

## Original Article

# Spleen-Saving or Spleen-Sacrificing? Rethinking Splenectomy Strategies in Thalassemia

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## Abstract

**Background:** Splenomegaly and hypersplenism are common complications in thalassemia that may require splenectomy. Although total splenectomy (TS) effectively improves hematologic parameters, it is associated with increased risks of infection and thrombosis. Partial splenectomy (PS) has been proposed as a spleen-preserving alternative to reduce these complications. This study compares the clinical outcomes of PS and TS in patients with thalassemia.

**Materials and Methods:** In this retrospective study, 74 thalassemia patients who underwent splenectomy from 2011 to 2018 were analyzed (median follow-up: 4 years). Twenty-five patients (33.8%) underwent PS, and 49 (66.2%) underwent TS. The outcomes, including hematologic improvement, transfusion intervals, incidence of diabetes mellitus, thrombotic events, and infection-related complications, were compared between the groups. The results were analyzed using an independent t-test, Fisher's exact test, and logistic regression.

**Results:** In this study, both PS and TS groups showed significant post-operative improvements in hemoglobin levels ( $P < 0.0001$ ). However, complications varied notably between the two groups. Diabetes mellitus developed in 12 patients (16.2% overall); only one case (4%) occurred in the PS group, while 11 cases (22.4%) were observed in the TS group. This corresponded to a significantly higher odds of diabetes after total splenectomy (OR = 6.9; 95% CI: 0.22–32.22;  $P = 0.04$ ). The wide confidence interval reflects the small number of events, particularly in the PS group. Moreover, 13 cases of infection were observed exclusively in the TS group.

**Conclusion:** Partial splenectomy may serve as a safer alternative to total splenectomy in thalassemia patients, providing hematologic benefits while reducing the risk of infectious and metabolic complications. Further prospective studies are warranted to validate this finding.

**Keywords:** Beta Thalassemia, Hypersplenism, Splenectomy, Thalassemia intermedia



## Introduction

Thalassemias are inherited hemoglobinopathies characterized by impaired globin chain synthesis and chronic hemolytic anemia. In  $\beta$ -thalassemia, defective  $\beta$ -globin production leads to ineffective erythropoiesis and the premature destruction of abnormal erythrocytes, resulting in marked splenic enlargement and hypersplenism (1-4). The reticuloendothelial system of the spleen sequesters malformed red cells (“pitting” and “culling”), causing progressive splenomegaly, peripheral cytopenias, and increased transfusion requirements. Over time, excessive extramedullary hematopoiesis in the spleen also contributes to its enlargement. Clinically, massive or symptomatic splenomegaly (characterized by pain, early satiety, or an increased risk of splenic rupture) and cytopenias (including anemia, thrombocytopenia, and leukopenia) define hypersplenism in thalassemia. These features often compel intensified transfusion and iron chelation, creating a vicious cycle of anemia and iron overload (2, 4, 5).

Splenectomy is a recognized therapy in thalassemia to interrupt this cycle. By removing the hyperactive spleen, residual red blood cells survive longer, and the need for transfusions declines (4, 6). Thalassemia guidelines generally recommend splenectomy for clinically significant hypersplenism, for example, when transfusion requirements are excessively high or cytopenias cause complications (e.g. bleeding or infection) despite optimal transfusion and chelation therapy (7, 8). In practice, splenectomy is typically delayed until after early childhood (usually after 5 years of age) to minimize the risk of infection. After total splenectomy, patients often experience a significant rise in hemoglobin and a marked reduction in transfusion frequency (4, 9, 10), thereby improving quality of life and slowing iron accumulation. These benefits underpin the longstanding rationale for splenectomy in transfusion-dependent thalassemia.

