

Laparoscopic Splenectomy in the Management of Benign and Malignant Hematologic Diseases

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ABSTRACT

Objectives: The use of laparoscopy to treat malignant hematological diseases is not completely accepted. Our aim was to analyze operative and postoperative results of laparoscopic splenectomy performed for benign versus malignant hematological disorders.

Methods: Between 1994 and 2003, 76 consecutive patients underwent laparoscopic splenectomy. The first 38 cases were performed by using an anterior approach, whereas in the remaining 38 cases a semilateral position was used.

Results: Baseline characteristics showed that patients with malignant diseases were significantly older (56.9 vs 32.6 years, $P < 0.001$). Seventy-two (94.7%) procedures were completed laparoscopically. Conversion was required in 4 cases (5.2%). Mean operative time was 138.5 minutes for benign and 151.0 minutes for malignant diseases, ($P > 0.05$, ns). The hand-assisted technique was used in 3 patients with massive splenomegaly. Pathologic features showed that spleen volume was higher in patients with malignant diseases (mean interpole diameter 18.1 cm vs 13.7 cm, $P < 0.001$). Massive splenomegaly (interpole diameter over 20 cm, weight over 1000 g) was present in 13 patients (17.1%); 9 had malignant diseases. Overall perioperative mortality was 1.3% and major postoperative complications occurred in 6 patients (7.8%). Postoperative splenoportal partial thrombosis was identified in 9.7% of patients.

Conclusions: Laparoscopic splenectomy is a well-accepted, less-invasive procedure for hematological disorders. Neoplastic diseases or splenomegaly, or both, do not seem to limit the indications for a minimally invasive approach after the learning curve.

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INTRODUCTION

The first laparoscopic splenectomies (LS) were performed more than a decade ago by Delaitre¹ in France (1991), Carrol² in the USA (1992), and Poulin³ in Canada (1992). Many other experiences have been reported since then, and indications for surgery have been expanded to include adults and children with nontraumatic diseases.⁴⁻⁶ Less surgical trauma and intraoperative blood loss, early hospital discharge, rapid return to normal activities, and better cosmetics have been proposed as major advantages of LS in adult.¹⁻³

The most frequent indication for LS is immune thrombocytopenic purpura (ITP),⁷⁻¹⁰ followed by hereditary spherocytosis and autoimmune hemolytic anemia. Several studies have demonstrated the feasibility and safety of the laparoscopic approach also in cases of massive splenomegaly (interpole diameter > 20 cm, spleen weight > 1000 g).^{11,12}

Successful experiences with LS have been reported as well in patients with hematological malignancies.^{7,13,14} However, concerns about technical difficulties have limited this approach in cases of malignancies, and only limited series have been reported. It is a common opinion that in cases of lymphomas, large spleen, perisplenitis, and hilar lymphadenopathy may negatively affect manipulation and removal of the spleen. Primary lymphomas, splenomegaly, staging (in select cases), restaging after radio/chemotherapy, and focal lesions (suspected recurrence) are reported as indications for LS.¹⁵

The aims of the present study were to analyze the results in 76 consecutive patients (adults and children) with either benign or malignant diseases and to evaluate the benefits of laparoscopy in patients with lymphomas and other hematological malignancies.

METHODS

Our database was reviewed for patients who had undergone laparoscopic splenectomy. Between May 1994 and

December 2003, 76 consecutive patients were operated on for hematological benign and malignant diseases. The preoperative workup included routine blood tests, chest x-ray, and electrocardiography. In all patients, additional diagnostic examinations for surgical purposes were obtained no more than 2 weeks before surgery, ie, abdominal ultrasound with measurement of the maximum interpole diameter of the spleen and computed tomography scan or magnetic resonance imaging of the abdomen in case of suspected hematological malignancies. The last 41 patients underwent routine pre- and postoperative (7th day) ultrasound color Doppler examination of the splenic vessels to identify postoperative splenic or portal thrombosis, or both. At least 1 week before surgery, all patients were vaccinated for pneumococcus (Pneumovax, Merck & Co, Inc, Whitehouse Station, NJ, USA), *Haemophilus influenzae* (Prohibit, Connaught Laboratories, Inc, Swiftwater, USA) and meningococcus (Meningokokken, Baxter GmbH, Deutschland). All patients received intravenous antibiotic prophylaxis (piperacillin 4 g) 2 hours before surgery.

