Laparoscopic Splenectomy for Immune Thrombocytopenic Purpura (ITP) Patients with Very Severe Thrombocytopenia

Shahana Gupta¹ · Raja Kalayarasan¹ · Sandip Chandrasekar¹ · Senthil Gnanasekaran¹ · Biju Pottakkat¹

Received: 23 May 2017 / Accepted: 18 November 2017 / Published online: 25 November 2017
© Indian Society of Hematology and Blood Transfusion 2017

Abstract Laparoscopic approach is considered as gold standard for splenectomy in patients with Immune Thrombocytopenic purpura (ITP). The evidence for safety and feasibility of laparoscopic splenectomy (LS) in patients with very severe thrombocytopenia ($< 10,000 \mu\text{L}$) is limited. A retrospective study of 32 ITP patients who underwent LS between July 2012 and November 2016. The ITP patients who had platelet counts $< 10,000 \mu\text{L}$ (Group A, $n = 15$) and $> 10,000 \mu\text{L}$ (Group B, $n = 17$) were compared with respect to operative time, blood loss, conversion rate, perioperative blood transfusion, the length of hospital stay and postoperative complications. There was no significant difference between the two groups with respect to operative time ($p = 0.07$), intraoperative blood loss ($p = 0.75$), postoperative complications ($p = 0.23$) and hospital stay ($p = 0.15$). None of the patients in the two groups required conversion to open procedure. No intra operative blood transfusion was required. In Group A, 3 patients (with platelet count less than $2000 \mu\text{L}$) received platelet transfusion at induction of anesthesia while 10 others received after ligation of the splenic artery. There was no difference in the operative time, blood loss, postoperative complications and hospital stay between them. LS is a safe and feasible procedure for ITP patients with very severe thrombocytopenia. In these patients, the timing of intraoperative platelet transfusion does not influence perioperative and anesthetic complications.

Keywords Laparoscopic splenectomy · Very low platelet counts · ITP · Platelet transfusion

Introduction

Immune (or idiopathic) thrombocytopenic purpura (ITP) is an idiopathic autoimmune disorder characterized by destruction of opsonized platelets in the reticuloendothelial system, especially in the spleen. The first-line therapy for ITP is oral corticosteroids [1]. Splenectomy is generally considered a second-line therapy in patients who are refractory to steroids and in those who relapse after an initial response to medical therapy [2]. Since its introduction in 1992, laparoscopic splenectomy (LS) has gained increasing attention. In several series reported in the literature, ITP is found to be the most common indication for LS [3]. In addition to well-known benefits of laparoscopic surgery, it is specifically associated with lower blood loss, morbidity, and mortality [4]. The laparoscopic approach makes complete visualization of potential sites for accessory spleens possible thereby minimizing the chance of recurrent disease [3].

LS has been performed in patients with low platelet counts. However, the safe level of platelet count, the need and the timing of platelet transfusion during LS remain uncertain [5–12]. The aim of this study is to determine the safety of LS for ITP patients with very severe thrombocytopenia and to determine the impact of platelet transfusion on the perioperative outcomes.

Methods

A retrospective study of patients with ITP who underwent LS between July 2012 and November 2016. LS was performed on patients with ITP who were evaluated and referred to the Surgical Department by the Hematology Unit. Informed consent was taken from all patients.

✉ Raja Kalayarasan
kalayarasanraja@yahoo.com

¹ Department of Surgical Gastroenterology, JIPMER, Room no 551, Fourth floor, Superspeciality block, Puducherry 605006, India

Indications for LS included steroid dependent and steroid refractory ITP. Very severe thrombocytopenia is defined as platelet count $< 10,000 \mu\text{L}$. All patients received preoperative vaccination with Pneumococcal, H. influenza and Meningococcal vaccine. LS was performed in right lateral decubitus position using standard approach via four ports. The specimen was retrieved through the 12 mm port in midclavicular line after morcellation within a retrieval bag. Platelet transfusion was given at induction of anesthesia or after ligation of the splenic artery at the discretion of the anesthetist. All patients received 3 doses of Co-amoxiclav injection perioperatively and antibiotic prophylaxis with Amoxicillin for a period of 2 years or till they reach 18 years whichever was earlier. Platelet counts were serially monitored in the preoperative and postoperative period. The postoperative counts were done on day 7 after surgery and repeated at 1 and 3 months. Parameters studied include operative time, blood loss, conversion rate, perioperative blood transfusion, need and timing of platelet transfusion, the length of hospital stay and complications. Complications were graded according to Clavien Dindo classification [13].