However, complete splenectomy involves well-recognized risks. Without splenic filtration, patients face a lifelong predisposition to overwhelming post-splenectomy infection (OPSI) from encapsulated organisms. *Streptococcus*

*pneumoniae*, *Haemophilus influenzae* type b, and *Neisseria meningitidis* account for the majority of serious post-splenectomy infections (7, 11). OPSI is rare but often fulminant, with reported mortality rates on the order of 40-70% without prompt treatment (11, 12). Children are at exceptionally high risks; splenectomy under age of five substantially increases the likelihood of early OPSI, thus generally discouraged (13). Thrombosis is another primary concern. Asplenic patients develop a hypercoagulable state, partly due to circulating phosphatidylserine-exposing erythrocytes and platelet activation (5, 14-16). Recent meta-analytic data in thalassemia confirm this risk. In one series, 93% of the observed thrombotic events occurred in the patients who had undergone splenectomy (16). For example, portal vein and deep vein thromboses, pulmonary embolism, and even cerebrovascular events have been reported as post-splenectomy complications. Current guidelines, thus, emphasize vaccination and often recommend aspirin or anticoagulation prophylaxis after splenectomy in thalassemia (4, 16, 17). In summary, total splenectomy sacrifices hematologic benefits for increased lifelong risks of infection and thrombosis.

Partial (subtotal) splenectomy has been proposed as a compromise to balance these risks. By removing only a portion of the spleen, clinicians aim to relieve hypersplenism while preserving some splenic immune function (18, 19). Early reports and reviews suggest that partial splenectomy is technically feasible and can significantly improve blood counts and reduce transfusion requirements, albeit to a lesser degree than total splenectomy (19, 20). Crucially, the retained splenic remnant may provide immunologic protection: As Attina et al. (19) note, in children with hemolytic anemia, partial splenectomy “ensures the desired hematologic effect” and maintains “good immunological function”. Theoretically, this lowers the risk of OPSI (19, 21). Indeed, recent pediatric series have found no episodes of overwhelming sepsis after partial splenectomy, even over extended follow-up (20, 22). Partial splenectomy also avoids the acute post-splenectomy thrombocytosis, potentially mitigating a thrombotic risk. In practice, however, partial splenectomy has drawbacks; the

hematologic response is often smaller (one study found hemoglobin rising ~2.4 g/dL after partial vs ~4.1 g/dL after total) (19), and substantial residual hemolytic activity may persist (often requiring later cholecystectomy for gallstones). Splenic regrowth is also common; some series report that remnant spleens enlarge over time, sometimes necessitating a complete splenectomy (19, 20). Thus, while partial splenectomy may preserve some immune function, its long-term durability and optimal patient selection remain uncertain.

Currently, there is no clear consensus on which approach is most effective. Most published evidence on partial vs total splenectomy comes from small case series or retrospective cohorts, often in pediatric hereditary spherocytosis rather than in thalassemia (19, 23). A recent systematic review has found that the existing studies are small and underpowered, preventing the development of definitive guidelines on partial splenectomy indications (19). Likewise, a 2019 Cochrane review concluded that high-quality comparative trials are essentially lacking for splenectomy in thalassemia, let alone for the specific question of partial versus total removal (4). In practice, surgical decisions vary by center and patient age, reflecting uncertainty in practice. This underscores the need for direct comparative data; that is, only by systematically evaluating outcomes (hematologic improvement, transfusion independence, infection and thrombotic events, etc.) in adults and children can it be clarified whether partial splenectomy offers a net advantage over total splenectomy in thalassemia.

## Material and Methods

### *Patients and procedure*

In this retrospective study, 74 patients with beta-thalassemia, including 47 transfusion-dependent thalassemia (TDT) patients and 27 non-transfusion-dependent thalassemia (NTDT) patients, who had undergone PS or TS, retrospectively, were investigated using a convenience sampling method from 2011 to 2018. In our practice, the choice of partial versus total splenectomy was individualized after discussion with the patients and their families. Generally, the older patients tended to opt for total splenectomy,

whereas the parents of the younger patients often favored partial splenectomy.

The inclusion criterion was any type of thalassemia along with receiving vaccination against pneumococcus with the pneumococcal 13-valent conjugate vaccine and pneumococcal polysaccharide vaccine before splenectomy.

After a total splenectomy, the patient had to receive penicillin V as a prophylactic antibiotic for at least one year. The indication for splenectomy in the studied patients was the signs and symptoms of hypersplenism and massive splenomegaly, leading to a narrow interval of regular transfusion in TDT, with or without thrombocytopenia or neutropenia.

The exclusion criteria were other indications for splenectomy, such as trauma, spherocytosis, or immune thrombocytopenia, as well as age less than 5 years.

