



Long-term outcomes of a 5-year follow up of patients with immune thrombocytopenic purpura after splenectomy

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Background

The long-term outcomes of adult patients with immune thrombocytopenic purpura (ITP) after splenectomy are not clear.

Methods

We retrospectively analyzed 31 patients who underwent splenectomy after diagnosis of ITP at our institution between 1990 and 2009. Long-term follow-up was defined as a follow-up that lasted 1 year or more from splenectomy to the last follow-up.

Results

The overall response rate to splenectomy was 84%. However, the response rate at 6 and 12 months decreased to 77% and 68%, respectively. During the 6 years of median follow-up after splenectomy, 11 patients (35%) relapsed. The long-term response rate was 55%. The long-term follow-up of 26 patients after responding to splenectomy showed that the median time from splenectomy to relapse was 19 months in the partial response (PR) group; however, there was no relapse after 9 months in the complete response (CR) group. Variables, including age, were not predictive of the long-term response after splenectomy. Additional treatment in patients who did not respond or relapsed after splenectomy was mostly effective. After a median follow-up of 7 years (range: 1-25 years) from the diagnosis, there were 2 deaths, including one due to spontaneous bleeding after repair of duodenal ulcer perforation.

Conclusion

Although splenectomy is safe and effective, the response rate after splenectomy continuously decreases over time. The duration of response is different between the patients that achieved CR and those that achieved PR. Factors, including age, were not predictors of a response to splenectomy.

Key Words Adult, Immune thrombocytopenic purpura, Long term, Splenectomy, Thrombocytopenia

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by accelerated destruction of platelets due to autoantibodies and insufficient production of platelets [1]. ITP is caused by the production of autoantibodies directed to platelet surface proteins. The mechanism by which the platelet surface proteins become antigenic and stimulate the immune system is not clear. However, this action results in accelerated platelet destruction and suppression of platelet production [1].

In adults, ITP typically has an insidious onset, without

preceding viral or other illnesses. Symptoms and signs vary from no symptoms to clinically significant hemorrhages. However, bleeding symptoms are uncommon unless the ITP is severe [2]. The diagnosis of ITP is based on clinical features and complete blood counts; other reactive causes of thrombocytopenia should be excluded [2].

Although patients presenting with clinically significant bleeding require emergency treatment and intravenous immunoglobulin therapy, the standard first-line treatment for patients without critical bleeding is oral corticosteroids. About 50% of patients respond to initial corticosteroid treatment, but only 10-20% of patients have a sustained response [2].



As a second line treatment, patients with very severe thrombocytopenia (platelet counts $<10,000/\mu\text{L}$), those with a high risk of bleeding (platelet counts $<30,000/\mu\text{L}$), or those who require continuous corticosteroid treatment to maintain safe platelet counts are candidates for therapeutic splenectomy. The response rate to splenectomy varies from 50% to 80% [3, 4]. A systematic review of splenectomy reported a complete response rate in 66% of patients with 1.0% mortality after a laparotomy and 0.2% mortality after laparoscopy [3]. However, the long-term results after splenectomy in patients with ITP are not clear.

There is little information on the patients that fail to respond after splenectomy. Currently available treatments for patients with refractory ITP include danazol, azathioprine, vinca alkaloids, cyclophosphamide, cyclosporine, and rituximab; however, there is limited evidence on the efficacy of any treatment [5]. The recently developed thrombopoietin-mimetic agents, such as romiplostim and eltrombopag, offer new options for managing patients with ITP that are refractory to splenectomy [6].

The purpose of this study was to investigate the long-term outcomes of patients with ITP after splenectomy and to evaluate the results of additional therapy in patients that did not respond to splenectomy. In addition, we analyzed the predictive factors associated with a response to splenectomy and the pharmacological therapy that was useful after failure of splenectomy.

