Surg Endosc (2001) 15: 1386–1389
DOI: 10.1007/s00464-001-8154-2

Surgical Endoscopy
Ultrasound and
Interventional Techniques

Are the favorable outcomes of splenectomy predictable in patients with idiopathic thrombocytopenic purpura (ITP)?

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Received: 26 March 2001/Accepted in final form: 18 June 2001/Online publication: 5 October 2001

Abstract
Background: Historically, splenectomy has been an accepted procedure in the management of immune thrombocytopenic purpura (ITP). However, it is also true that the response to splenectomy in patients with ITP seems to be unpredictable. Therefore, the purpose of this study was to identify clinical variables that might predict a favorable response to splenectomy in patients with ITP.
Methods: Data were collected retrospectively for 40 adult patients with ITP who underwent laparoscopic (LS) and open (OS) splenectomy at Emory University Hospital between 1992 and 1999. Demographics and outcomes were recorded. Age, sex, disease duration, comorbidities (ASA > 2), previous response to steroids and/or other medications, and preoperative platelet count were analyzed by univariate (*t*-test, Fisher's exact test) and multivariate statistical methods.
Results: Of the 20 patients in each group, improved platelet counts were noted in 18 patients (90%) in the LS group and 20 patients (100%) in the OS group. Follow-up (16 ± 3 months) was obtained in 19 LS patients (95%) and 16 OS patients (80%), with 84% and 87.5% sustained response rates, respectively. After univariate analysis, two variables (age and disease duration) were found to be significantly related to the outcome of splenectomy ($p < 0.01$). However, after multiple logistic regression analysis, only disease duration (relative risk = 1.083; CI, 1.004–1.167) was an independent prognostic factor for a sustained response to splenectomy.
Conclusion: These results suggest that the response to splenectomy (laparoscopic and open) in patients with ITP cannot be adequately predicted on the basis of presplenectomy clinical variables. However, disease duration and patient age should be taken into consideration when selecting patients for splenectomy.

Key words: Immune thrombocytopenic purpura — Splenectomy — Laparoscopy — Spleen

Immune thrombocytopenic purpura (ITP) is the most common and thoroughly studied benign hematologic disease, affecting > 14,000 new patients every year in the United States [9, 13]. The aim of surgical treatment is to remove the major site of platelet destruction and antibody production—the spleen. Splenectomy is now regarded as the most effective means of treating ITP. Moreover, medical treatment is prohibitively expensive and often associated with troublesome side effects (corticosteroids).

Data on the surgical management of ITP have shown that the immediate postoperative response rates range from 75% to 93% and that major complications occur very rarely [1, 5, 15]. Furthermore, since laparoscopic splenectomy (LS) was first described in 1991 [4], several large series of laparoscopic splenectomy have been reported [2, 8, 13, 18]. However, in these series, as previously, the response to splenectomy was unpredictable.

Several groups have attempted to establish useful predictors of splenectomy outcomes in patients with ITP. The most frequently mentioned prognostic factors are age, previous response to steroids, interval from diagnosis to splenectomy, site of platelet sequestration, and platelet survival [1, 5, 6, 16]. However, other studies [7, 10, 11, 14] have failed to confirm the predictive value of these preoperative clinical variables.

The aim of this study was to identify the clinical variables that predict a favorable response to splenectomy in patients with ITP.

Patients and methods

Retrospectively, we collected and analyzed data for 40 consecutive adult patients with ITP who underwent either laparoscopic ($n = 20$) or open ($n = 20$) splenectomy at Emory University Hospital between 1992 and 1999. The diagnosis of ITP was established according to the following generally

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Table 1. Demographics and characteristics of patients with ITP ($n = 40$)

Parameter	*n* (%)
Age (yr)	42.5 ± 19[a]
Weight (kg)	81 ± 21[a]
Sex (F/M)	25/15
Comorbidities (ASA >2)	14 (35)
Preoperative treatment	
Steroids	35 (87.5)
IVIG	17 (42.5)
WinRho	3 (7.5)
Spleen weight (g)	240 ± 176[a]
Accessory spleen	6 (15)

[a] Mean ± SD

accepted criteria: thrombocytopenia with abundant or sufficient megakaryocytes and the absence of systemic diseases, splenomegaly, coagulation disorders, or medication side effects [1].

The indications for splenectomy in these patients were unsuccessful treatment with corticosteroids or other medications and/or the requirement of high dosages of steroids for prolonged periods of time to maintain platelet count > 30 G/L. Prior to surgery, all patients were treated with corticosteroids and/or intravenous immunoglobulin (IVIG) to raise the platelet count and thus minimize the risk of intraoperative bleeding. All of them received pneumococcal vaccine (Pneumovax), and 19 of them received hemophilus and meningococcus vaccine before surgery to avoid overwhelming postsplenectomy sepsis (OPSS).

