

Late Results After Splenectomy in Adult Idiopathic Thrombocytopenic Purpura

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ABSTRACT

Background: We performed a retrospective study on patients with idiopathic thrombocytopenic purpura (ITP) to evaluate the response to splenectomy in relation to preoperative platelet count.

Materials and Methods: Two groups of patients operated on with laparoscopic or open splenectomy for ITP, with a platelet count $\leq 30,000/\mu\text{L}$ (study group: 22 patients) and $>30,000/\mu\text{L}$ (control group: 18 patients), respectively, were compared. The two groups were homogeneous in relation to age, sex, length of preoperative steroid therapy, and time interval between diagnosis and surgery (Student *t* test with $P > .1$). The results of surgery were evaluated at one year after splenectomy. Positive response to surgery, according to the American Society of Hematologic Guidelines, was considered in patients with a postoperative platelet count $\geq 100,000/\mu\text{L}$ or in patients with a postoperative platelet count $\geq 30,000/\mu\text{L}$ and a twofold increase in platelet count from baseline, in the absence of bleeding.

The postoperative platelet count increase rate was statistically related to preoperative platelet count in both the study and control groups. Statistical analysis was performed using the Student's *t* test for independent sample and the Pearson correlation in a 2-tailed test.

Results: No relationship between preoperative platelet count and postoperative platelet percent increase was observed in the control group ($r = -0.41$; $P = .089$), whereas a significant negative correlation ($r = -0.68$; $P = .0004$) was found in the study group.

Conclusions: A higher increase of postoperative percent platelet count may be predicted in patients with a low preoperative platelet count.

Key Words: Idiopathic thrombocytopenic purpura, Splenectomy, Laparoscopic splenectomy.

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune hematological disorder resulting in low platelet count (diagnosed with the presence of a platelet count $<100,000/\mu\text{L}$), which may lead to spontaneous bleeding.

Based on ITP's autoimmune pathogenesis, immunosuppressive or immune-modulating therapy has been the standard initial treatment for adults with moderate to severe thrombocytopenic purpura, and splenectomy, performed either by the laparoscopic or traditional approach, has been indicated only in cases refractory to medical therapy.¹⁻⁶

Complete response after splenectomy has been observed in 66% to 100% of cases.⁵⁻⁹ Response to splenectomy has been related to several predictive factors⁴⁻¹⁴ but is still uncertain, with no definitive results reported on this issue.

Only few studies have addressed the results of splenectomy in patients with a very low platelet count.¹⁵ Preoperative platelet count, however, has never been related to a postsplenectomy platelet increase.

In this study, we retrospectively analyzed the results of splenectomy in patients with ITP, comparing 2 groups of patients with preoperative platelet count, respectively, inferior and superior to $30,000/\mu\text{L}$.

MATERIALS AND METHODS

We evaluated retrospectively 40 consecutive patients affected by ITP who underwent laparoscopic or open splenectomy from January 2002 to December 2011. Among these patients, in 22 cases (study group) the preoperative platelet count was $\leq 30,000/\mu\text{L}$ (mean 15,954, range 8000-30,000), whereas in the remaining

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Table 1.
Patients' Data

	Study Group (Preoperative Platelet Count $\leq 30,000/\mu\text{L}$)	Control Group (Preoperative Platelet Count $> 30,000/\mu\text{L}$)
No. patients	22	18
Mean age, y (range)	30.18 (19–50)	29.56 (17–45)
Sex ratio (M/F)	11/11	7/11
Open/laparoscopic splenectomies	8/14	12/6
Mean preoperative platelet count, μL (range)	15,954/ μL (8000–30,000)	55,833/ μL (34,000–90,000)
Mean postoperative platelet count, μL at 1 year (range)	300,364/ μL (22,000–750,000)	221,333/ μL (24,000–600,000)
Rate of response to splenectomy	90.9%	72.2%

18 patients (frequency-matched control group), the preoperative platelet count was $30,000/\mu\text{L}$ (mean $55,833$, range $34,000$ – $90,000$). **Table 1** summarizes data for each group of patients.

