomy, and, similarly, Rijcken et al[23] had negative results for the predictive value of age in their examination of 72 patients.

Several studies have analyzed the predictive role of response to preoperative steroids.[23,24] In our study, all the surgical patients who were steroid dependent (n = 17) were in the CR group, although all the PR (n = 5) and NR (n = 7) patients fell into the preoperative steroid-refractory group. There were significantly more NR patients in the steroid-refractory group (P = .027). In the case of patients showing a persistent response (n = 21), 12 were steroid dependent and 9 were steroid refractory; in the loss-of-response group (n = 12), 5 patients were steroid dependent and 7 were steroid refractory. Rijcken et al[23] and Aleem[24] among others, found response to steroids to be a predictive factor in their studies.

Perhaps the least controversial fact is that CR significantly predicts the probability of a long-term stable response.[23,25] Wang et al[26] followed up 92 patients and found platelet count in the third postoperative month to be an independent predictor of long-term outcome. Rijcken et al[23] found a greater increase in platelet count in the postoperative period ($>150,000/\mu$L) to be a predictor of long-term response. Montalvo et al[27] examined 150 patients and found an immediate response after surgery ($\geq$150,000) to be the 1-year CR predictor. In addition, Vianelli et al[10] followed up 233 patents for at least 10 years and confirmed no stable predictors of long-term response. During our follow-up, we reached the same findings. Results were found to be permanent in 71% of the CR patients, but a long-term response occurred in only 20% of the patients in the PR group.

In the future, lifespan and sequestration studies of platelets labelled with indium would be useful (if the literature data show that splenectomy is effective in 90% of cases),[25] although such data were not available in our study.

Finally, we compared our results to the literature data and examined both the number of published studies that used the consensus guidelines to follow up on patients in the long term after laparoscopic splenectomy since the 2011 introduction of the standardized guidelines[8] and the predictive factors in these publications.

Xu et al[28] analyzed 114 patients in whom age and postoperative peak platelet count were independently associated with the response. Vecchio et al[29] also examined patients with laparoscopic and open surgeries for a 2015 publication and found that a higher increase in postoperative platelet count may be predicted in patients with a low preoperative platelet count. In the investigation by Rijcken et al[23] with 72 patients (noted above), perioperative platelet counts were predictive factors of long-term response. Navez et al[30] studied 82 patients in 2014, primarily examining the predictive value of platelet sequestration; the platelet sequestration site was not found to be a predictive factor, but age was. Montalvo et al[27] reviewed data on 150 patients and found no predictive factors of long-term response besides immediate CR (response $>150,000$ platelets/mL during the first week). In 2013, Wang et al[26] reported that platelet count in the third

postoperative month was a significant independent predictor of long-term favorable hematologic outcomes.

In summary, literature data have been exceedingly heterogeneous with regard to predictive factors, even since the consensus guidelines were published. In addition, potentially prospective studies are necessary to determine predictive factors. Furthermore, long-term follow-up of patients with various imaging techniques is important to screen the accessory spleen and its possible role in non-responsive and refractory ITP.

CONCLUSION

Although several medications are available for second-line ITP therapy, splenectomy provides the longest lasting results. LS is the gold standard, as it can be performed safely and with great efficacy in centers experienced in the technique. In our study, young age and a preoperative response to steroids (steroid-dependent cases) were positive predictors for the success of splenectomy. In the case of an immediate complete response to splenectomy, relapse occurred significantly less often during long-term follow-up.

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