The patients were divided into two groups, PS vs TS, and each group was further subdivided into children (age < 18 years) and adults (age > 18 years) at the time of splenectomy. Three pediatric surgeons performed partial splenectomy.

In the pediatric subgroup (n = 20), 10 were female and 10 were male, while, in the adult subgroup (n = 54), 21 were female and 33 were male. The follow-up period was 2, 7, and 14 days after operation, and then every month. The follow-up for each patient continued until his or her last clinic visit (up to 7 years after surgery, median ~4 years). This method has already been published by our pediatric surgeon colleagues (1). During the operation, 20-30% of the splenic size for the appropriate age (or approximately 10% of the patient's splenic volume) was maintained. Based on the patient's age, normal splenic volume, and primarily the blood supply to the remaining tissue, the pediatric surgeon decided to manage the volume reduction of the spleen during the operation. Due to massive splenomegaly, laparoscopic partial and total splenectomy was not done.

### *Clinical outcomes and assessment methods*

Post-splenectomy outcomes and complications were systematically assessed and compared for the PS and TS groups as described here. We compared the PS and TS groups (and their age subgroups)

with respect to post-splenectomy complications (cardiac, hepatic, endocrine), transfusion interval (for TDT patients), thrombotic events, and infection complications. These outcomes were assessed via echocardiography (for cardiac function) under a cardiologist's supervision, endocrine evaluations (hormonal assays for endocrine complications), liver function tests and abdominal ultrasonography (for hepatic complications), and close clinical observation.

The patients were contacted for follow-up information as necessary. Post-splenectomy infection was defined as any serious infection (e.g., pneumonia, abscess, sepsis) confirmed by clinical evaluation and appropriate investigations. Endocrinopathy was defined as new-onset diabetes mellitus or hypothyroidism following splenectomy, ascertained by standard diagnostic criteria. For baseline transfusion management, the NTDT patients were maintained on folic acid and hydroxyurea and were followed in the clinic for every 1 to 3 months. The TDT patients had transfusion visits every 2-4 weeks.

### *Ethical considerations*

All the patients were registered at the Thalassemia Clinic affiliated with Shiraz University of Medical Sciences. The demographic, clinical, and laboratory data were collected from their medical records using a designed questionnaire.

Written informed consent was also obtained from the individual patients or their legal guardians. All the procedures that followed were in accordance with the ethical standards of the responsible committee on human experimentation of Shiraz University of Medical Sciences, Iran, and with the 1975 Declaration of Helsinki, as revised in 2008.

### *Statistical analysis*

The data were analyzed by SPSS version 23. The descriptive data were presented as means, standard deviations, frequencies, percentages, and appropriate charts and tables. A comparison was also performed of the qualitative variables between the patients with partial and total splenectomy using Fisher's exact test. The quantitative variables

were compared by an independent t-test for the two groups. The normality and homogeneity of variances were assessed (e.g., Levene's test), and nonparametric tests were considered if assumptions were violated. A multiple logistic regression model with the Enter method was employed to identify the independent variables influencing endocrinopathy. Moreover, univariate analysis was performed to determine the association between endocrinopathy and various variables, including the method of splenectomy, age, ferritin levels, changes in hemoglobin levels before and after splenectomy, NRBC percentage, and transfusion intervals. Multivariable logistic regression was performed for endocrinopathy. In this regard, similar regression analysis was not feasible for infection and thrombosis due to the absence of infections or thromboses in the PS group and the low event counts. A two-sided P-value less than 0.05 was considered statistically significant.

### **Results**

74 patients were in the range of 6-45 years. One patient who underwent splenectomy at < 5 years of age (for refractory iso-immune hemolysis) was excluded. Twenty five patients (33.8%) underwent partial splenectomy, and 49 (66.2%) underwent total splenectomy.

Most patients in this series had massive splenomegaly at the time of surgery. In our research population, 31 patients (41.9%) were female, and 43 (58.1%) were male. The values are given as the number of the patients (percentage of the total 74 patients). Mean age  $\pm$  standard deviation (SD) is shown for each subgroup. There was no significant difference in mean age between the male and female patients ( $P = 0.12$ ) (Table 1). As shown in Figure 1, the patients who underwent PS were significantly younger than those who underwent TS (mean ages  $\sim 18$  vs  $\sim 28$  years,  $P < 0.001$ ). Post-operative bleeding occurred in two patients initially scheduled for PS; both were converted intraoperatively to total splenectomy, as previously reported by our pediatric surgeons (23).