The mean age of patients was 30.2 years (range 19–50) in the study group, and 29.6 years (range 17–45) in the control group. The male-to-female ratio was 1.00 (11 males, 11 females) in the study group and 0.64 (7 males, 11 females) in the control group.

Alternative etiologies of thrombocytopenia were accurately ruled out before treatment in all patients.

When surgery was proposed, all patients were symptomatic with various degrees of mucocutaneous bleeding, and menorrhagia in the females. Surgery was indicated for recurrent bleeding episodes or for risks of bleeding resulting from the patients' lifestyle (2 patients in the control group performed heavy sports) or secondary to associated pathologies (2 patients in the control group had, respectively, peptic ulcers and ulcerative colitis).

All patients were previously treated with corticosteroid therapy (prednisone 1–2 mg/kg/d), and the length of presurgical medical treatment ranged from 2 weeks to 28 months (mean 8.45) in the study group and from 2 weeks to 36 months (mean 11.19) in the control group.

Overall, 24 patients (60%) did not respond to steroids (13 in the study group, 11 in the control group), whereas in 16 cases (40%) (9 in the study group, 7 in the control group) corticosteroid therapy was associated with temporary remission but relapse of the disease with the interruption of medical treatment.

The interval between diagnosis and splenectomy ranged from 4 to 60 months (mean 18.9) in the study

group and from 4 to 45 months (mean 19.7) in the control group.

Open and laparoscopic splenectomies were performed in the traditional fashion reported elsewhere.¹⁶ In 9 cases, cholecystectomy was performed associated with splenectomy using the standard technique.¹⁷

All patients were followed up for at least one year after the surgery. Results of the surgery were evaluated at one year after splenectomy through the assessment of blood platelet count and remission of symptoms in both the study and control groups. Based on the recommendations of the International Working Group reported by the American Society of Hematology (ASH),¹⁶ a positive response was considered when the postoperative platelet count was $\geq 100,000/\mu\text{L}$ or in patients with a postoperative platelet count $\geq 30,000/\mu\text{L}$ and a twofold increase in platelet count from baseline, in the absence of bleeding.

The postoperative platelet count increase rate was statistically related to the preoperative platelet count in both the study and control groups.

Statistical analysis was performed using the Student *t* test for independent sample and the Pearson correlation in a 2-tailed test.

RESULTS

The study and the control groups were statistically homogeneous. The Student *t* test for independent sample showed a *P* value $> .1$, with no significant differences when age, sex, length of preoperative steroid therapy, and diagnosis-to-splenectomy interval were compared between the study and control groups.