Patients with malignant and benign disease were compared for the following characteristics: age, sex, operative time (measured from incision to skin closure), transfusions, weight, and interpole diameter (ID) of the spleen, intraoperative complications, causes of conversion to open surgery, postoperative mortality, 30-day morbidity, reoperations, and length of hospital stay.

Specific late complications related to laparoscopy and to the histopathological diagnosis were also taken into account. Massive splenomegaly was defined as splenic interpole diameter (ID) >20 cm or as splenic weight >1000 g.

Values are expressed as mean \pm standard deviation ($M \pm SD$). All continuous variables were compared using the Student *t* test, and proportions were compared using the chi square test or Fisher's exact test. $P < 0.05$ was considered statistically significant (confidence interval 95%).

Surgical Approach

Anterior Approach

In the first 38 consecutive cases (May 1994 through February 1999), an anterior approach was adopted. The patient was placed in the lithotomy position, with the surgeon standing between the legs of the patient, and the assistant holding the camera on his right. Pneumoperitoneum was created with a Veress needle, in the majority of the cases inserted at the left subcostal margin. A 30-degree laparoscope was routinely used. The first 10-mm to

12-mm port was inserted in the umbilicus or at the left subcostal margin (depending on the spleen size and body mass index). A subxiphoid 5-mm port and a 10-mm to 12-mm left flank port were inserted. The position of the fourth port was based on the size of the spleen, but generally was between the xiphoid and camera port.

The first step of the procedure consists of the exploration of the abdominal cavity looking for accessory spleens in case of benign diseases or for lymphadenopathy and hepatic lesions in malignancies. In case of massive splenomegaly, to reduce the spleen size and the risk of bleeding, the main trunk of the splenic artery on the superior edge of the body of the pancreas was clipped. Exposure of the spleen was facilitated by the reverse Trendelenburg position and right-side rotation. Mobilization of the spleen began at the inferior pole dividing the spleno-colic ligament. Then the spleno-gastric ligament and the short gastric vessels were divided using clips or Harmonic scalpel (Ultracision, Ethicon Endo-Surgery, Cincinnati, OH, USA). The spleen mobilization was completed along its lateral and superior attachment with the diaphragm. The main splenic vessels were clipped or stapled using linear endoscopic cutter with vascular cartridge (ETS 30/45-2.5, Ethicon or Endo-Gia II 30/45-2.5, US Surgical, Tyco, Norwalk, CT, USA). A retrieval bag (Endocatch II, Tyco) was inserted percutaneously at the site of the left flank port, and the spleen was grasped and packed into the plastic bag. In case of benign diseases, the spleen was morcellated into the plastic bag before extraction. When malignancy was suspected, the spleen was introduced into the bag and divided into large pieces (3 cm) before retrieval through the enlarged port site.

Semilateral Approach

Since February 1999, a semilateral position with the left side elevated at 45 degrees and a reverse Trendelenburg has been used. This position has the advantage of splenic dislocation due to gravity (ie, medial retraction of the spleen), and it also allows a more comfortable access in case of hand-assistance. The same position of the surgical team is used as above. LS is typically a 2-surgeon operation, both facing the patient's abdomen and a single monitor over the patient's left shoulder for in-line operating. Three or 4 ports along the left subcostal margin are used. The position of the most lateral port must be 4cm to 5cm below the inferior tip of the spleen to manage large organs. Proceeding from the lower pole, the peritoneal attachments are sharply divided using the Harmonic scalpel. After the mobilization of the inferior pole, the dissection proceeds lateral to medial approaching the short

gastric vessels. The hilar pedicle is stapled using a linear endoscopic stapler with vascular cartridge (Endo-Gia II 45-2.5, US Surgical), taking care to preserve the tail of the pancreas. The mobilization is completed by dividing the attachment of the superior pole from the stomach and diaphragm.