MATERIALS AND METHODS

After approval by the institutional review board, the patient database at Kyung Hee University Medical Center in Seoul, the Republic of Korea, was retrospectively reviewed to identify 44 adult (age ≥ 16 years) patients with ITP that underwent splenectomy between March 1, 1990 and June 1, 2009. Of the 44 patients, 31 patients having a follow-up time of more than 12 months were included in this study. All patients met the diagnostic criteria reported by the American Society of Hematology Practice Guidelines [7]. The medical records of these patients were reviewed for the clinical and laboratory information regarding their diagnosis, initial treatment, splenectomy, and post-splenectomy follow-up. The severity of bleeding at diagnosis was classified into four categories according to the severity: asymptomatic, minor purpura or easy bruisability, mucosal bleeding that might require clinical intervention, and severe life-threatening bleeding. The severity of thrombocytopenia was classified into four groups: very severe, $<10 \times 10^9/\text{L}$; severe, $10 \times 10^9/\text{L}$ - $30 \times 10^9/\text{L}$; moderate, $30 \times 10^9/\text{L}$ - $50 \times 10^9/\text{L}$; and mild, $>50 \times 10^9/\text{L}$.

All patients received oral corticosteroids 1 mg/kg/day for initial treatment, except for 4 patients that required a rapid increase in the platelet counts. Fourteen patients initially received intravenous immunoglobulin (IVIG) and were later started on steroids. The indications for splenectomy were: 1) not responding to medical therapy for 4 weeks; 2) relapse

during the tapering of steroids; 3) side effects to steroids; 4) poor compliance with the medication. Patients with platelet counts less than $50 \times 10^9/\text{L}$ were treated with IVIG before splenectomy. The size and weight of spleen were measured during surgery; however, this was limited in those cases involving a laparoscopic splenectomy. The platelet counts at 1 week, 1 month, 6 months, and 12 months after the splenectomy were assessed to determine the response to splenectomy. A response to the splenectomy was defined as a response at 1 month after splenectomy. The long-term response to splenectomy was defined as a response from 12 months to the last follow-up. The correlation between gender, age at diagnosis, symptoms at diagnosis, platelet counts at diagnosis, anti-platelet antibody, response to pre-splenectomy treatment, reasons for splenectomy, age at splenectomy, platelet counts before splenectomy, time to splenectomy, methods of splenectomy, weight of the spleen, and the likelihood of a response after splenectomy were analyzed. In the patients that were unresponsive to splenectomy, additional treatment with corticosteroids, IVIG, danazol, vinca alkaloids, or a combination of these preparations were attempted.

1. Definitions of response to treatment and relapse

The response criteria to pharmacological treatment were defined: complete response (CR), platelet counts $>150 \times 10^9/\text{L}$ for ≥ 4 weeks; partial remission (PR), platelet counts ≥ 50 - $150 \times 10^9/\text{L}$ for ≥ 4 weeks; transient response for <4 weeks; and no response (NR), platelet counts $<50 \times 10^9/\text{L}$ for 4 weeks of therapy [8, 9]. The definitions were also used to define CR and PR after splenectomy. Non-responders to splenectomy were defined as patients that failed to achieve platelet counts $\geq 50 \times 10^9/\text{L}$ at any time after splenectomy. Relapse after splenectomy was defined as a decrease in platelet counts $<50 \times 10^9/\text{L}$.

2. Statistics

The remission duration was determined in 26 patients that responded to splenectomy during the interval from the splenectomy to the date of relapse. The time to progression was defined in all 31 patients as the interval from the splenectomy to the date of decrease of the platelet counts $<50 \times 10^9/\text{L}$. Curves of the remission duration and time to progression were constructed using the life-table technique by Kaplan-Meier. Data on patients still in remission or that died were censored at the time of the last follow-up or death. The log-rank test was used for comparison of the remission duration between the CR and PR groups. For comparisons between groups, Fisher's exact test was used for nominal data. Mann-Whitney *U*-test was performed for non-parametric data and t-test for parametric data. All *P* values were two-sided and statistical significance was defined as a *P* value <0.05 . All statistical analyses were carried out with SPSS software (SPSS, Inc., Chicago, IL, USA).