The post-splenectomy complications were compared for age groups (children  $\leq 18$  years vs adults  $> 18$  years), as shown in Table 2. The rate of

severe infection was higher in the pediatric group than in the adults (35% vs 11% developed a severe infection,  $P = 0.01$ ). By contrast, there were no significant age-group differences in rates of post-splenectomy thrombocytosis, endocrinopathy, or thrombosis. Each cell shows the number of patients in that age group with the complication (the percentage of that age group is reported in parentheses). The pediatric group ( $< 18$  years,  $n = 20$ ) had a significantly higher rate of severe infections than the adult group ( $\geq 18$  years,  $n = 54$ ;  $P = 0.01$ ). There were no statistically significant age-group differences in thrombocytosis ( $P = 0.36$ ), endocrinopathy ( $P = 0.95$ ), or thrombosis ( $P = 0.17$ ) (Table 2). Table 3 summarizes the laboratory findings in the PS and TS groups. In this table, the data are presented as mean  $\pm$  SD. The mean differences between the groups (Total vs Partial) are given at 95% confidence intervals (CI). The  $P$  values are from independent t-tests comparing the partial vs total splenectomy groups ( $n = 25$  vs  $n = 49$ ). An asterisk (\*) indicates statistical significance ( $P < 0.05$ ).

The patients who underwent partial splenectomy had significantly lower post-splenectomy levels of ferritin [ $t(72) = 2.1$ ,  $P = 0.036$ ], white blood cell count [ $t(72) = 3.07$ ,  $P = 0.003$ ], platelet count [ $t(72) = 4.5$ ,  $P < 0.001$ ], and nucleated RBC percentage [ $t(72) = 2.9$ ,  $P = 0.004$ ] compared to those who underwent total splenectomy. The left ventricular ejection fraction was significantly higher in the PS group than in the TS group [ $t(72) = -7.4$ ,  $P < 0.001$ ] (Table 3). Both groups demonstrated significant within-group improvements in hemoglobin after surgery. The mean hemoglobin level before PS ( $M = 7.5$ ,  $SD = 0.4$  g/dL) rose to  $9.2 \pm 0.7$  g/dL after PS [ $t(48) = 10.5$ ,  $P < 0.0001$ ]. Similarly, mean hemoglobin before TS ( $M = 7.7$ ,  $SD = 0.5$ ) increased to  $9.4 \pm 1.6$  g/dL after TS [ $t(96) = 7.09$ ,  $P < 0.0001$ ]. Thus, both partial and total splenectomy types were associated with significant hematologic improvement in our cohort, and the degree of post-operative hemoglobin increase did not differ significantly between the two procedures.

Figure 2 illustrates the frequency of complications in the two patient groups. Higher rates of infectious complications were observed in patients with TS compared to those with PS, with

statistical significance only in the frequency of severe infections, including pneumonia, liver abscess, abdominal abscess, pericarditis, and urinary tract infection ( $P = 0.003$ ).

After PS, 5 (20%) patients consumed aspirin due to platelets above 600,000 cells/ $\mu$ L. However, after TS, 35 (65.3% of patients) needed aspirin, which was a statistically significant difference ( $P < 0.001$ ). Five patients (10.2%) used warfarin after TS, but no one required warfarin in the PS group. There was no statistically significant difference in this case ( $P < 0.16$ ). Besides, for six patients (24%) in the PS group, we had to use Hydroxyurea again, while, in the TS group, 15 patients (30.6%) started Hydroxyurea again. There was no statistically significant difference ( $P < 0.59$ ) in this respect. The mean of the transfusion intervals before splenectomy was  $7.8 \pm 6.6$  weeks for the PS patients and  $5.4 \pm 5.3$  weeks for the TS ones ( $P = 0.113$ ). Since thrombosis occurred in only five out of 74 patients (all in the TS group), no statistical comparison or further analysis of thrombosis was feasible.

