

**Predictive prognostic factors after splenectomy in patients with idiopathic thrombocytopenic purpura**

Splenectomy is an important treatment option in patients with idiopathic thrombocytopenic purpura (ITP). We retrospectively analyzed 52 ITP patients splenectomized in our hospital in the past 31 years, and found that 4 factors might indicate a better prognosis: younger age ( $p=0.011$ ), higher pre-operative minimum platelet count ( $p=0.033$ ), lesser prednisolone dosage ( $\leq 40\text{mg/day}$ ) for maintaining the maximum platelet count before splenectomy ( $p=0.013$ ); and the lowest platelet count  $\geq 50 \times 10^9/\text{L}$  within 14 days after splenectomy ( $p<0.005$ ). Multivariate analysis showed that age and steroid dosage for maintaining the maximum platelet count preoperatively were the predictive factors before splenectomy in the ITP patients who received splenectomy.

Splenectomy is an important treatment option for idiopathic thrombocytopenic purpura (ITP), especially in those patients refractory to corticosteroid therapy. Much effort has been devoted to trying to discover possible factors predictive of successful splenectomy,<sup>1-5</sup> but the results are equivocal. In this study we analyzed the records of ITP patients splenectomized in our hospital during the past 31 years to discover the prognostic factors, if any.

Among 905 patients diagnosed with ITP in our hospital from 1970 to 2000, a total of 74 received splenectomy. Of them, 52 had data available for analysis (mean age:  $35.3 \pm 19.5$  years, range 4-69 years). Prednisolone was the first-line therapy in these patients and the dosage was 1 mg/kg body weight. The response to steroid was divided into 3 categories when the response could be maintained for  $> 2$  months in the following conditions: complete (platelet count  $\geq 100 \times 10^9/\text{L}$ , prednisolone  $\leq 10$  mg per day), partial (platelet count  $\geq 50 \times 10^9/\text{L}$ , prednisolone  $\leq 15$  mg per day), and non-response (platelet count  $< 50 \times 10^9/\text{L}$  and/or prednisolone  $> 15$  mg per day). Five patients showed partial response to steroids before splenectomy, 38 showed no response, and 9 patients could not be evaluated well because of incomplete records of the steroid dosage.

The criteria for evaluating the response to splenectomy were the same as above, except that the maintenance period was at least 3 months. Fisher's exact test and the Mann-Whitney test were used to calculate the difference ( $p$  value) of the response to splenectomy in different conditions.

After splenectomy, 25 patients (48.1%) and 11 patients (21.1%) had complete and partial responses, respectively; 16 patients (30.8%) had no response. Of them, 8 had a platelet count  $< 200 \times 10^9/\text{L}$  and 8 had a count of  $20-50 \times 10^9/\text{L}$ . No bleeding episodes were recorded in these 16 patients. We then subdivided the 52 patients into responders (complete or partial) and non-responders, and found that gender, the time from diagnosis to splenectomy, hemoglobin concentration, white cell count, blood group, and the response to steroid were not significantly different between them (Table 1). However, the responders were found to be significantly younger and have significantly higher pre-operative minimal platelet counts ( $p=0.011$  and  $0.033$ , respectively, Mann-Whitney test, Table 1). Taking a cut point of prednisolone 40 mg/day, we found that the patients needing higher dosages of prednisolone to raise their platelet count to the maximum achievable level pre-operatively tended to have a poorer post-operative response ( $p=0.013$ , Fisher's exact test, Table 1). Examining post-operative platelet count nadir and taking  $50 \times 10^9/\text{L}$  as the cut point, we found that the patients whose post-operative lowest platelet count within 2 weeks of the operation remained above this level had a more favorable prognosis ( $p< 0.005$ , Fisher's exact test, Table 1).