RESULTS

1. Characteristics of patients at diagnosis

The median age at diagnosis was 46 years (range: 14-74 years). Four patients (13%) were males and 27 (87%) were females. Eight of the 31 patients (26%) were asymptomatic at diagnosis. Fifteen patients (48%) presented with minor purpura or easy bruisability and 8 patients (26%) with clinically significant bleeding symptoms at diagnosis. None of the patients showed severe life-threatening bleeding symptoms at diagnosis. The median platelet count at diagnosis was $14 \times 10^9/L$ (range: 1-72, missing data in 3 patients); 9 patients (29%) were very severe, 14 patients (45%) were severe, 2 patients (6%) were moderate, and 3 patients (10%) were mild. Anti-platelet antibodies were positive in 7 patients (23%) and negative in 16 patients (52%, missing data in 8 patients). Twenty patients (65%) had other medical conditions, with 6 having 2 conditions: diabetes mellitus (N=5), hypertension (N=4), thyroid disease (N=4), iron deficiency anemia (N=3), stomach cancer (N=1), asthma (N=1), ulcerative colitis (N=1), chronic hepatitis (N=1), alcoholic liver disease (N=1), intra-hepatic duct stone (N=1), coronary artery

disease (N=1), ureter and renal stone (N=1), active pulmonary tuberculosis (N=1), and pregnancy (N=1). The median follow-up duration was 7 years (range: 1-25 years) (Table 1).

2. Initial response to treatment before splenectomy

Sixteen patients received steroids and 2 patients received IVIG for first line therapy. Thirteen patients received steroids and IVIG. Overall response was obtained in 20 patients (64%) with CR in 5 patients (16%) and PR in 15 patients (48%). Eleven patients (36%) had no response to initial therapy (Table 1).

3. Characteristics of patients at splenectomy

The median age at splenectomy was 46 years (range: 16-74 years). The median duration from diagnosis to splenectomy was 5 months (range: 0-155 months). The median platelet count before splenectomy was $9 \times 10^9/L$ (range: $1-77 \times 10^9/L$). The median follow-up duration after splenectomy was 6 years (range: 1-21 years). Twenty-one patients (68%) did not respond to corticosteroids or dependent on corticosteroids, 5 patients (16%) experienced severe side effects to steroids, and 2 patients (6%) had poor compliance with the medications. Other reasons for the splenectomy in the remaining 3 patients (10%) were: active pulmonary tuberculosis, a splenectomy performed during a subtotal gastrectomy in a patient with stomach cancer, and a splenectomy performed before pregnancy. Fifteen patients (48%) underwent open splenectomy and 16 patients (52%) underwent laparoscopic splenectomy. The median weight of the spleen was 110 g (range: 37-400 g). An accessory spleen was found

Table 1. Patient characteristics at diagnosis.

Variables	N=31	%
Age (years), median (range)	46 (14-74)	
Gender		
Male	4	13
Female	27	87
Initial presentation		
Asymptomatic	8	26
Skin purpura or bruisability	15	48
Clinically significant bleeding	8	26
Platelet count ($\times 10^9/L$) ^a , median (range)	14 (1-72)	
Very severe	9	29
Severe	14	45
Moderate	2	6
Mild	3	10
Anti-platelet antibody		
Positive	7	23
Negative	16	52
Unknown	8	25
Initial treatment		
PDL	16	52
IVIG	2	6
PDL+IVIG	13	42
Response to initial therapy		
Complete response	5	16
Partial response	15	48
No response	11	36

Thirty-one of the 44 patients who were available for follow-up for at least 1 year were analyzed. The median follow-up duration was 7 years (range: 1-25 years). No patients showed life threatening bleeding at diagnosis.

^aVery severe: $< 10 \times 10^9/L$; Severe: $10 \times 10^9/L-30 \times 10^9/L$; Moderate: $30 \times 10^9/L-50 \times 10^9/L$; Mild: $> 50 \times 10^9/L$.

Abbreviations: PDL, prednisolone; IVIG, intravenous immunoglobulin.

Table 2. Patient characteristics at splenectomy.