A total of 13 patients (17.5%) developed severe infections after splenectomy; all the 13 were in the TS group. Likewise, all the five observed thrombotic events occurred in the TS patients. ( $n.s.$  = not significant)

The prevalence of diabetes mellitus in our patients was 16.2%. Of the 12 patients who developed diabetes mellitus, only one (4%) belonged to the PS group, and 11 (22.4%) belonged to the TS group. The difference was statistically significant (95% CI: 0.22-32.22,  $P = 0.04$ ).

A statistically significant relationship was found between endocrinopathy and the type of splenectomy, as 13 (92.9%) of the patients with endocrinopathy had undergone total splenectomy, compared to 36 (60%) with no endocrinopathy ( $P = 0.026$ ). In the next step, the variables with a  $p$ -value less than 0.2 (splenectomy, age, and transfusion interval before splenectomy) were included in a logistic regression model to identify the independent factors influencing endocrinopathy. After adjustment, there was no significant association between endocrinopathy and any of the evaluated variables, as reported in Table 4. In this table, the outcome variable is the

occurrence of endocrinopathy (diabetes mellitus or hypothyroidism), and the regression coefficient (B), adjusted odds ratio (OR) with 95% CI, and P value are shown for each covariate in the model (the “Splenectomy” covariate is coded as 0 = partial and 1 = total splenectomy).

Regarding infection, it was not possible to perform regression analyses like endocrinopathy because all the total splenectomized patients were in the infection group, and the frequency in the partial splenectomy group was zero.

Likewise, there was only a statistically significant association between infection and the type of splenectomy, as 13 (100%) of the patients with infection had undergone total splenectomy, compared to 36 (59%) who had no infection ( $P = 0.003$ ). All the patients with a history of infection were included in the total splenectomy group. In the next step, to adjust for the possible confounding effect of age, we stratified the research population into two groups, those over 25 years and those 25 years or younger. The relationship between splenectomy and the occurrence of infection was re-evaluated. In this stratification, the significant association was only observed in the population under 25 years. Four patients (100%) in the infection group, compared to 11 (33.3%) in the non-infection group, had undergone total splenectomy ( $P = 0.021$ ).

Because thrombosis occurred in only five patients out of 74, all of whom were totally splenectomized, the incidence was low. However, total splenectomy could be considered a significant risk factor for thrombosis in both TDT and NTDT patients; it was not possible to find a cut-off point and conduct further analysis.

*Table I: Demographic characteristics of the patients by sex*

Sex	Number of patients n (%)	Partial splenectomy n (%)	Total splenectomy n (%)
Female	31 (41.9%)	10 (32.3%)	21 (67.7%)
Male	43 (58.1%)	15 (34.9%)	28 (65.1%)
Total	74 (100%)	25 (33.8%)	49 (66.2%)

The results are based on Fisher's Exact Test.

Table II: Comparison of post-splenectomy complications in the pediatric vs adult patients

Complication	Pediatric (< 18) n (%)	Adult (≥ 18) n (%)	P-value
Thrombocytosis	12 (60.0%)	28 (51.9%)	0.36
Severe infection	7 (35.0%)	6 (11.1%)	0.01*
Endocrinopathy	3 (15.0%)	9 (16.7%)	0.95
Thrombosis	0 (0.0%)	5 (9.3%)	0.17

The results are based on an independent t-test.

Table III: Comparison of the laboratory findings for the patients with partial vs total splenectomy

Laboratory variable	Partial splenectomy (Mean ± SD)	Total splenectomy (Mean ± SD)	95% CI of difference (Lower–Upper)	P-value
Ferritin (ng/mL)	973.4 ± 892.1	1958.6 ± 2219.0	62.3 – 1908.1	0.036*
WBC (cells/μL)	12,304 ± 9,811	23,235.9 ± 16,322.6	3.8 – 18.0 < sup > a </ sup >	0.003*
Hemoglobin before splenectomy (g/dL)	7.5 ± 0.4	7.7 ± 0.5	-0.43 – 0.08	0.077
Hemoglobin after splenectomy (g/dL)	9.2 ± 0.7	9.4 ± 1.6	-0.88 – 0.48	0.554
Platelet count (× 10 <sup>9</sup> < sup > / L)	456.9 ± 197.2	681.2 ± 204.0	125.4 – 323.2	< 0.001*
NRBC (% of RBC)	34.3 ± 69.3	108.2 ± 115.2	23.7 – 124.0	0.004*
Ejection fraction (%)	66.0 ± 4.8	53.6 ± 7.4	-15.5 – -9.0	< 0.001*

The results are based on an independent t-tests comparing the partial vs total splenectomy groups.