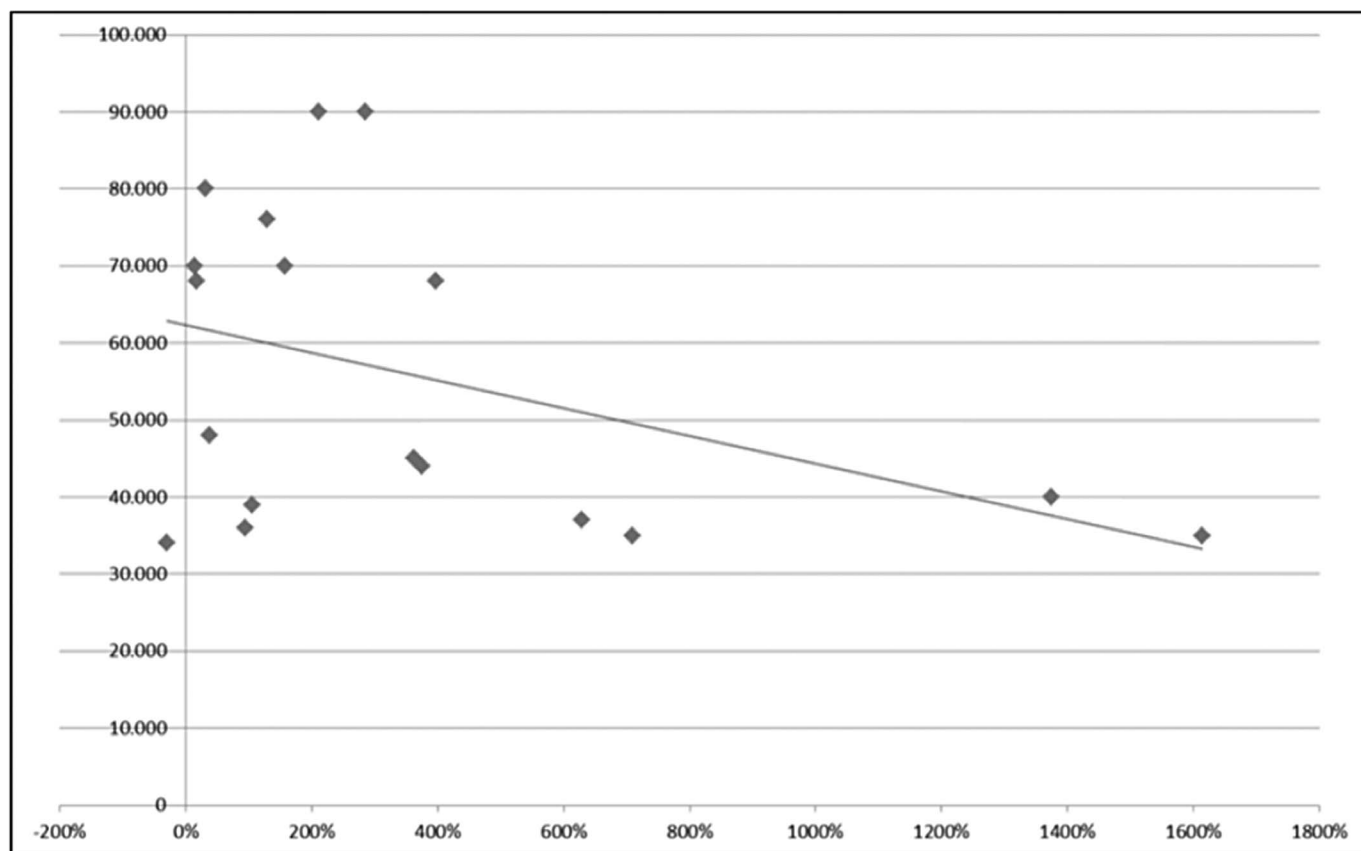


Figure 1. The correlation between preoperative platelet count and postsplenectomy platelet count increase (percentage of preoperative value) in patients with a preoperative platelet count $>30 \times 10^9/L$ (no correlation found: $r = -0.41$; $P = .089$).

Accessory spleens were found and removed in 6 patients (15%): in 2 patients with a preoperative platelet count $\leq 30,000/\mu L$ and in 4 patients with a preoperative platelet count $>30,000/\mu L$.

According to the criteria of the International Working Group reported by ASH,¹⁸ in this study response to splenectomy was observed in 13 of 18 patients (12 complete responders with a postoperative platelet count $>100,000/\mu L$ and 1 patient responder with a platelet count $\geq 30,000$ but $<100,000/\mu L$ and a doubling platelet count from baseline) in the control group (overall rate 72.2%) and in 20 of 22 patients (19 complete responders with a postoperative platelet count $>100,000/\mu L$ and 1 patient responder with a platelet count $\geq 30,000$ but $<100,000/\mu L$ and a doubling platelet count from baseline) in the study group (overall rate 90.9%).