The immediate impact of the surgery on the platelet count was evaluated on the day of discharge from the hospital. All patients were evaluated at a mean of 16 ± 3 months after surgery. Five patients were not available for follow-up; however, this did not alter the statistical analysis.

To rule out the presence of missed accessory spleen as a cause of failure, ^{99m}Tc heat-denaturated red blood cell scintigraphies (DRBCS) were performed in patients who failed to respond or relapsed after splenectomy.

We looked at a total of seven potentially prognostic clinical variables, including age, sex, disease duration, comorbidities not related etiologically to immune thrombocytopenia (ASA > 2), previous response to corticosteroids, preoperative platelet count, and type of splenectomy (open or laparoscopic). The prognostic significance of these presplenectomy clinical variables was initially evaluated by univariate analysis (*t*-test, chi-square, and Fisher's exact tests). The variables found to be significantly related to the achievement of the favorable outcomes were subsequently subjected to multiple logistic regression analysis. Results are presented as mean ± standard deviation (SD).

To facilitate the statistical analysis of the data, we established the following two groups for comparison: (a) responders (patients with sustained increase of platelet count > 50 G/L not requiring further treatment) and (b) nonresponders, (patients with platelet count < 50 G/L or with normal platelet count requiring maintenance of medical treatment during follow-up).

Results

Response to splenectomy

Of the 40 patients who underwent splenectomy for ITP, 20 had a laparoscopic procedure. A total of five complications were seen in five patients (pleural effusion, anemia, and pneumonia). No reoperations were necessary, and there were no deaths. No LS patients were converted to laparotomy. Patient demographics and other characteristics are listed in Table 1.

The mean preoperative platelet count before medical preparation was 31.0 ± 25.1 G/L; after preparation, it was 70.5 ± 58.0 (all patients were treated with steroids and/or IVIG to raise their platelet count prior to surgery). After splenectomy, there was an immediate increase in the platelet count of most patients. Between the day before surgery and the day of discharge, the mean platelet count rose significantly from 70.5 ± 58.0 G/L to 242.0 ± 156.7 G/L ($p < 0.001$) and remained high (230.0 ± 151.0 G/L) at the time of follow-up (16 ± 3 months) (Fig. 1).

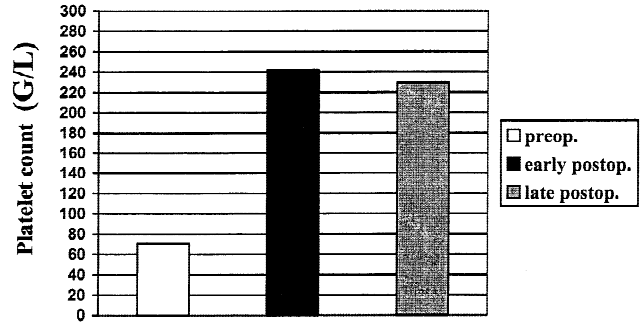

Fig. 1. Effect of splenectomy on platelet count ($p < 0.05$, ANOVA, Tukey's test). Preop. = platelet count prior to surgery, early postop. = platelet count on the day of discharge, late postop. = platelet count 16 ± 3 months postoperatively.

In the immediate postoperative period, 18 LS patients (90%) and 20 OS patients (100%) responded to the splenectomy. No response was seen in two LS patients (5%). Figure 2 shows the overall response rate for both types of splenectomy (open and laparoscopic).

Follow-up (16 ± 3 months) was obtained in 19 LS patients (95%) and 16 OS patients (80%). A sustained response was noted in 30 patients (85.7%). None of these patients required additional medical therapy during the follow-up period. Five patients (14.3%) failed to achieve any kind of sustained remission (Fig. 3).

At the time of surgery, six accessory spleens were found in six patients (15%), three of whom had undergone a laparoscopic procedure. Patients who failed to respond or relapsed after splenectomy underwent postoperative DRBCS, which did not reveal any persistence of splenic tissue.

Identification of preoperative prognostic factors

All of the presplenectomy variables were examined by univariate analysis (*t*-test, chi-square, and Fischer's exact tests) in relation to the achievement of a sustained remission (complete or partial.) Only two variables were found to be significantly related to the outcomes of splenectomy ($p < 0.01$) (Table 2).

Age at the time of splenectomy had a prognostic value; older patients responded less often than younger patients did. Likewise, patients with a sustained remission after splenectomy had a significantly shorter diagnosis-to-splenectomy interval. Most patients who responded to steroids did well after splenectomy; but at the same time, a large number of patients who did not respond to steroids before surgery did well too. Preoperative platelet count had no prognostic value for the results of splenectomy.