Statistical analysis was performed using the statistical software SPSS version 16.0. Mann–Whitney U test was used for comparison of continuous variables and Chi square test was used for categorical variables. A p value of < 0.05 was taken as significant.

Results

During the study period, thirty-two patients underwent LS for ITP. Of the 32 patients, 5 patients had steroid dependent ITP and the remaining 27 patients had steroid refractory ITP. Preoperatively, 23 patients were on steroids along with azathioprine, intravenous immunoglobulin (IVIG), cyclophosphamide, rituximab or dapsone while the rest were only on high dose steroids. Of the 23 patients, IVIG (1 g/kg) was administered in 9 patients. The age of the patients included in the study ranged from 14 to 65 years and 22 were females. Of the 32 patients, 15 had a very severe thrombocytopenia (Group A) and in the remaining 17 patients, the platelet count was more than $10,000 \mu\text{L}$ (Group B). There was no significant difference between two groups in terms of the demographic parameters, body mass index, disease type and duration, duration of medical treatment and the type of medical treatment received in the preoperative period (Table 1).

The median (range) platelet count in Group A was $4000 \mu\text{L}$ (1000 – $9000 \mu\text{L}$). Of the 15 patients, 3 had platelet count $< 10,000 \mu\text{L}$ despite preoperative IVIG. In Group B, 12 patients had platelet counts more than $10,000$ but less than $50,000 \mu\text{L}$. The other 5 had counts between $50,000$

and $90,000 \mu\text{L}$. Of the 17 patients who received platelet transfusion, the majority (13/15, 86.7%) were in Group A. In Group A, 3 patients who had platelet count below $2000 \mu\text{L}$ received platelet transfusion at the time of induction of anesthesia and 10 patients received platelets after ligation of the splenic artery. Two patients in Group A who did not receive platelet transfusion had a preoperative platelet count of $9000 \mu\text{L}$ without any bleeding manifestations in the preoperative period. In Group B, 4 patients received platelet transfusion after ligation of the splenic artery as they had significant bleeding manifestations in the preoperative period. There was no conversion to open procedure in either group. The commonest complication was port site hematoma, which developed in 3 patients in Group A and 1 in Group B. All were treated conservatively. None of the patients had Grade III/IV postoperative complications. There was no significant difference in the operative time ($p = 0.07$), blood loss ($p = 0.75$), complications ($p = 0.23$) and hospital stay ($p = 0.15$) between Group A and B (Table 2). Also, there was no significant difference in these parameters in Group B patients with platelet count more than $10,000$ but less than $50,000 \mu\text{L}$ and those with counts $\geq 50,000 \mu\text{L}$. In Group A, there was no difference in the median (range) operative time [120 (120–180) mins], blood loss [50 (50–60) mL], and hospital stay [3 (2–4) days] between patients who received platelet transfusion at induction and after splenic artery ligation. Also, there was no significant difference in the Grade I/II complications between two subgroups in Group A (1/3 and 1/10, $p = 0.37$). None of the patients required intraoperative packed red blood cell (PRBC) transfusion. All except 6 patients (Group A-3, Group B-3) had a rise in platelet count to more than $50,000 \mu\text{L}$ by the first postoperative week which was sustained at 3 months follow up. Five of the nonresponders were in the age group of 50–60 years and the remaining one patient was aged 31 years. None of them had any response to preoperative immunosuppressive therapy.

Discussion

LS has become the preferred approach for elective treatment of many splenic diseases, particularly for ITP patients refractory to medical treatment. While many authors have reported a longer operative time for LS than for open splenectomy (OS), a significant decrease in operative time with increasing experience in LS has been reported [14, 15]. Benefits of laparoscopic approach are well established and it is now accepted as the “gold standard” for splenectomy. A meta-analysis of 51 published series with a total of 2940 patients reported that LS was associated with significantly reduced procedure-related morbidity

Table 1 Comparison of demographic and clinical parameters of patients with platelet count < 10,000 μL (Group A) and platelet count > 10,000 μL (Group B) undergoing laparoscopic splenectomy

Parameter	Group A (n = 15)	Group B (n = 17)	p value
Median age, years	23	25	0.45
Gender (male: female)	4:11	6:11	0.60
Median body mass index (BMI), kg/m^2	19.5	20.1	0.56
Primary ITP, n (%)	15 (100)	17 (100)	–
Median duration of disease, months	18	16	0.13
Median duration of medical treatment, months	17	16	0.26
Preoperative medical treatment			
Only steroids	5	4	0.53
Steroid with other Immunosuppressives [#]	10	13	
Accessory spleen, n (%)	2 (13.3)	2 (11.8)	0.89