Variables	N=31	%
Age (years), median (range)	46 (16-74)	
Platelet count ($\times 10^9/L$), median (range)	9 (1-77)	
Time to splenectomy (months), median (range)	5 (0-155)	
Reasons for splenectomy		
Non-responders or relapse after tapering steroid	21	68
Adverse effects to steroid	5	16
Noncompliance to steroid	2	6
Others ^a	3	10
Method of splenectomy		
Open	15	48
Laparoscopy	16	52
Weight of spleen (g), median (range)	110 (37-400)	
Accessory spleen		
Removed during splenectomy	3	10
No accessory spleen	28	90
Perioperative complications		
Hemoperitoneum	2	
Wound abscess	1	

The median follow-up duration after splenectomy was 6 years (range, 1-21 years).

^aActive pulmonary tuberculosis, splenectomized during subtotal gastrectomy, splenectomy was done before pregnancy.

in 3 patients (10%) during the surgery and was removed. Three patients (10%) had complications after the splenectomy. Two patients underwent reoperation due to hemoperitoneum and 1 patient had a wound abscess (Table 2).

4. Response to splenectomy and predictors of response

The overall response rate to splenectomy was 84% with CR in 14 and PR in 12. The response rate at 6 and 12 months was 77% and 68%, respectively. The long-term response rate to splenectomy was 55%. Of the remaining patients, 35% relapsed and 10% were non-responders (Table 3). Nine patients relapsed within 24 months after splenectomy and 2 patients relapsed at 70 and 104 months. The median time for the progression of survival after splenectomy was 70 months (Fig. 1). In the 26 patients that responded to splenectomy, the curve of the proportion of patients remaining in remission plateaued after 9 months in the CR group; however, this rate continuously decreased in the PR group, in which the median time between splenectomy and relapse was 19 months (Fig. 2).

There was no statistically significant difference between

the responders (CR+PR) and non-responders with regard to gender, platelet counts at diagnosis, time to splenectomy, platelet counts before splenectomy, weight of the spleen, severity of symptoms at diagnosis, initial response to medical treatment, anti-platelet antibody, reasons for splenectomy, and method of splenectomy (Table 4).

5. Treatment of patients after splenectomy failure

At 1 month after surgery, 5 patients were non-responsive to the splenectomy; 1 patient maintained platelet counts over $30 \times 10^9/L$ and was observed without further treatment. One other patient achieved CR after 1 month without oral corticosteroid. The remaining 3 patients achieved PR or CR with oral corticosteroids only.

Eleven patients relapsed during the median of 6 years of follow-up. One patient was non-responsive to splenectomy, but his platelet counts were maintained over $30 \times 10^9/L$ and he was observed without further treatment. Prednisone with or without IVIG was the most commonly used treatment and achieved CR (N=1) and PR (N=5). Danazol with or without IVIG was the second most common treatment and achieved CR (N=1) and PR (N=2). The remaining patients achieved PR with vincristine after failing to respond to oral steroids, IVIG and danazol treatment. Three of the 11 relapsing patients maintained their response when treatment tapered off after the long-term follow-up (Table 5).

6. Morbidity and mortality

Two patients (6%) died during follow-up. One patient had coronary artery disease before the diagnosis of ITP and achieved PR 7 years after splenectomy. This patient was admitted to the hospital with congestive heart failure and pulmonary edema; the cause of death was ventricular fibrillation. Another patient had a primary closure of the perforation of duodenal ulcer. This patient achieved PR to splenectomy, but relapsed after 1 year and achieved PR at

Table 3. Response status during the follow-up period after splenectomy.

Status	1 month	6 months	12 months	Last follow-up
Complete response	14 (45%)	14 (45%)	13 (42%)	13 (42%)
Partial response	12 (39%)	10 (32%)	8 (26%)	4 (13%)
Relapse	NA	4 (13%)	7 (22%)	11 (35%) ^{b)}
Non-responders	5 (16%) ^{a)}	3 (10%)	3 (10%)	3 (10%)

Overall response rate of splenectomy was 84% at 1 month and 55% at long-term follow-up.

^{a)}Two non-responders achieved complete response after 1 month of follow-up; ^{b)}Nine patients relapsed within 24 months after splenectomy, and 2 patients relapsed at 70 and 104 months, respectively. Abbreviation: NA, not applicable.