In select cases of massive spleen, a hand-assisted procedure (without specific device) was adopted, with the surgeon's left hand through an enlarged umbilical incision (7 cm).

RESULTS

From May 1994 to December 2003, 76 consecutive patients (M=33, F=43), with a mean age of 40.2±20.9 years (range, 4 to 73) underwent LS. Eleven (14.4%) patients (M=5, F=6) were younger than 18 years of age (mean age, 10.8±5.4). Mean operative time was 143.6±42.0 minutes (range, 60 to 240), and mean hospital stay was 5.5±3.2 days (range, 2 to 24). Baseline clinical and operative characteristics for patients with benign diseases (group I - 52 patients) and malignant diseases (group II - 24 patients) are shown in **Table 1**. Surgical indications are summarized in **Table 2**.

Seventy-two (94.7%) of 76 procedures were completed laparoscopically. Intraoperative bleeding from major splenic vessels occurred in 3 patients: 2 in group I (3.8%) and 1 in group II (4.1%) with Hodgkin's disease (HD) for failure of the endoscopic linear cutter (EndoGIA, 30±2.5mm, vascular cartridge). Conversion was required to control splenic bleeding in 1 patient from group I. Three conversions were necessary for massive splenomegaly (ID 22 cm) in a patient with pancytopenia and a

Table 2.
Indications for Laparoscopic Splenectomy in the Benign and Malignant Disease Groups

Indications in Benign Diseases	No.	Indications in Lymphoproliferative Diseases	No.
Spherocytosis	17	Splenomegaly: primary diagnosis	8
Cooley disease	8	Splenomegaly (DL 13-19): primary diagnosis	6
Immune thrombocytopenic purpura	7	Splenomegaly: suspicion of recurrence	1
Autoimmune hemolytic anemia	4	Splenic lesions: primary diagnosis	5
Splenic cyst	2	Splenic lesions: suspicion of recurrence	2
Splenic hematoma	2	Splenomegaly nonresponder to chemotherapy	2
Others	12	—	

large incisional hernia; multiple splenic abscesses with perisplenitis in a patient with non-Hodgkin's lymphoma (NHL); marked splenomegaly (ID 25 cm) in 1 patient with NHL. Conversion rate was higher, although not statistically significant (Fisher's exact test, F = 0.41), in cases of LS performed for malignant (8.3%) versus benign diseases (3.8%).

Postoperative data are reported in **Table 3**. Patients received a soft diet on the second postoperative day. Major postoperative complications occurred in 6 patients (7.9%). Three patients had left subphrenic abscesses (2 of group II), successfully treated by percutaneous drainage. One group I patient had hemoperitoneum on the first postoperative day, successfully treated by percutaneous embolization of the splenic artery. Two patients were reoperated

Table 1.
Demographics and Surgical Data

Characteristics	Benign (N=52)	Malignant (N=24)	P
Age (years)	32.6±19.0	56.9±14.0	<0.001
Operative time (minutes)	138.5±43.5	151±34.5	NS
Intraoperative complications	2 (3.8%)	1 (4.2%)	NS, 0.9
Conversion	2 (3.8%)	2 (8.3%)	NS, 0.4
Mean ID* (cm)	13.7±3.2	18.1±5.8	<0.001
Massive splenomegaly ID* >20 cm	4 (7.6%)	9 (37.5%)	—

*ID=splenic interpole diameter.

Table 3.
Postoperative Data

Characteristics	Group I	Group II	P
Transfusions	2 (3.8%)	2 (8.3%)	NS, 0.4
Complications	3 (5.7%)	3 (12.5%)	NS, 0.3
Postoperative splenoportal vein thrombosis	2 (3.8%)	2 (8.3%)	NS, 0.4
Hospital stay (days)	5.5 (2-11)	5.9 (3-10)	NS, 0.3
Reoperations	1 (1.9%)	1 (4.1%)	NS, 0.1

on, one for hemoperitoneum (group I) and one for enteric fistula (group II). The last patient died of a pulmonary embolism 30 days after surgery.