**Table 1. Comparison of the variables of the post-operative responders and non-responders.**

	Responders* (36)	Non-responders* (16)	p value
Male/Female	11/25	6/10	0.751 <sup>#</sup>
Time from diagnosis to operation (days)	1041.6 $\pm$ 1713.9	504.4 $\pm$ 580.1	0.317 <sup>a</sup>
Maximum platelet count ( $\times 10^9/\text{L}$ )	114.3 $\pm$ 74.0	99.5 $\pm$ 132.0	0.053 <sup>a</sup>
Minimum platelet count ( $\times 10^9/\text{L}$ )	20.6 $\pm$ 19.8	9.33 $\pm$ 7.4	0.033 <sup>a</sup>
Hemoglobin (g/L)	127 $\pm$ 21	114 $\pm$ 29	0.139 <sup>a</sup>
WBC count ( $\times 10^9/\text{L}$ )	9.0 $\pm$ 3.9	9.4 $\pm$ 4.6	0.874 <sup>a</sup>
Response to steroid (partial/none) <sup>†</sup>	5/28	0/10	0.320 <sup>#</sup>
Blood group:			
A	7	3	
B	11	5	
O	13	8	
AB	3	0	
Not recorded	2	0	0.774 <sup>#</sup>
Age (years)	30.5 $\pm$ 18.0	46.0 $\pm$ 19.0	0.011 <sup>a</sup>
Minimum steroid dose maintaining the pre-operative platelet count to maximum level			
Prednisolone $> 40$ mg/day	11	8	
Prednisolone $\leq 40$ mg/day	22	2	0.013 <sup>#</sup>
Highest platelet count within 14 days after splenectomy <sup>§</sup>			
Platelet $\geq 300 \times 10^9/\text{L}$	15	2	
Platelet $< 300 \times 10^9/\text{L}$	21	13	0.06 <sup>#</sup>
Lowest platelet count within 14 days after splenectomy <sup>§</sup>			
Platelet $\geq 50 \times 10^9/\text{L}$	31	5	
Platelet $< 50 \times 10^9/\text{L}$	5	10	$< 0.005$ <sup>#</sup>

\*Number of patients; <sup>†</sup>Overall only 43 patients could be evaluated; <sup>#</sup>Fisher's exact test; <sup>a</sup>By Mann-Whitney test; <sup>§</sup>Only 51 patients have adequate data for analysis.

**Table 2. Possible pre-operative predictive factors of successful splenectomy in ITP patients.<sup>#</sup>**

	Odds ratio	95% confidence interval of O.R.		p value
		Lower	Upper	
Age	1.078	1.014	1.147	0.017
Steroid40*	12.230	1.548	96.609	0.018

<sup>#</sup>Using multivariate logistic regression analysis. \*Steroid40: using prednisolone 40 mg/day as the cut point for maintaining the maximum platelet level.

When multivariate analysis was used to test the pre-operative parameters, we found that age and steroid dosage for maintaining the maximum platelet count were two predictive factors for ITP patients receiving splenectomy (Table 2).

With a median follow-up of 1,420 days (range 17-4,290) from the time of splenectomy, there were 5 and 0 relapses among complete and partial responders, respectively. The median time

to relapse after surgery was 1,121 days (at 73, 1,361, 296, 3,833, and 40 days in the 5 relapsing responders). After treatment 3 of these relapsed patients, 2 treated with steroids and 1 with cyclophosphamide, achieved another complete response. The criteria for treating the post-splenectomized patients were platelet count  $<50 \times 10^9/L$  and a bleeding tendency.

The prognostic factors of successful splenectomy in ITP patients have been of much interest for decades. Some have claimed that prognosis is correlated with PAIgG levels, the site of splenic platelet sequestration,<sup>1,3,6</sup> the pre-splenectomy response to corticosteroids,<sup>3</sup> a younger age,<sup>3,7</sup> a higher platelet count after splenectomy,<sup>3,8</sup> and the response to intravenous immunoglobulin administration.<sup>4,7</sup> Yet, others have not found the same correlations.<sup>2,5</sup>

Our results and those of others, highlight different predictive factors which might not be universally accepted. We still seem a long way off discovering whether it is the heterogenous nature of ITP that counts, or whether there really are some universal predictive factors.

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