Abbreviations: WBC = white blood cell count, NRBC = nucleated red blood cells. 95% CI for WBC difference is given in units of ×10<sup>3</sup>/μL (same units as provided for WBC). \*Statistically significant (P < 0.05).

Table IV: Multivariate logistic regression analysis for the risk factors of endocrinopathy

Covariate	B coefficient	Adjusted OR (95% CI)	P-value
Age (years)	- 0.01	0.99 (0.913–1.074)	0.815
Transfusion interval (weeks)	- 0.07	0.94 (0.814–1.078)	0.361
(Splenectomy total vs Partial)	- 2.15	0.12 (0.012–1.128)	0.063

The results are based on a Logistic Regression test.

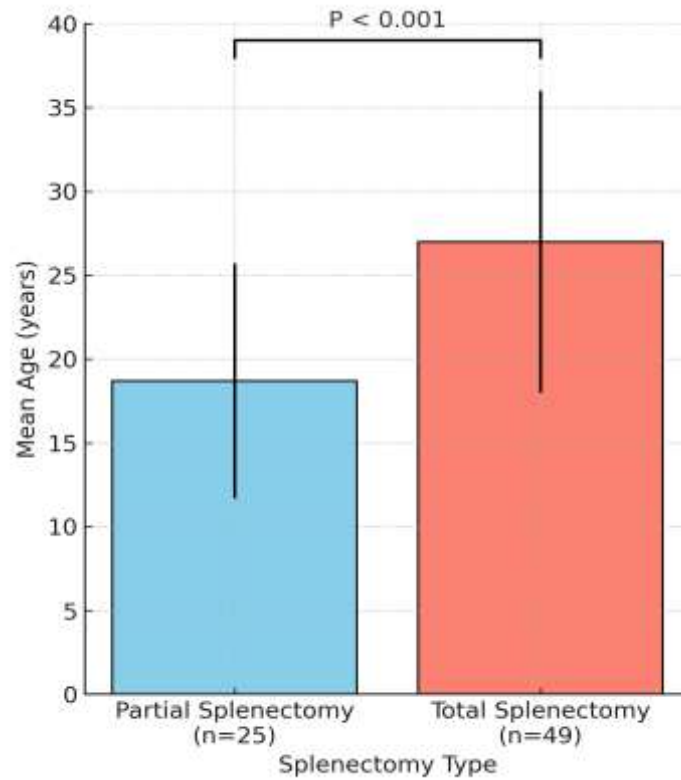


Figure 1. Comparison of the mean age of the patients in the partial vs total splenectomy groups

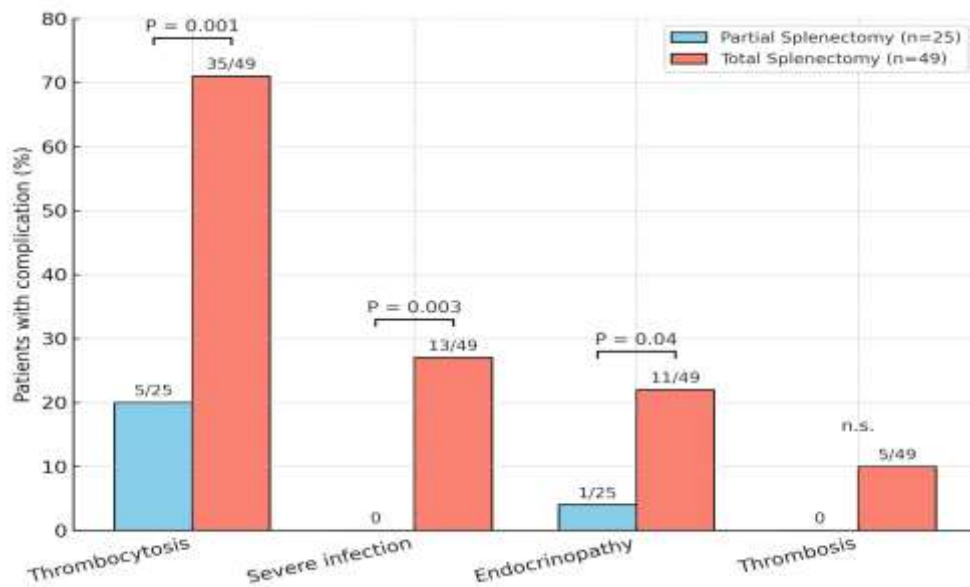


Figure 2. Comparison of the complication frequencies in the partial and total splenectomy groups

