Ligasure versus EndoGIA Stapler for Hilar Vascular Control During Laparoscopic Splenectomy for Adult Chronic ITP

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Background: The major procedural risk associated with laparoscopic splenectomy (LS) for adult chronic immune thrombocytopenia (ITP), is uncontrollable intraoperative bleeding, requiring conversion to laparotomy. There are several methods of achieving hemostasis, including clips, sutures, Ligasure and EndoGIA stapler.

Patients and methods: Between April 2015 and May 2017, 32 adult patients with chronic ITP indicated for LS, were divided into two equal groups, according to the method of hilar vascular control (group 1, Ligasure Vessel Sealing System; group 2, EndoGIA stapler). The perioperative course was documented and the follow up data were recorded.

Results: Two patients (6.25%) were converted to open splenectomy. Four patients (12.5%) had persistent thrombocytopenia after surgery. The cost was higher in group B. No significant difference was found between both groups regarding post-operative complications.

Conclusion: For adult chronic ITP, both Ligasure and EndoGIA stapler are safe and effective for hilar vascular control during LS. The results are similar and comparable, but Ligasure is less costly than EndoGIA stapler.

Key words: Laparoscopic splenectomy, Ligasure, EndoGIA stapler, chronic ITP, hilar vascular control.

Introduction

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized mainly by immune-mediated accelerated platelet destruction by autoantibodies and suppressed platelet production in the bone marrow, leading to cutaneous and mucosal bleeding.[1] It is characterized by a platelet count>100x109 cells/L in the absence of any recognized cause of thrombocytopenia.[2] The new terms for ITP are: 'newly diagnosed' (from diagnosis until 3 months), 'persistent ITP' (3–12 months) and 'chronic ITP' (ITP lasting for more than 12 months).[2]

Recent studies indicate that there may be a component of impaired platelet production when compared to the exuberant peripheral destruction.[3] ITP is triggered by upper respiratory infections in two thirds, occasionally by specific viral illness or immunization with a live virus vaccine in the preceding 2–3wk.[3,4] Immune response elicits anti-platelet antibodies against platelet antigens (GPIIb/IIIa). Antibody coated platelets are cleared by the reticulo-endothelial system, predominantly in the spleen. Antibodies reactive against the platelets target megakaryocytes in the marrow as well, resulting in decreased platelet production along with peripheral destruction.[3]

Laparoscopic splenectomy (LS) is considered to be the second-line treatment in the following situations: (1) refractory symptomatic thrombocytopenia after 3–6 months of corticosteroids therapy, (2) contraindications to corticosteroid or intolerant doses of steroids are required to achieve remission and (3) relapse of thrombocytopenia after an initial response to medical therapy.[5] Following splenectomy there is an early response rate of 80% but over time relapses occur and the long-term response rate is closer to 66%.[6] Even if splenectomy fails to induce a complete remission, many patients may still experience a partial response to splenectomy with a platelet count that is higher than that before splenectomy.[7]

Laparoscopic approach to diseases related to solid organ such as spleen and liver has lagged behind operations on hollow viscous because of problems related to hemostasis and extraction of specimen. Intraoperative bleeding is the major concern with LS, because of the complex splenic blood supply and the difficulty of dissection. The high blood loss is harmful to the patient and makes the dissection difficult because of inadequate visualization of anatomical structures. Furthermore, reported conversion rates are usually between 5% and 10%,[8] and most conversions are related to uncontrollable bleeding from hilar vessels or capsular injury. Satisfactory hemostasis is essential for good results in LS.

There are several methods of achieving hemostasis, including clips, sutures, ultrasonic coagulation, and

monopolar and bipolar coagulation. Clips are easily placed but can become dislodged while sutures are time consuming in laparoscopic surgery. Standard bipolar and ultrasonic coagulation can be used to coagulate small vessels (1-3 mm). The surgical stapler was applied for en bloc transection of the splenic pedicle, and is currently used widely in LS. The Ligasure vessel-sealing system was developed as an alternative to suture ligatures, hemoclips and ultrasonic coagulators for ligating vessels. The Ligasure is FDA approved to seal vessels that are 7 mm in diameter or less, by denaturing collagen and elastin within the vessel wall and surrounding connective tissue. The hemostatic seal is characterized at 20 days by intrinsic fibrosis with minimal inflammation.[9] The aim of this study was to evaluate the use of Ligasure versus EndoGIA stapler for hilar vascular control during LS for adult chronic ITP.