The Pearson correlation test, used to find an association between preoperative platelet count and postoperative platelet percent increase at one year after surgery, showed no relationship in the control group (preoperative platelet

count $>30,000/\mu L$), with $r = -0.41$ and $P = .089$ (**Figure 1**). In the study group, in which the preoperative platelet count was $\leq 30,000/\mu L$, a significant negative correlation ($r = -0.68$; $P = .0004$) was found between the 2 variables, demonstrating a higher increase in postoperative percent platelet count in patients with a lower preoperative platelet count (**Figure 2**).

DISCUSSION

ITP is an autoimmune hematological disease characterized by the destruction of opsonized platelets in the reticulo-endothelial system,^{6-15,19} particularly in the spleen or by suppression of platelet production,¹⁹ resulting in a persistent low platelet count, which may lead to spontaneous bleeding.⁶

ITP is a relatively common hematological disorder affecting people of all ages, with an incidence of roughly 2 in 100,000 per year and spontaneous remission of 5% to 11% in adult patients.²⁰ Primary ITP was defined by the Inter-

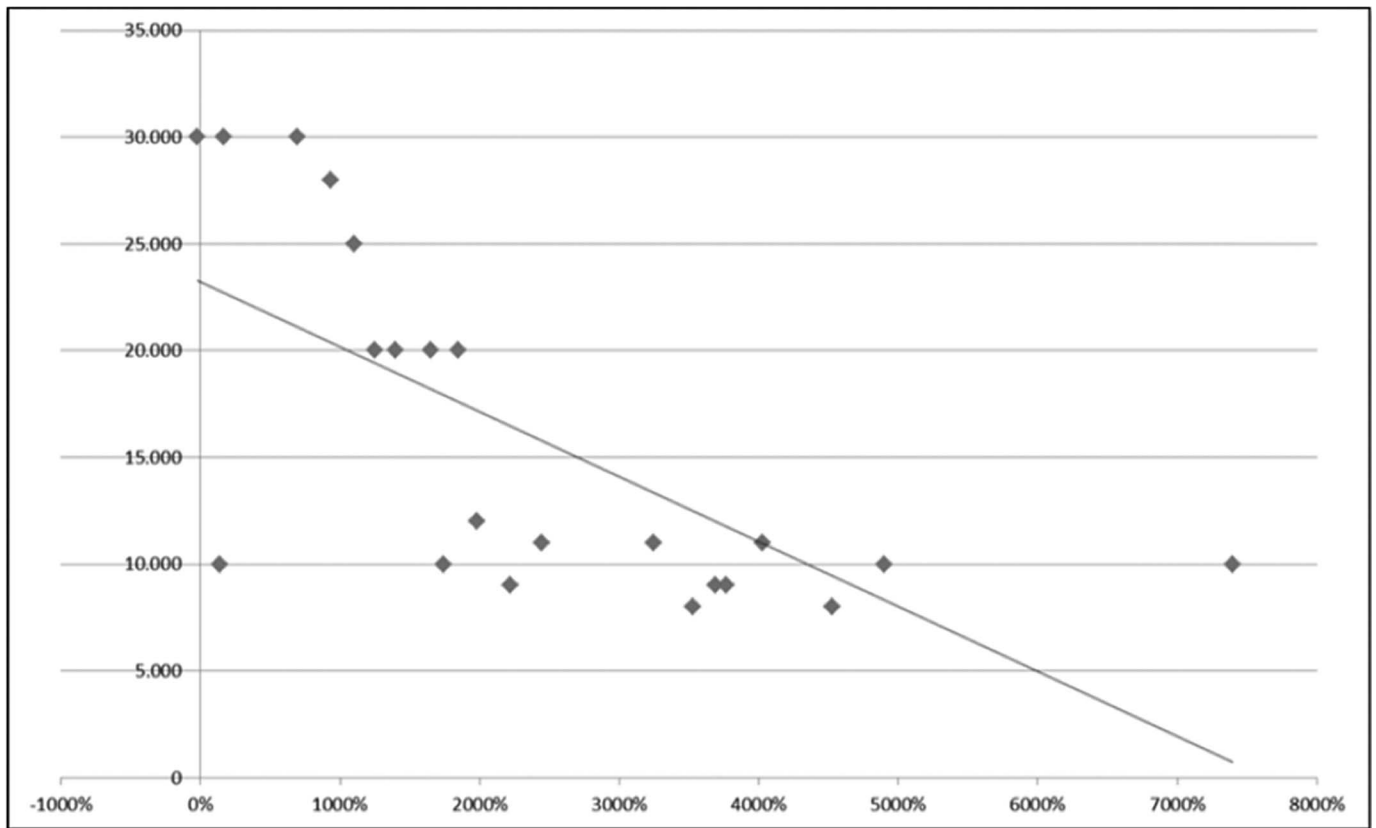


Figure 2. The correlation between preoperative platelet count and postsplenectomy platelet count increase (percentage of preoperative value) in patients with a preoperative platelet count $\leq 30 \times 10^9/L$ (significant negative correlation demonstrating a higher increase of postoperative percent platelet count in patients with a lower preoperative platelet count: $r = -0.68$; $P = .0004$).

national Working Group as a platelet count $<100,000/\mu L$ in the absence of other causes or disorders that may be associated with thrombocytopenia.

There is no evidence in the literature that could allow determination of a threshold platelet count under which a patient with ITP should be treated. According to the 1996 ASH guidelines,¹ treatment for newly diagnosed ITP should be indicated for patients with a platelet count $<30,000/\mu L$ or in patients with a platelet count $<50,000/\mu L$ with significant bleeding or risk of bleeding (such as in hypertension, peptic ulcer disease, or having a vigorous lifestyle). In the 2011 ASH guidelines, however, it is outlined that there is limited evidence for treatment recommendation based on platelet count in ITP patients.