[#]Other immunosuppressives include azathioprine, Cyclophosphamide, Intravenous immunoglobulin, Rituximab or Dapsone

and a shorter hospital stay than OS [15]. However, it has been difficult to determine a platelet level for safe operative intervention. The results of the present study suggest that LS is a safe procedure even in patients with very severe thrombocytopenia. The operative time, intra-operative blood loss, complications and hospital stay in ITP patients with very severe thrombocytopenia were comparable to patients with platelet count > 10,000 μL . A limited number of studies evaluated the role of LS in patients with very severe thrombocytopenia. The operative outcomes of the present study compare favorably to the previously reported series (Table 3) [5, 8–11, 16–18]. In a series of 11 patients with a platelet count < 10,000 μL , only a mild bleeding tendency was noted during the operation and it did not alter the perioperative course. Only 3 patients with a platelet count close to zero in this series, received intraoperative platelet transfusion [17]. Advancements in laparoscopic energy devices with improvement in surgical skills contribute to better postoperative outcomes in these high-risk patients.

The need and timing of platelet transfusion in ITP patients requiring splenectomy is controversial. In patients with ITP, about one-third of transfused platelets are sequestered in the splenic pool where they are destroyed; and their measured survival time is shortened, ranging from 2 to 3 days to a matter of minutes [6]. The immunological destruction of platelets in the spleen limits the value of

platelet transfusion in the presence of functioning spleen. Also, platelets are a scarce resource and transfusion is associated with risks of alloimmunization, transmission of infection, allergic reactions, thromboembolic complications and transfusion-related acute lung injury. However, perioperative bleeding due to low platelet count is of major concern to both the surgeon and the anesthetist. It has been a standard practice for the past four decades to give platelet transfusion to severely thrombocytopenic patients as supportive care. The British Committee for Standards in Hematology (BCSH) guideline recommends platelet transfusion after ligation of splenic artery in patients with platelet count < 10,000 μL [19]. American Society of Hematology also provided a similar recommendation [20]. Yoneoka et al. [12] reported a successful emergency LS for a patient whose platelet count was below the measurable limit, with continuous platelet transfusion at a rate of 2 U/h. However, Chen et al. [6] reported that perioperative platelet transfusion for ITP patients with very low platelet count may be unnecessary. In a report on 10 patients with ITP who had a platelet count less than 10,000 μL , platelet transfusion was given to only 2 patients after ligation of the splenic artery. The mean operating time was 157 min and the mean intraoperative blood loss was 44 mL. None of the patients had any significant complications [8]. No significant correlation between conversion rate and platelet counts has been reported [7, 21, 22]. An important concern

Table 2 Comparison of perioperative parameters of patients with platelet count < 10,000 μL (Group A) and platelet count > 10,000 μL (Group B) undergoing laparoscopic splenectomy

Parameter	Group A (n = 15)	Group B (n = 17)	p value
Median operative time (minutes)	120	120	0.07
Median blood loss (ml)	60	60	0.75
Transfusion requirement (PRBC)	0	0	–
Complications (Grade I/II), n (%)	3 (20)	1 (5.9)	0.23
Median hospital stay (days)	3	2	0.15

Table 3 Studies on laparoscopic splenectomy in patients with very severe thrombocytopenia

Author	No of patients (platelet counts < 10,000 μ L)	Operative time (mins)	Blood loss (ml)	Complications Grade I/II (%)	Complications Grade III/IV (%)	Conversion rate (%)
Keidar [5]	12	80	–	16.5	16.5	0
Chen [6]	30	162	65	6.6	0	6.6
Wu [8]	10	157	44	0	0	6.6
Cai [16]	42	115	60	11.4	0	2.4
Szold [17]	11	56.5	–	4.8	2.9	0
Balague [26]	19	115	263	16	–	10
Present series	15	120	60	20	0	0