## Discussion

Our findings indicate that partial splenectomy can achieve hematologic outcomes comparable to total splenectomy while potentially reducing certain complications. Both PS and TS led to significant increases in hemoglobin levels, reflecting the relief of hypersplenism in both approaches. Importantly, we observed that PS patients experienced lower post-operative ferritin levels, WBC and platelet counts, and nucleated RBC percentages than TS patients (Table 3). These differences suggest that removing only part of the spleen attenuates the rebound erythropoiesis and thrombocytosis seen after total splenectomy. In practical terms,

the more modest rise in WBC and platelets after PS translated into a reduced need for aspirin prophylaxis and presumably a lower prothrombotic risk in the PS group. The significantly higher ejection fraction in the PS patients may have likewise stemmed from a lower iron overload (owing to fewer transfusions and lower ferritin levels), resulting in better preserved cardiac function. Consistent with this, our PS patients had a smaller increase in iron stores after splenectomy, which probably reduces the risk of cardiac siderosis and iron-related endocrine dysfunction over time. The immune advantage of partial splenectomy was evident in the markedly lower infection rate in the PS group. All the 13 episodes of severe post-splenectomy infection in our study occurred in the totally splenectomized patients (none in the PS patients,  $P = 0.003$ ), underscoring the higher vulnerability to post-splenectomy infections following total removal, over a median 4-year follow-up period. This dramatic difference highlights the protective role of the residual splenic tissue in immune surveillance and pathogen clearance. It aligns with prior observations that preserving the splenic tissue significantly lowers the risk of OPSI. Our findings reinforce that, particularly for young or infection-prone patients, avoiding complete asplenia can diminish long-term infection-related morbidity.

We also noted a lower incidence of new-

onset diabetes mellitus in the PS group (4% vs 22%,  $P = 0.04$ ). Patients with thalassemia major are predisposed to endocrinopathies (especially iron-induced pancreatic damage leading to diabetes) due to iron overload and other factors (8). By reducing transfusion requirements and ferritin levels, partial splenectomy might indirectly mitigate this risk. On the other hand, the PS group in our study was significantly younger, which may have contributed to their lower diabetes rate (the younger patients had less cumulative iron exposure). Age is a known determinant of endocrinopathy in thalassemia (4). Thus, while our PS patients had better glucose metabolism outcomes during the observed follow-up, this advantage may reflect both the selection of younger patients for PS and the beneficial effect of spleen preservation on iron balance. In the long term, maintaining a lower iron burden with partial splenectomy could translate into fewer endocrine complications, though continued follow-up is needed to confirm this trend.

Several studies have examined the outcomes of partial splenectomy in both pediatric and adult populations. As our results and the literature suggest, partial splenectomy may offer clinical benefits with fewer complications compared to total splenectomy (20, 23-25).

For example, retrospective series in hereditary spherocytosis and thalassemia have reported improved blood counts and reduced transfusion needs after PS without the full infectious risk of TS (19). A large systematic review by Costi et al. (26) found low OPSI rates in over 2,000 partial splenectomy cases. Our data concur with these reports; despite a smaller spleen remnant, PS provided significant hematologic improvement and maintained splenic immune function, thereby avoiding OPSI in our cohort. Notably, even in children under 5 (in whom TS is contraindicated due to the risk of infection), partial splenectomy has been cautiously attempted in NTDT patients to manage hypersplenism while mitigating the risk (16, 27).

We did not include such young patients in this series (given our institutional practice of deferring any splenectomy until  $\geq 5$  years old),

but our results on older children suggest that partial splenectomy can be performed safely in pediatric thalassemia with careful patient selection and appropriate prophylaxis (28, 29).