These individually significant variables were subsequently included in the multiple logistic regression analysis, which revealed that only disease duration (relative risk = 1.083; CI, 1.004–1.167) was an independent prognostic factor for a sustained response to splenectomy.

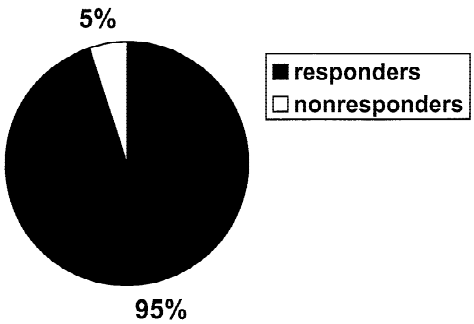

Fig. 2. Response to splenectomy on the day of discharge.

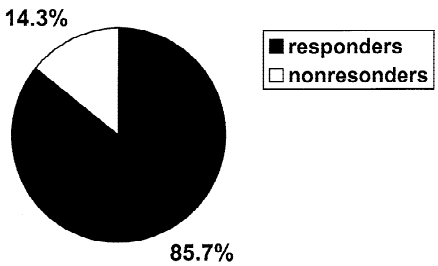

Fig. 3. Response to splenectomy at the time of follow-up (16 ± 3 months).

Table 2. Presplenectomy variables: univariate analysis in relation to the achievement of a stable remission

	Responders	Nonresponders	*p* value
Age (yr)[a]	39 ± 18	64 ± 16	0.0013
Sex (F/M)	20/10	2/3	NS
Disease duration (mo)[a]	14 ± 11	61 ± 46	0.0001
Preoperative platelets (G/L)[a]	82 ± 62	31 ± 19	NS
ASA >2	11 (37%)	3 (60%)	NS
Steroid responders/nonresponders	15/15	0/5	NS
LS/OS	16/14	3/2	NS

[a] Mean ± SD
NS, not significant; ASA, American Society of Anesthesiologists; LS, laparoscopic splenectomy; OS, open splenectomy

Discussion

In our study 71.4% of patients achieved platelet counts > 150 G/L in the late postoperative period (16 ± 3 months). This pattern of response is similar to the average complete response rate of 75% reported by other investigators [1, 13]. Splenectomy (open or laparoscopic) is a successful treatment for ITP because the spleen is not only an important location of platelet destruction but also the site of antiplatelet antibody production. Although the morbidity and mortality rates are low with splenectomy, it should be helpful to establish preoperative clinical variables that can predict which patients are likely to benefit from splenectomy. Several previous studies [1, 5, 6, 11, 16] have examined this subject. The factors that most often predicted a good outcome were age, previous response to prednisone, interval between diagnosis and splenectomy, site of platelet sequestration, and platelet survival.

It is frequently said that the response to steroids predicts the response to splenectomy. One study [15] reported a postsplenectomy remission rate of 92% in patients who had responded to steroids before operation, as compared to a 65% response rate in those who had not shown response to preoperative steroids. In other reports, the remission rate among patients who showed a preoperative response to steroids ranged from 67% to 82% and was not different from the overall response rate of 56–85% [1]. In our study, all patients who responded to steroids did well after splenectomy. At the same time, many of the patients (75%) who did not respond to steroids before surgery responded to splenectomy, and there was no statistically significant difference between these two groups of patients.

Although age was an important predictor of response to splenectomy in some studies [5, 6, 7], it had no prognostic value in others [10, 11]. Likewise, in our series, the univariate analysis selected age as a prognostic factor. However, after the assessment by multiple logistic regression analysis, age lacked significance.

Preoperative platelet count failed to predict response to splenectomy in most series [1, 6, 10, 11], as evidenced by the statistically insignificant rates of platelet count for both responders and nonresponders (82 ± 62 vs 31 ± 19 G/L in our series). Likewise, most authors [7, 10, 11] could not confirm that the disease duration prior to splenectomy had a prognostic value. However, in our study, this preoperative variable was a significant factor even after the assessment by multiple logistic regression analysis. On the other hand, the magnitude of the relative risk (1.083; CI, 1.004–1.167) shows that disease duration is weak predictor of outcome.

Several series of successful LS in ITP patient have been reported [2, 8, 13, 18]. However, none of these studies examined the influence of preoperative clinical variables on the outcomes of LS vs. OS. Our study failed to show any statistically significant difference between the open and laparoscopic procedures as a prognostic factor predictive of a favorable outcome.