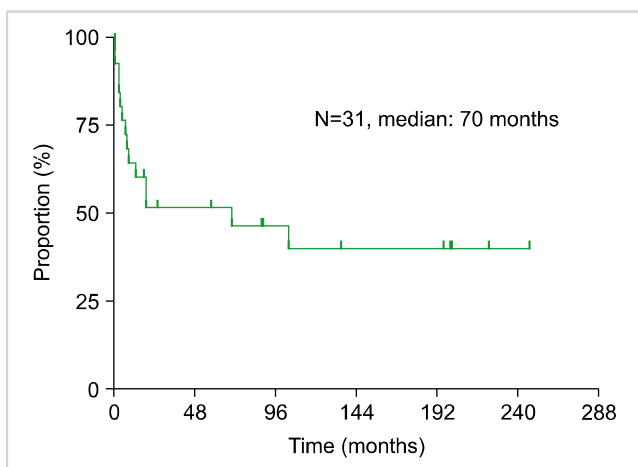


Fig. 1. Progression-free survival of all 31 patients after splenectomy. Median time of progression-free survival was 70 months.

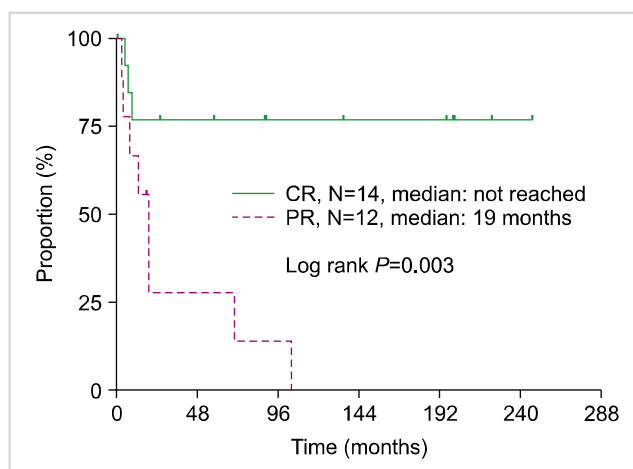


Fig. 2. Kaplan-Meier curve of remission (CR+PR) duration in 26 patients after responding to splenectomy. Median time from splenectomy to relapse was 19 months in PR patients. However, no relapse occurred after 9 months in CR patients. CR, complete response; PR, partial response.

Table 4. Comparison between responsive group and non-responsive group after splenectomy.

	Responsive group ^{a)} N=17 (%)	Non-responsive group N=14 (%)	P
Gender			0.607
Male	3 (18)	1 (7)	
Female	14 (82)	13 (93)	
Age at diagnosis (years)	38 (14-74)	50 (23-69)	0.222
Age at splenectomy (years)	43 (16-74)	51 (23-72)	0.235
Severity of symptoms at diagnosis			0.204
Asymptomatic	2 (12)	6 (43)	
Minor skin purpura	10 (59)	5 (36)	
Clinically significant bleeding	5 (29)	3 (21)	
Anti-platelet antibody			0.799
Positive	3 (18)	4 (29)	
Negative	9 (53)	7 (50)	
Unknown	5 (39)	3 (21)	
Response to initial medical treatment			0.553
Complete response	4 (24)	1 (7)	
Partial response	8 (47)	7 (50)	
No response	5 (29)	6 (43)	
Method of splenectomy			0.200
Open	10 (59)	5 (36)	
Laparoscopy	7 (41)	9 (64)	
Reasons for splenectomy			0.542
Non-responders or relapsed	12 (70)	9 (64)	
Adverse effects to steroid	2 (12)	3 (22)	
Noncompliance to steroid	2 (12)	0 (0)	
Others	1 (6)	2 (14)	
Platelet count at diagnosis ($\times 10^9/L$)	11 (1-45)	15 (2-72)	0.118
Platelet count before splenectomy ($\times 10^9/L$)	7 (1-77)	10 (1-33)	0.463
Time to splenectomy (months)	10 (0-155)	5 (0-56)	0.313
Weight of spleen (gram)	105 (52-222)	110 (37-400)	0.457

Median (range).