Patients and methods

This study was a comparative, prospective, randomized clinical trial. This study was carried out in El-Demerdash hospital. An informed consent was obtained from the patients for participation in this study according to the Ethical Committee of the Faculty of Medicine, Ain Shams University.

For this study, 32 adult patients with chronic ITP who did not achieve sustained remission or refractory to medical treatment, underwent elective LS between April 2015 and May 2017. They were divided into two equal groups, according to the method of hilar vascular control; Group 1, Ligasure Vessel Sealing System (Covedien, Philadelphia, Pennsylvania, USA); Group 2, EndoGIA stapler (Ethicon, Johnson and Johnson Co. USA). Patients were referred from hematology department in Ain Shams University hospitals.

All patients aged more than 15 years and not having any contraindication for general anesthesia or laparoscopic surgeries were included. Patients with a history of open upper abdominal surgery were excluded. Complete history and physical examination were carried out, including laboratory investigations and abdominal ultrasound to determine the splenic size. Bone marrow examination was performed for all patients. The typical finding in a bone marrow biopsy was an increase in megakaryocytes without other concomitant abnormalities.

Bruising, epistaxis and gum bleeding were the commonest clinical presentations. All patients received meningococcal, pneumococcal and haemophilus influenzae type B vaccines, two weeks pre-operatively. The pre-operative platelet count ranged from 3 to 43×10^9/L. Platelet and red blood cell transfusions were given till the platelet count was around 50×10^9/L and hemoglobin level around 10 g/dl. After the splenic hilum was transected, platelet transfusion was done to increase the platelet count promptly and stop the oozing of blood. A drain was left in the operative bed in all patients.

Clinical data, including age, gender, operative time, estimated blood loss, intraoperative blood transfusion, postoperative morbidity, post-operative platelet count, hospital stay, and rate of conversion to laparotomy were compared. We defined a platelet count that failed to double and remained under 100×10^9/L as failure to respond, while doubling of the platelet count which nevertheless remained under 100×10^9/L, as partial response, and a platelet count over 100×10^9/L with resolution of clinical symptoms and no further need for steroid therapy as complete response. No combined surgery was performed. Patients were followed up for 8-24 months post-operative, for early and late complications.

Surgical technique

Under general anesthesia with nasogastric tube and Foley catheter inserted, the patient was positioned in the semi-lateral position (left side up). The surgeon and assistant stood facing the patient, with the video monitor sited opposite. Via the open technique, a 10 mm port was placed just above the umbilicus, for laparoscopy and for CO2 pneumoperitoneum up to a pressure of 14 mmHg. A 5-mm port was placed in the epigastrium for liver retraction. A 5-mm port was placed in the left mid-clavicular line, immediately below the left costal margin. Another 5-mm port was placed in the left mid-axillary line immediately below the costal margin, and if the EndoGIA stapler was used, it was replaced for a 12-mm port. An additional 5-mm port was placed more laterally to facilitate retraction and dissection.

A search for accessory spleens was made before commencing dissection of the spleen. Dissection was performed from the caudal to cranial direction with gentle dissection of the omentum from the lower pole and visceral aspect and/or splenic hilum. Dissection was close to the spleen but without tearing the capsule. In this phase, the short gastric vessels were also severed. With the spleen rotated towards the midline, the posterior peritoneal attachments were divided away from the splenic capsule. The spleen was progressively mobilized towards the midline, exposing the "splenic mesentery," which contains the main splenic vessels inferiorly, the short gastric vessels superiorly, and the tail of the pancreas.

In group A, hilar vessels were sealed with Ligasure (Covedien, Philadelphia, Pennsylvania, USA)

(Figure 1), as close as possible to the parenchyma and good hemostasis was checked. The operation proceeded with the dissection of the short gastric vessels **(Figure 2)**, and finally with the division of the splenorenal ligaments up to the splenodiaphragmatic attachments. In group B, the vascular attachments were divided using a 45-mm endoscopic linear cutting stapler (white cartridge) (Ethicon, Johnson and Johnson Co. USA) **(Figure 3)**. This was applied sequentially across the splenic mesentery commencing inferiorly, and usually multiple applications of the stapler were required (two to three) **(Figure 4)**. The stapler was placed adjacent to the splenic capsule at the hilum, to minimize the risk of damaging the pancreatic tail. When applying the stapler, the spleen was lifted up by a blunt instrument passed through the most medial port and complete separation of the spleen from its remaining attachments was done **(Figure 5)**.