By preserving a small portion of spleen, PS might reduce the stimulus for such extramedullary hematopoiesis, as evidenced by the absence of EMH-related complications in our PS patients. This is whereas rare cases of spinal cord compression from EMH have been reported after TS (30). Such a speculative benefit requires further investigation, but it is another rationale for spleen-conserving approaches in thalassemia.

Our study also compared the outcomes for the pediatric and adult patients after splenectomy. We found that the children had a significantly higher post-splenectomy infection rate than the adults (Table 2), which is consistent with the heightened OPSI susceptibility in younger patients. In contrast, the rates of thrombosis, thrombocytosis, and endocrinopathy were similar for the pediatric and adult subgroups in our cohort. This suggests that age did not substantially influence those particular complication rates beyond the effect of the type of splenectomy performed. Nevertheless, the younger patients in our study more often underwent PS (by both our practice and parental preference), which probably conferred them a lower risk profile for complications like infection and thrombosis as compared to the older patients who underwent TS.

This study has several limitations. It was retrospective and observational, with a relatively small sample size, which may limit statistical power for some outcomes. The treatment assignment was not randomized; partial splenectomy was preferentially performed in the younger and pediatric patients, while the older patients more often underwent total splenectomy. This selection bias (due to convenience sampling and patient/parent preference) could confound direct comparisons between the groups. For instance, age and baseline health differences might have influenced the complication rates independently of the splenectomy type. The

follow-up duration varied (some patients had only months of follow-up, but the others up to several years), and we did not systematically capture very long-term outcomes such as late thrombosis, overwhelming infection beyond five years, or splenic remnant regrowth. We also did not perform a formal sample size or power calculation in advance, which means the study may have been underpowered to detect smaller differences in outcomes like thrombotic events. Finally, our definitions of complications focused on clinically significant events (e.g., severe infections requiring medical intervention, diabetes mellitus requiring therapy); milder subclinical differences may not have been recorded. These limitations should be considered when interpreting our results. It is valuable for prospective studies or trials to confirm the benefits of partial splenectomy as suggested by our data.

In summary, our experience suggests that partial splenectomy can effectively alleviate hypersplenism in thalassemia while preserving partial immune function and reducing certain risks. Careful patient selection is crucial; factors such as spleen size, patient age, transfusion dependence, degree of hypersplenism, and comorbid conditions must all be weighed when deciding between PS and TS. With appropriate vaccinations and prophylactic measures, partial splenectomy offers thalassemia patients hematologic improvement with a lower incidence of overwhelming infection and potentially fewer metabolic complications than total splenectomy. Ongoing vigilance is also needed, as partial splenectomy is not without drawbacks (incomplete symptom relief or need for re-splenectomy in some cases). Nevertheless, our findings add to the growing body of evidence favoring spleen-conserving surgery in well-selected patients.

## Conclusion

Regarding thalassemia patients, our findings suggest that partial splenectomy is associated with a lower risk of post-operative complications, particularly severe infections, compared to total splenectomy. By maintaining a portion of the splenic tissue, this spleen-saving

approach may reduce long-term infection-related morbidity while providing similar hematologic benefits. For younger or higher-risk individuals, partial splenectomy can be considered as an alternative to total splenectomy, though careful patient selection and rigorous follow-up are essential. The decision between partial and total splenectomy should be individualized, taking into account the spleen size, patient age, transfusion requirements, degree of hypersplenism, and concomitant comorbidities. Tailoring the surgical approach to the patient's profile can help maximize clinical outcomes, avert unnecessary complications, and preserve quality of life. Future multicenter studies are needed to refine selection criteria and to evaluate the long-term hematologic and immunologic outcomes of partial splenectomy in thalassemia.

### Availability of Data

Not applicable

### Acknowledgements

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### Conflict of Interest

The authors declare no competing financial or non-financial interests regarding this article.

### Funding

No fund was received for this study.

### Ethical Considerations

The study was approved by the Ethics Committee of Shiraz University of Medical

Sciences, with the ethical code IR.sums.med.rec.1397.330. It was also performed by following the ethical standards as laid down in the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards.

### Authors' Contributions

The study conceptualization and design were done by MS, NS, and SAB.

SH, NS, and AB analyzed and interpreted the data.

Acquisition of the data was done by MS, SH, SAB, and AB

MS and NS drafted the manuscript.

All the authors did the critical revisions.

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