^{a)}Patients who achieved complete response and partial response at long-term follow-up after splenectomy were included.

10 years after splenectomy. The cause of death was disseminated intravascular coagulopathy after primary closure.

Two patients that underwent laparoscopic splenectomy had reoperation due to hemoperitoneum. One patient was admitted to the hospital 1 month after an open splenectomy due to a wound abscess. A 17-year-old woman had overwhelming post-splenectomy infection approximately 18 months after a laparoscopic splenectomy. This patient was admitted due to a changed mental status, and was diagnosed with meningococcal meningitis. Four patients had other, newly developed medical problems after the splenectomy: steroid-induced severe acne, bilateral total hip replacements due to avascular necrosis of the femoral head, lupus nephritis, and coronary stent insertion due to unstable angina.

DISCUSSION

Spleen is the major site of removal of immunized or damaged RBCs, WBCs, and platelets that contribute to cytopenia. For this reason, splenectomy has been used as therapy for patients with ITP or hemolytic anemia. For the patients with ITP who were not responsive to initial corticosteroid therapy, splenectomy could be effective and curative [2,

7, 10]. In this study, the response rate to splenectomy was 84% at 1 month after the splenectomy. The initial response rate of this study was similar to that of the prior reports [9, 11-18]. However, the response rate decreased to 77% at 6 months after the splenectomy and further decreased to 68% at 12 months and 55% at the last follow-up. This data is consistent with the findings reported by other studies with 57-65% response rates after more than 5 years of post-splenectomy follow-up [17-19]. Some studies reporting higher long-term response rate, averaging 72-89%, had a median follow-up duration of less than 5 years. This study included only 13% males compared to over 25% males in other studies with higher response rates [9, 13, 14, 16]. In addition, the patients in this study might include more severe ITP patients; this explains the difference in the long-term responses [20, 21]. Recent studies reported that relapse continued to occur during the first 2-4 years after splenectomy [11, 14, 17, 22]. In this study, all the relapsed patients except for 2 had relapsed in the first 24 months after splenectomy.

The difference in the duration of remission between the CR and PR patients was statistically significant ($P=0.003$). No relapse occurred in patients with CR since 9 months after the splenectomy. However, patients in the PR group continuously relapsed during the follow-up period; the me-

Table 5. Treatment after splenectomy of 14 patients that were non-responders or relapsed at the long-term follow-up.

No.	Sex	Age at splenectomy (years)	Response to splenectomy	Therapy	Response	Follow-up duration (years)	Last platelet counts (/ μ L)	Status at last follow-up
1	F	25	Relapse	Prednisone+IVIG	PR	5	129,000	Admitted five times due to ITP symptoms Dependent on therapy
2	F	32	Relapse	Prednisone+Danazol+IVIG	PR	14	77,000	On therapy
3	F	30	Relapse	Prednisone	PR	6	76,000	Dependent on therapy
4	M	39	Non-responder	Prednisone	CR	4	580,000	Off therapy, Use mesalazine due to ulcerative colitis
5	F	51	Relapse	Prednisone	PR	7	84,000	Off therapy
6	F	61	Relapse	Prednisone+Danazol+IVIG	CR	13	504,000	On therapy
7	F	30	Relapse	None	NR	1	34,000	Observation without treatment
8	F	72	Relapse	MPD	PR	3	91,000	Off therapy
9	F	55	Relapse	Prednisone+Danazol	PR	3	41,000	Dependent on therapy
10	F	51	Non-responder	Prednisone	PR	1	75,000	Off therapy
11	F	26	Non-responder	None	PR	8	87,000	Observation without treatment
12	F	69	Relapse	Prednisone+IVIG	CR	3	339,000	Admitted three times due to ITP symptoms Off therapy
13	F	69	Relapse	Prednisone	PR	11	136,000	Died of DIC after duodenal ulcer operation ^{a)}
14	F	69	Relapse	MPD+Danazol+IVIG+Vincristine	PR	2	43,000	Dependent on vincristine

^{a)}The cause of death was spontaneous bleeding associated with disseminated intravascular coagulopathy after surgery due to duodenal ulcer perforation.