In both groups, the spleen was extracted through a small Pfannenstiel incision. A drain was left in situ in all patients. The 10 mm and 12 mm ports puncture sites were closed to prevent port site hernia and the Pfannenstiel incision was closed in layers. All wounds were infiltrated with long acting local anesthetic to reduce post-operative pain and analgesia requirements. The Foley catheter was removed at the end of surgery.

Fig 1: Hilar vessels were sealed with Ligasure.

Fig 2: Dissection of the short gastric vessels with Ligasure.

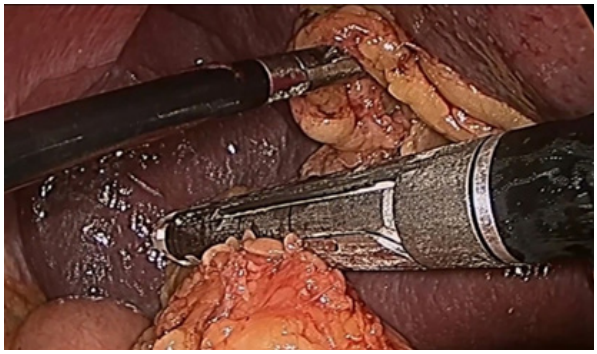

Fig 3: Vascular attachments were divided using a 45-mm linear cutting stapler (white cartridge).

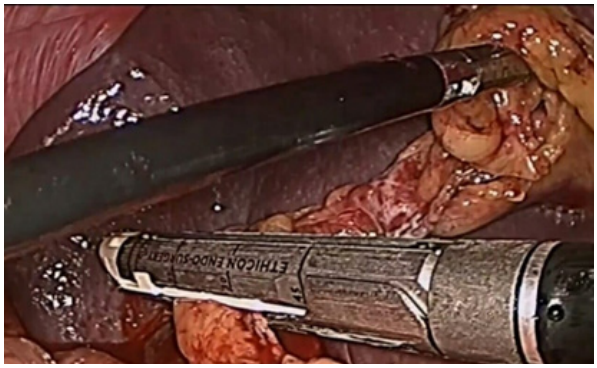

Fig 4: Hilar transection via multiple applications of the stapler.

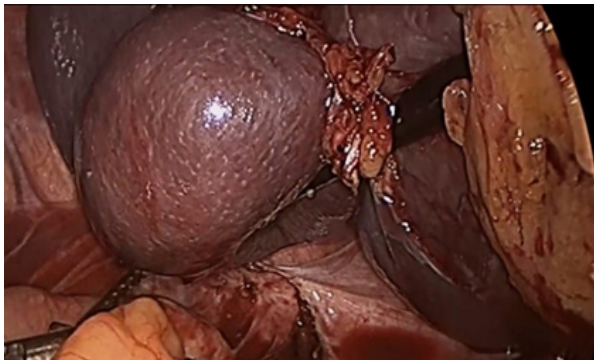

Fig 5: Complete separation of the spleen from its remaining attachments via stapler.

Results

Statistical analysis

Data were collected and analyzed using computer program IBM SPSS (version 21). Continuous data were presented as mean ± standard deviation (SD). Categorical data were presented as percentages. Analysis of variance (ANOVA) and the rank-sum test were used to analyze continuous data. The results were regarded significant (S) with $P<0.05$ & highly significant (HS) with $P<0.01$. $P\geq0.05$ was regarded non-significant (NS). $\chi 2$ test (with Yates correction and Fisher's exact test) and the Student t or Mann Whitney U tests were used according to the characteristics of the study variables and the conditions of applicability.

Patients' demographics (Table 1)
The study included 32 patients, 24 females (75%) and 8 males (25%). In group A, the age ranged (16-41 years) with a mean age of 27.75± 8.7063 years, while in group B, the age ranged (17-43 years) with a mean age of 28.0625±7.5318 years. The P value was 0.457 by t-test, which was statistically nonsignificant.

Pre-operative platelet count
In group A, the mean pre-operative platelet count was 21±11.758 x 10^9/L, ranging from 3 to 37x10^9/L. In group B, the mean pre-operative platelet count was 22.9375±11.767 x 10^9/L, ranging from 7 to 43x10^9/L. The P-value was 0.6446 by t-test, which was statistically nonsignificant.