¹⁸ Therefore there is currently no evidence on which to base an indication for treatment in relation to platelet count. Several authors^{9,21-25} suggest that the decision to treat should be made on an individual basis considering severity of bleeding, bleeding risk (such as previous bleeding

episodes, hypertension, age, and sex), the patient's preferences, and a lifestyle that increases the risk of bleeding.

The primary aim of ITP treatment is to maintain a stable platelet count at a level that prevents bleeding events.^{2,18} The International Working Group proposed the definition of complete response when a platelet count $>100,000/\mu L$ is achieved with treatment. Therapeutic response is also considered in patients with a platelet count $>30,000/\mu L$ if a doubling platelet count from the baseline is observed in symptomless patients.¹⁸ Although it is regarded as the second-line therapy in refractory disease after medical treatment, splenectomy is a well-established modality found in the literature and appears to be the single best option to convert a patient with ITP to a "nonpatient."²⁶ The percentage of patients who need splenectomy is unclear and is usually reported to be 20% to 45% according to two large series.^{19,22}

Nevertheless, it appears that the popularity of splenectomy has decreased dramatically in the past few years,

despite increasing reports of its high rate and durable response with surgery.²⁶

There are discordant opinions, however, about the indication for splenectomy and the timing of surgery. Splenectomy should not be performed as the initial therapy, and it should be reserved for patients who did not respond to medical therapy first.

The British Committee for Standards in Haematology guideline recommended splenectomy with a platelet count $<30,000/\mu\text{L}$ in cases refractory to medical treatment.³ This platelet threshold is considered a trigger for treatment, either medical or surgical with splenectomy, by several clinicians. However, this is not the only criterion, and indications for splenectomy are the same as for first-line medical treatment, which were mentioned earlier.