Abbreviations: MPD, methylprednisolone; CR, complete response; PR, partial response; NR, no response; ITP, immune thrombocytopenic purpura; DIC, disseminated intravascular coagulopathy.

dian time for relapse was 19 months. Johansson et al. also reported a plateau in the progression-free survival curve; however, there was no disease progression after 12.1 and 7.3 years in patients with CR or PR, respectively [22]. Patients that achieved PR after splenectomy may have an unstable disease status and show a different clinical course in comparison to patients that achieved CR after splenectomy. Further studies are needed to determine the long-term clinical course of patients that achieve PR to splenectomy.

Various predictors of response to splenectomy, such as age, gender, duration of illness, response to steroids, pre-operative platelet counts, severity of bleeding, and anti-platelet antibody were studied. In previous studies, younger age was the most common variable associated with a good response to splenectomy; however, there was no specific age cutoff point that defined the younger group of patients [3, 12-14]. Age was not a predictive factor in this study. In this study, there was no statistically significant difference between the response group and non-response group with regard to gender, platelet counts at diagnosis, time to splenectomy, the lowest platelet counts before splenectomy, weight of the spleen, severity of symptoms at diagnosis, initial response to medical treatment, anti-platelet antibody, reasons for splenectomy, and methods of splenectomy. Patients that underwent splenectomy were at increased risk for overwhelming infection and death [15, 22, 23]. The complication rate after splenectomy was 13% (N=4); 2 patients had hemoperitoneum after laparoscopic splenectomy, 1 patient had a wound abscess after an open splenectomy, and 1 patient

had an overwhelming infection 18 months after laparoscopic splenectomy. Four additional patients (13%) developed other medical problems. Portielje et al. reported that patients with ITP who underwent splenectomy had a postoperative complication rate of 33% [23]. The complication rates in the study by Kojouri et al. were 13% with laparotomy and 10% with laparoscopic splenectomy [3]. Laparoscopic splenectomy is now more widely used than open splenectomy; however, there is no proof that laparoscopic splenectomy is safer than open splenectomy [3, 10, 23].

In this study, patients with platelet counts less than $50 \times 10^9/L$ were considered non-responsive or in relapse after splenectomy. This might have included many patients who might not have required treatment. Three patients in the current study were observed without treatment. The platelet counts in these patients remained over $30 \times 10^9/L$ during the follow-up, with no significant bleeding. Patients with platelet counts more than $30 \times 10^9/L$ have a minimal risk of severe bleeding, and may be safely observed without treatment with more severe thrombocytopenia [23-25].

Although only 55% of patients were considered responders to splenectomy during the long-term follow-up, most non-responsive patients achieved CR or PR with additional treatment. Other studies have reported similar results; that is, most patients that had refractory ITP or relapsed after splenectomy achieved good responses to additional treatment [26, 27]. Two of the 4 non-responders achieved CR or PR without any treatment. Three of the 11 patients that relapsed after splenectomy also achieved CR or PR without any

treatment. The suppression of platelet production can play a role in the pathogenesis of ITP, and removal of the spleen might be the most effective therapy for some patients with ITP.

According to the Maastricht III consensus conference, detection and eradication of *Helicobacter pylori* (*H. pylori*) is indicated in patients with ITP [28]. With *H. pylori* eradication, CR and overall response of 42.7% and 50.3% has been reported [29]. The response rate tended to be higher in countries with a high prevalence of *H. pylori* [29]. *H. pylori* infection was not evaluated in this study. The association between *H. pylori* and ITP requires further study.

In conclusion, splenectomy may be considered as safe and effective for patients with ITP who failed to respond to first-line corticosteroid treatment. However, the initial response rate continuously decreases over time. The duration of response is different in patients that achieved CR and those that achieved PR during long-term follow-up after splenectomy, and most of them relapsed in the first 2 years after splenectomy. Additional treatment in patients who did not respond or relapsed after splenectomy was mostly effective, with some patients in this group sustaining a response without any treatment. None of the factors, including age, were reliable in identifying patients who are likely to respond to splenectomy.

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