Operative time and accessory spleen detection
In group A, the mean operative time was 98.125±5.302 min, ranging from 90 to 104 min. In group B, the mean operative time was 99.125±8.663 min, ranging from 88 to 116 min. The P-value was 0.348 by t-test, which was statistically nonsignificant. Accessory spleens were recognized and removed in six patients (13%), three patients in each group.

Intra-operative blood loss
In group A, the mean intra-operative blood loss was 90.625±53.475 ml, ranging from 50 to 250 ml. In group B, the mean intra-operative blood loss was 92.5±61.779 ml, ranging from 40 to 300 ml. The P-value was 0.463 by t-test, which was statistically nonsignificant.

Rate of conversion to open surgery
All laparoscopic splenectomies were successfully carried out except two (6.25%) patients, one patient in each group. In group A, conversion to open surgery was due to splenic artery bleeding which could not be stopped by laparoscopic instruments. In group B, conversion was due to that the stapler got broken and locked while trying to transect the vascular pedicle.

Table 1: Patients' demographics and operative data

	Ligasure group	EndoGIA Stapler group
Age	years 8.7063 27.75±	years 7.5318±28.0625
Sex (M:F)	3:13	4:12
Pre-operative platelet count	x 10^9/L 11.758 ± 21	x 10^9/L ١1.767 ± 22.9375
Operative time	min 5.302 ± 98.125	min 8.663 ± 99.125
Accessory spleen detection	3	3
Intra-operative blood loss	ml 53.475 ± 90.625	ml 61.779 ± 92.5
Rate of conversion to open surgery	% 3.125	% 3.125

Hospital stay and cost and post-operative complications (Table 2).

In group A, the mean hospital stay was 3.8125±0.91 days, ranging from 3 to 6 days. In group B, the mean hospital stay was 4.375±1.927 days, ranging from 3 to 10 days. The P-value was 0.299 by t-test, which was statistically nonsignificant. The cost was high in group B than group A due to the higher price of the EndoGIA stapler.

Three (9.375%) patients developed port-site haematomas treated conservatively. One (3.125%) patient developed a haematoma of the Pfannensteil wound requiring surgical evacuation. Four (12.5%) patients developed chest infection with good response to medications and chest physiotherapy, none of which required ventilatory support. One (3.125%) patient developed a pancreatic fistula, for which the drain was left in place and the fistula was treated conservatively with octreotide. There were six (18.75%) cases of urinary retention, all of which settled spontaneously, and three (9.375%) port-site infections in the absence of haematomas requiring antibiotic treatment. One (3.125%) patient had left pleural effusion. Two (6.25%) patients were readmitted for fever of unknown origin. There was no case of overwhelming post-splenectomy sepsis or post-operative thrombotic complications. Two (6.25%) patients had incisional hernia of the Pfannensteil incision. Regarding post-operative complications, the difference between both groups was statistically nonsignificant.

Post-operative platelet count
In the immediate post-operative period, in group A, the mean post-operative platelet count was 52.125±13.093x109/L, ranging from 33 to

77x10^9/L. In group B, the mean post-operative platelet count was 55.937±17.467 x 10^9/L, ranging from 31 to 92x10^9/L. The P-value was 0.490 by t-test, which was statistically nonsignificant.

Late hematological response of splenectomy
All 32 patients have been followed-up to at least 8 months after splenectomy (8-24 months). None was lost to long-term follow-up, and none has died. Overall, 28 (87.5%) patients responded, with 23 (71.875%) showing CR and 5 (15.625%) showing PR, to a combination of splenectomy and adjunctive medical therapy without relapse. At the last follow-up, only four patients (12.5%) (two in each group) had persistent thrombocytopenia and the platelet count did not increase after splenectomy. The difference between both groups was statistically nonsignificant.