The timing of performing splenectomy is also still controversial. In 1996, ASH guideline panelists considered indications to splenectomy after 6 weeks from initial diagnosis when the platelet count is $<10,000/\mu\text{L}$ or after 3 months with a platelet count $<30,000/\mu\text{L}$ (with or without bleeding symptoms). In the same consensus conference, the panelists considered splenectomy to be inappropriate in symptomless patients who have had the diagnosis for 6 months and have a platelet count $>50,000/\mu\text{L}$ and low hemostatic risk.¹

Other authors²⁷ accordingly, to reduce the duration and morbidity of medical treatment, have recommended early splenectomy in patients who do not respond rapidly to initial glucocorticoid treatment. However, in their 2010 consensus review, Provan et al noted that in most reported series, splenectomy was deferred at least 6 months after diagnosis.² In our series, we primarily performed splenectomy in patients who did not respond to medical treatment after at least 6 months of therapy.

Despite the high response rate of splenectomy, the number of postsurgical failures remains significant and the knowledge of predictive factors of response to splenectomy could help select patients for surgery, avoiding unnecessary operations.¹⁰

Several studies^{7,11,12,19} have been carried out to evaluate the response to splenectomy in ITP patients according to some hypothetic predictive factors. Predictive factors such as age and sex, length of the disease and time interval between diagnosis and surgery, and length and response to the preoperative corticosteroid therapy have been related to the response to splenectomy.

In some studies, a better response to splenectomy was observed in patients ≤ 52 years,^{6–8,12} complete or partial preoperative response to steroid therapy,^{5,7} in cases with short length of disease,⁶ and in patients responding with a temporary increase in platelet count to high-dose preoperative intravenous antibody therapy.^{5,7} Alternately, other investigators failed to demonstrate that age and sex,^{5,11,13,14} length of the disease and time between diagnosis and splenectomy,^{5,23} response to medical treatment,^{5,25} and preoperative platelet count^{5,13} could predict the success of splenectomy.

All of the studies reported in the literature relating the aforementioned predictive factors of response to splenectomy, however, are not conclusive, and further investigations are needed.

Only a few studies have addressed the response to splenectomy in relation to the preoperative platelet count. Radaelli et al,⁵ in a series of 65 adult patients with ITP who underwent splenectomy did not find any relationship between response to splenectomy and preoperative platelet count. Balagué et al,¹³ studying 103 patients treated by splenectomy in their univariate and multivariate statistical analysis, were unable to demonstrate that preoperative platelet count was a predictive factor of response to splenectomy, because there was not a significant difference in the response comparing patients with preoperative platelet counts less or more than $20,000/\mu\text{L}$. In this latter study, response was considered when a stable postoperative platelet count $\geq 50,000/\mu\text{L}$ was obtained. Duperier et al,¹² in their study of 67 patients, observed a successful response to splenectomy in patients with a preoperative platelet count $>70,000/\mu\text{L}$. In their univariate analysis, a statistical difference with a *P* value of .005 between patients groups with more or less than $70,000/\mu\text{L}$ was observed. In their multivariate analysis, younger patients (*P* = .005) and a higher preoperative platelet count (*P* = .007) again predicted a successful response to splenectomy.

In the present study, we found that a higher increase in postoperative percent platelet count with a stable positive response can be found in patients with a preoperative platelet count $\leq 30,000/\mu\text{L}$. In one of our previous studies comparing laparoscopic and open splenectomies groups,⁴ we observed that this greater increase of postoperative platelet count in patients with a lower preoperative platelet count seemed not to be related to the type of surgery. We used the cutoff of $30,000/\mu\text{L}$ because a recent recommendation in the ASH Guidelines (published in 2011) suggest using this

value of platelet count to decide whether to begin a treatment in adult ITP patients.

It is currently difficult to find any explanation for these results. However, the results of this study could be relevant when indication to splenectomy in ITP patients has to be considered. Splenectomy should be better performed in patients who are not responding to medical treatment when the preoperative platelet count is $\leq 30,000/\mu\text{L}$. This cutoff in the indications to splenectomy does not increase surgical morbidity. The risk of bleeding seems not to be augmented, especially when splenectomy is performed laparoscopically, which, according to the literature,^{15,28,29} could be responsible for hematological benefits, significantly reduce the need for platelets transfusion, and lower the perioperative blood loss and complications when compared with open surgery.

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