It seems evident that other approaches are needed to identify those patients more likely to be permanently cured by splenectomy. Presumably, a better understanding of the various emerging pathogenic subtypes of ITP will allow for an improved choice of the available therapeutic options. ITP actually encompasses a variety of thrombocytopenias with different pathogenic mechanisms. It includes cases with IgG-type antiplatelet antibodies and cases with IgM antibodies [3]. There are also at least three major patterns of platelet sequestration: splenic, hepatic, and hepatosplenic [12]. Furthermore, kinetic studies have shown a wide range of platelet survival times and turnover rates [16]. In addition, other investigators have shown that there is a subgroup of patients with moderate thrombocytopenia, a decreased platelet half-life, but normal rates of platelet production [17]. It thus appears that ITP includes a heterogeneous group of disorders. Most likely, this is the reason why there are no prognostic factors that can be applied to all patients.

In conclusion, our data show that favorable outcomes following splenectomy (laparoscopic or open) in patients with ITP cannot be adequately predicted on the basis of preoperative clinical variables. However, disease duration and patient age should be taken into consideration when selecting patients for splenectomy.

References

1. Akwari OE, Itani KMF, Coleman RE, Rosse WF (1987) Splenectomy for primary and recurrent immune thrombocytopenic purpura: current criteria for patient selection and results. Ann Surg 206: 529–541
2. Cadiere GB, Verroken R, Himpens J, Bruyns J, Efira M, De Wit S (1994) Operative strategy in laparoscopic splenectomy. J Am Coll Surg 179: 596–601
3. Cines DB, Wilson SB, Tomaski A, Schrieber AD (1985) Platelet antibodies of the IgM class in immune thrombocytopenic purpura. J Clin Inv 75: 1183–1190
4. Delaitre B, Maignien B (1991) Splenectomy by the coelioscopic approach [Letter]. Presse Med 20: 2263
5. Di Fino SM, Lachant NA, Kirshner JJ, Gottlieb AJ (1980) Adult idiopathic thrombocytopenic purpura: clinical findings and response to therapy. Am J Med 69: 430–442
6. Fabris F, Zanatta N, Casonato A, Randi ML, Luzzatto G, Girolami A (1989) Response to splenectomy in idiopathic thrombocytopenic purpura: prognostic value of the clinical and laboratory evaluation. Acta Haemat 81: 28–33
7. Fenaux P, Caulier MT, Hirschauer MC, Beuscart R, Goudemand J, Bauters F (1989) Reevaluation of the prognostic factors for splenectomy in chronic idiopathic thrombocytopenic purpura: a report of 181 cases. Eur J Haematol 42: 259–264
8. Friedman RL, Hiatt JR, Korman JL (1997) Laparoscopic or open splenectomy for hematologic disease: which approach is superior? J Am Coll Surg 185: 49–54
9. George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ, Blanchette VS, Bussel JB, Cines DB, Kelton JG, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood 88: 3–40
10. Gugliotta L, Isacchi G, Guarini A, Ciccone F, Motta MR, Lattaran C, Bachetti G, Mazzuconi MG, Baccarani M, Mandelli F, et al. Chronic idiopathic thrombocytopenic purpura: site of platelet sequestration and results of splenectomy. Scand J Haematol 26: 407–412
11. Julia A, Araguas C, Rossello J, Bueno J, Domenech P, Olona M, Guardia R, Petit J, Flores A (1990) Lack of useful clinical predictors of response to splenectomy in patients with chronic idiopathic thrombocytopenic purpura. Br J Hematol 76: 250–255
12. Karpatkin S (1997) Autoimmune (idiopathic) thrombocytopenic purpura. Lancet 349: 1531–1536
13. Katkhouda N, Hurwitz MB, Rivera RT, Chandra M, Waldrep DJ, Gugenheim J, Mouiel J (1998) Laparoscopic splenectomy: outcomes and efficacy in 103 consecutive patients. Ann Surg 4: 568–578
14. Kernoff LM, Malan E (1983) Platelet antibody levels do not correlate with response to therapy in idiopathic thrombocytopenic purpura. Br J Hematol 53: 559–562
15. Mintz SJ, Petersen SR, Cheson B, Cordell LJ, Richards RC (1981) Splenectomy for immune thrombocytopenic purpura. Arch Surg 116: 645–650
16. Siegel RS, Rae JL, Barth S, Coleman E, Reba RC, Kurlander R, Rosse WF (1989) Platelet survival and turnover: important factors in predicting response to splenectomy in immune thrombocytopenic purpura. Am J Hematol 30: 206–212
17. Stoll D, Cines DB, Aster RH, Murphy S (1985) Platelet kinetics in patients with idiopathic thrombocytopenic purpura and moderate thrombocytopenia. Blood 65: 584–588
18. Tsiotos G, Schlinkert RT (1997) Laparoscopic splenectomy for immune thrombocytopenic purpura. Arch Surg 132: 642–646