not addressed by platelet transfusion after ligation of splenic artery is safety of endotracheal intubation in the presence of very low platelet counts. Airway bleeding due to intubation trauma and intracranial hemorrhage due to coughing induced by tracheal tube represent major sources of morbidity or mortality [23]. Owing to lack of evidence, it is difficult to draw firm conclusion about the safe level of platelet count for laryngoscopy and endotracheal intubation. In general, before any surgical procedure, transfusion of platelet concentrates is indicated in patients with platelet count < 50,000 μ L [22]. Also, precautions should be undertaken to minimize trauma to the upper airway during laryngoscopy for tracheal intubation. Recently, two case reports described the anesthetic management in ITP patients with a very low platelet count [24, 25]. In a series, 20 patients with platelet count < 10,000 μ L underwent uneventful endotracheal anesthesia without platelet transfusion. Therefore, a platelet count < 10,000 μ L seems to be reasonably safe for this procedure [6]. In the present study 3 out of 15 patients in Group A received platelet transfusion at induction. These three had a platelet count of less than 2000 μ L. Ten others were given platelets after ligation of the splenic artery. However, the timing of platelet transfusion did not influence the perioperative outcomes in these patients. IVIG is an alternative to platelet transfusion to improve platelet count in the preoperative period [7]. Following IVIG administration platelet count reaches the peak value on the first week but soon declines and returns to pre-administration level by the third week due to the short half-life of IVIG. Both high dose (2 g/kg) and low dose (1 g/kg) IVIG were found to be equally effective in increasing platelet count [26]. However, the disadvantages of IVIG are high cost, adverse effects including anaphylactic reaction in patients with IgA deficiency and failure to improve platelet count in all patients. In the present series, the response rate of preoperative administration of IVIG is 66.7% (6/9).

Hematologic response to splenectomy in patients with very low platelet counts has been reported to be good [5, 27]. The increase in platelet counts is expected 24–48 h

after splenectomy. Predictors of success of splenectomy include young age, at least a partial response to preoperative steroid therapy and the long interval between diagnosis and surgery [28]. In the present study, the 6 patients in whom the platelet count did not rise above 50,000 μ L at 1 week and at 3 months follow up after surgery did not have any response to preoperative immunosuppressive therapy. Five of them were in the age group of 50–60 years, a negative predictor of response to splenectomy. Preoperative platelet count was not a predictor of response to splenectomy as there were three non-responders in each group. A major limitation of the present study is the small sample size of the study groups.

Conclusions

LS is a safe and feasible procedure for ITP patients with very severe thrombocytopenia. In these patients, the timing of intraoperative platelet transfusion does not influence perioperative and anesthetic complications.

Compliance with Ethical Standards

Conflict of interest Authors declare that they have no conflicts of interest.

Ethical Standards All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Rodeghiero F (2008) First-line therapies for immune thrombocytopenic purpura: re-evaluating the need to treat. *Eur J Haematol Suppl* 80:19–26
2. Cordera F, Long KH, Nagorney DM, McMurtry EK, Schleck C, Ilstrup D, Donohue JH (2003) Open versus laparoscopic splenectomy for idiopathic thrombocytopenic purpura: clinical and economic analysis. *Surgery* 134:45–52
3. Vecchio R, Cacciola E, Lipari G, Privitera V, Polino C, Cacciola R (2005) Laparoscopic splenectomy reduces the need for platelet