Control of the main vessels was obtained either with clips (60%), stapler (30%) or Endoloop (Polypropylene or Vicryl) (10%). Drains were left in place in 15 patients (19.7%), 6 of them affected by malignancy. The reasons were marked perisplenic adhesions, perisplenic abscesses, and intraoperative bleeding. Drains were removed in all patients within 48 hours. The spleen was extracted through the umbilical port in case of an anterior approach and through the left subcostal port in case of a semilateral approach. An enlargement of the port site (3 cm to 4 cm) was necessary in 3 patients. A Pfannenstiel incision was used in 3 women (3.9%). To retrieve the spleen in 3 cases of massive splenomegaly, the hand-assisted technique was used, in 2 group II patients and 1 group I patient.

Twenty-eight patients had splenic ID <13 cm, and 35 patients had ID between 14 cm and 19 cm. Massive splenomegaly (ID >20 cm) was noticed in 13 (17%) patients (mean ID, 23 ± 4.1 cm). The operative time for these last patients was 176.6 ± 30.5 minutes with a mean hospital stay of 6.6 ± 3.9 days. Prevalence of massive splenomegaly was registered in group II (9 patients), 8 of them with NHL and one with hairy cell leukemia. Four patients from group I had massive splenomegaly (pancytopenia, Newmann-Pick disease, autoimmune hemolytic anemia, and Cooley disease).

Postoperative mortality was 1.3% (1 case in group II). Blood transfusion was necessary in 4 patients (5.2%), 2 from each group.

The incidence of accessory spleen in ITP/spherocytosis patients was 8.7% (2 of 23 patients). The accessory spleen was localized at the splenic hilum (1.5 cm in diameter) and in the great omentum (7 mm in diameter). Two other cases of accessory spleen were registered in 2 patients with NHL.

Histopathological results for group II are shown in **Table 4**.

Postoperative Splenoportal Thrombosis

The incidence of postoperative thrombosis of the splenoportal branch was routinely examined in the last 41 patients undergoing LS. Partial thrombosis was registered in 4 (9.7%) of the 41 patients examined, 2 from group I (3.8%) and 2 from group II (8.3%). Only 1 patient with splenoportal thrombosis (group II) had massive spleno-

Histological Findings	No.
Recurrence of lymphoma	14
Non-Hodgkin lymphoma	7
Hodgkin disease	1
Hair cells leukaemia	1
Myelofibrosis	1

megaly. All patients were asymptomatic, and all received low-weight molecular heparin 100 UI/kg twice for 45 days, with complete resolution at Doppler ultrasound examinations within 30 days.

Group I Outcomes (52 Patients)

Mean follow-up for benign diseases was 84 months (range, 24 to 126). One HIV-positive patient with splenomegaly died 4 years after surgery. Two of 7 patients with ITP did not have a significant increase in platelet count (<30000), even though scintigraphy excluded accessory spleen. All other patients with ITP, spherocytosis, and autoimmune hemolytic anemia are disease free. Patients with beta-thalassemia had certain improvement, with a delay in the interval between transfusions (from a mean of 11.1 days before intervention to 19.8 days after).

Group II Outcomes (24 Patients)

The mean follow-up was 54 months (range, 26 to 138). Three patients were lost to follow-up. One patient with acute myeloid leukemia died 60 days after surgery from hepatic failure due to progression of the disease. Three patients with NHD and 1 with HL died after a mean interval of 13.2 months, and 2 patients with NHL died 71 months after LS for disease progression. At last follow-up, 14 patients were disease free, while 3 patients had recurrences and are being treated.