Table 2: Post-operative course and complications

	Ligasure group	EndoGIA Stapler group
Hospital stay	3.8125 ± 0.91 days	4.375 ± 1.927 days
Urinary retention	4	2
Port-site haematoma	1	2
Haematoma of the Pfannensteil wound	none	1
Chest infection	3	1
Pancreatic fistula	none	1
Port-site infection	1	2
Left pleural effusion	1	none
Overwhelming post-splenectomy sepsis	none	none
Incisional hernia	none	2
Post-operative platelet count	52.125 ± 13.093 x 10^9/L	55.937 ± 17.467 x 10^9/L
Non response of splenectomy	6.25%	6.25%

Discussion
ITP is an autoimmune disorder defined by an isolated decrease of platelet count (>100x10^9 cells/L) resulting from accelerated clearance and destruction of antibody-coated platelets by tissue macrophages, predominantly in the spleen. Splenectomy is a second-line treatment for adult ITP and should be considered whenever steroid-based therapy fails to achieve or sustain remission, or is intolerable for the patient due to severe adverse reactions.

LS was first performed in 1991.[10] Splenectomy has become a well-established treatment in patients with ITP or primary immune-mediated thrombocytopenia,[11,12] either in addition to, or even preferable to, medical therapy.[13] Laparoscopic splenectomy compares favourably with open splenectomy with regard to postoperative pain, length of hospital stay and return to normal daily activity.[5,14,15]

LS is a technically challenging procedure and this can be handled by learning and practicing the proper technique. The secure control of splenic pedicles is crucial, especially in high-risk patients with idiopathic thrombocytopenic purpura. Uncontrollable hemorrhage when it occurs requires the conversion to laparotomy in most cases.

Multiple haemostatic devices are available for the vascular management during LS, including clips, bipolar and ultrasonic coagulation. However, these methods lack consistent and reliable hemostatic effect, prolonging the time required for pedicular division and increasing the risk of bleeding. Therefore, the use of these approaches is usually limited to the transection of vessels <3 mm in diameter.

During LS, the best technique should have low risk of bleeding, to avoid conversion to open surgery with its complications. In this study, 32 adult patients with chronic ITP indicated for laparoscopic splenectomy, were divided into two equal groups, according to the method of hilar vascular control (group 1, Ligasure Vessel Sealing System; group 2, EndoGIA stapler). The aim of this study was to determine the efficacy of Ligasure versus EndoGIA stapler for hilar vascular control during LS for adult chronic ITP.

There were no statistically significant differences between the two groups regarding age, operative

time, intra-operative blood loss, rate of conversion to open surgery, hospital stay and postoperative complications. Patients in the EndoGIA stapler group had higher cost in comparison with the patients in the Ligasure group.

In group A, the operative time ranged from 90 to 104 min, while in group B, the operative time ranged from 88 to 116 min. This operative time was considerably less than that of other studies which reported operative times in the range of 88 minutes to 188 minutes.[16]

Though it was said that, there is significant risk of bleeding due to spleen's rich vascularity and intimate relationship with adjacent organs, LS could be carried out with less blood loss if care is taken to the anatomical details and usage of modern equipment. The average blood loss in this study was in group A, 90.625±53.475 ml, while in group B, the mean intra-operative blood loss was 92.5±61.779 ml, which is comparatively less than other published studies.[17]

All laparoscopic splenectomies were successfully carried out except two (6.25%) patients, either due to splenic artery bleeding or due to stapler malfunction. This rate of conversion was less than that of Delaitre et al.,[18] who reported that a conversion was necessary in 36 cases (17.2%) because of hemorrhage.

There was statistically significant difference between the two groups regarding the cost which was high in group B than group A, due to the higher price of the EndoGIA stapler. This result matched the study conducted by Ji et al.[19] who stated that "the costliness of the delicate Endo-GIA staplers restricted its use in our practice, and was a heavy burden on the public health care system".

In this study, 87.5% of patients responded to splenectomy. This was similar to the study conducted by Rosen et al.,[20] with a remission rate of 78-93 % and the study conducted by Katkhouda et al., with a remission rate between 75% and 94%.[21]

Only four patients (12.5%) (two in each group) had persistent thrombocytopenia and the platelet count did not increase after splenectomy, this was similar to the study conducted by Khan and Nixon who reported in their study that 13 % of patients had no remission post splenectomy.[22]

Conclusion

Ligasure is a cost-effective alternative for achieving hemostasis, it is less expensive than the endostapler. The Endo-GIA stapler is an effective instrument, but its application for pedicular control requires proper positioning as close as possible to the hilum, accurate vascular dissection, and cautious skeletonization to avoid injury to tail of pancreas and subsequent pancreatic fistula.

Conflicts of interest

There are no conflicts of interest.

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