- transfusion in patients with idiopathic thrombocytopenic purpura. *JSLs* 9:415–418
4. Silecchia G, Boru CE, Fantini A, Raparelli L, Greco F, Rizzello M et al (2006) Laparoscopic splenectomy in the management of benign and malignant hematologic diseases. *JSLs* 10:199–205
 5. Keidar A, Sagi B, Szold A (2003) Laparoscopic splenectomy for immune thrombocytopenic purpura in patients with severe refractory thrombocytopenia. *Pathophysiol Haemost Thromb* 33:116–119
 6. Chen X, Peng B, Cai Y, Zhou J, Wu Z, Chen S (2011) Laparoscopic splenectomy for patients with immune thrombocytopenia and very low platelet count: is platelet transfusion necessary? *J Surg Res* 170:e225–e232
 7. Keidar A, Feldman M, Szold A (2005) Analysis of outcome of laparoscopic splenectomy for idiopathic thrombocytopenic purpura by platelet count. *Am J Hematol* 80:95–100
 8. Wu Z, Zhou J, Pankaj P, Peng B (2011) Laparoscopic splenectomy for immune thrombocytopenia (ITP) patients with platelet counts lower than 1×10^9 L. *Int J Hematol* 94:533–538
 9. Wanachiwanawin W, Piankijagum A, Sindhvananda K, Vathanophas V, Visudhiphan S, Na-Nakorn S (1989) Emergency splenectomy in adult idiopathic thrombocytopenic purpura. A report of seven cases. *Arch Intern Med* 149:217–219
 10. Stiemer B, Opri F, Senger D, Kreuser ED, Berdel W, Hopp H et al (1996) Successful emergency splenectomy during pregnancy in a patient with life-threatening idiopathic thrombocytopenia case report. *J Perinat Med* 24:703–706
 11. Pastore Y, Wacker P, Ozsahin H, Humbert J, Hanquinet S, Lironi A (1999) Emergency splenectomy in the management of intracranial hemorrhage in childhood immune thrombocytopenic purpura. *J Pediatr Hematol Oncol* 21:306–307
 12. Yoneoka Y, Tokita K, Yamauchi JI, Takeda N, Ohta H, Shindo T (2004) Successful management of spontaneous intracranial haemorrhage despite critical thrombocytopenia (platelets $< 1000 \text{ mm}^3$) due to adolescence-onset idiopathic thrombocytopenic purpura. *Acta Neurochir* 146:199–201
 13. Dindo D, Demartines N, Clavien P (2004) Classification of surgical complications a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240:205–213
 14. Qu Y, Xu J, Jiao C, Cheng Z, Ren S (2014) Long-term outcomes of laparoscopic splenectomy versus open splenectomy for idiopathic thrombocytopenic purpura. *Int Surg* 99:286–290
 15. Winslow ER, Brunt LM (2003) Perioperative outcomes of laparoscopic versus open splenectomy: a meta-analysis with an emphasis on complications. *Surgery* 134:647–653 **discussion 654–655**
 16. Cai Y, Liu X, Peng B (2014) Should we routinely transfuse platelet for immune thrombocytopenia patients with platelet count less than 10×10^9 L who underwent laparoscopic splenectomy? *World J Surg* 38:2267–2272
 17. Szold A, Kais H, Keidar A, Nadav L, Eldor A, Klausner JM (2002) Chronic idiopathic thrombocytopenic purpura (ITP) is a surgical disease: long term results in 100 patients. *Surg Endosc* 16:155–158
 18. Delaitre B, Blezel E, Samama D, Barrat C, Gossot D, Bresler L et al (2002) Laparoscopic splenectomy for idiopathic thrombocytopenic purpura. *Surg Laparosc Endosc Percutaneous Tech* 12:412–419
 19. George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ et al (1996) Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood* 88:3–40
 20. British Committee for Standards in Haematology General Haematology Task Force (2003) Guidelines for the investigation and management of idiopathic thrombocytopenic Purpura in adults, children and in pregnancy. *Br J Haematol* 120:574–596
 21. Kam PC (2008) Anesthetic management of a patient with thrombocytopenia. *Curr Opin Anesthesiol* 21:369–374
 22. Martin Arnau B, Turrado Rodriguez V, Tartaglia E, Bollo Rodriguez J, Targarona EM, Trias Folch M (2016) Impacto del recuento plaquetario preoperatorio en la evolución perioperatoria tras la esplenectomía laparoscópica por purpura trombocitopénica idiopática. *Cir Esp* 94:399–403 **(English translation available)**
 23. Sadowitz D, Terndrup TE (1994) Subglottic airway hemorrhage associated with idiopathic thrombocytopenic purpura. *Ann Emerg Med* 23:591–595
 24. Felbinger TW, Posner M, Eltzschig HK, Kodali BS (2007) Laparoscopic splenectomy in a pregnant patient with immune thrombocytopenic purpura. *Int J Obstet Anesth* 16:281–283
 25. Trimmings AJ, Walmsley AJ (2009) Anaesthesia for urgent splenectomy in acute idiopathic thrombocytopenic purpura. *Anaesthesia* 64:226–227
 26. Qin YH, Zhou TB, Su LN, Lei FY, Zhao YJ, Huang WF (2010) The efficacy of different dose intravenous immunoglobulin in treating acute idiopathic thrombocytopenic purpura: a meta-analysis of 13 randomized controlled trials. *Blood Coagul Fibrinolysis* 21:713–721
 27. Balagué C, Targarona EM, Cerdán G, Novell J, Montero O, Bendahan G et al (2004) Long-term outcome after laparoscopic splenectomy related to hematologic diagnosis. *Surg Endosc* 18:1283–1287
 28. Katkhouda N, Grant SW, Mavor E, Friedlander MH, Lord RV, Achanta K (2001) Predictors of response after laparoscopic splenectomy for immune thrombocytopenic purpura. *Surg Endosc* 15:484–488