DISCUSSION

Laparoscopic splenectomy is generally accepted as a safe procedure, and many authors consider LS the gold standard in the treatment of benign hematological diseases with normal spleen size.^{8,11,16} Many retrospective studies have demonstrated a reduction in postoperative pain, hospital stay, and costs compared with a historical group of open splenectomies, including adults and children with ITP.^{4,17} Missing accessory spleens is reported as a down-

side of the laparoscopic approach, especially in ITP. However, even if studies with long-term follow-up are lacking, LS seems to provide results similar to those of open splenectomy in terms of identification of the accessory spleens. Our results (8.3% in ITP, 5.2% in total) are comparable to the incidence described in larger series.^{9,18}

The analysis of the present series of 76 consecutive LS, performed in nonselected patients, confirms that the laparoscopic approach is feasible and safe both in malignant and benign hematological diseases. LS must be considered an advanced laparoscopic procedure with specific pitfalls (ie, organ manipulation, specimen removal) because the spleen is a friable organ, with a close relationship to other organs, such as the stomach, colon, and pancreas. In addition, it must be removed intact for pathological evaluation, in case malignant hematological disorders are suspected. On the other hand, patients may receive advantages from a laparoscopic approach, because these patients usually have co-morbidities.

LS can be carried out with very low morbidity and mortality rates, comparable to or lower than those of open splenectomy, after the learning curve period.^{19–21} In the present study, LS was completed in 94.7% of cases (conversion rate 5.3%) with an overall morbidity and mortality of 7.9% and 1.3%, respectively. The conversion rate was higher, although not statistically significant in cases of LS performed for malignant versus benign diseases. Furthermore, in the last 57 patients, only 1 conversion was required (NHD with massive splenomegaly, ID 22 cm).

No intraoperative complications were recorded in patients with splenomegaly. There was no significant difference in the hospital stay between the 2 groups. Operative time was longer in patients with malignant diseases than in patients with benign conditions, without reaching a statistically significant difference. It could be in part justified by the fact that subdiaphragmatic staging of lymphoma requires liver and lymph node biopsies and, at the same time, by the fact that spleen size was smaller in group I.

LS for massive splenomegaly and malignancy remains a controversial issue.^{11,12,22–24} Spleen size is considered the single most important condition affecting the conversion rate, operative time, and complication rate.²⁵ Some authors¹² consider massive splenomegaly as a relative contraindication to LS. Initial reports of LS in cases of splenomegaly showed higher operative complication rates and led to lower acceptance of laparoscopy in these patients. During the last few years, however, good results have been reported even in the presence of splenomegaly.^{9,23} Standardization of the technique, increasing experience,

and technical innovations have shown that an enlarged spleen can be managed successfully by laparoscopy. In a previous report of 57 patients,²⁶ the morbidity rate was higher in lymphoma patients than in patients with benign diseases. Standardization of the procedure has induced a significant reduction in operative time, conversion and complication rates.

Although one limit of the study is the different sample size of the 2 groups (52 vs 24), the comparative analysis did not show a significant statistical difference between malignant and benign diseases concerning conversion rate, postoperative hospital stay, and morbidity. No differences in morbidity were observed in patients with massive splenomegaly versus those with a normal size spleen, suggesting that splenomegaly is not a contraindication to laparoscopy.

Initially, we adopted an anterior approach, because we were more comfortable with it, especially during the learning curve. Afterwards, we started using the semilateral approach, which allows a quick dissection of the splenic attachments and safe management of the splenic hilum. In addition, in case of splenomegaly and malignancy, with hilar adenopathy and perisplenitis, the lateral or semilateral approach offers the advantages of gravity in medial retraction of the organ and limits the amount of tissue manipulation required.

During recent years in select cases, the hand-assisted procedure has gained increasing acceptance.^{27–29} We adopted the hand-assisted technique in cases of massive splenomegaly, following the evidence in the literature, for nontraumatic handling of the spleen, a “finger control” of bleeding, and rapid conversion if necessary.^{30,31}

Splenoportal thrombosis is a severe complication after splenectomy, described both after open and laparoscopic procedures,^{32,33} with an unknown true incidence.³³ Early recognition is of great importance for successful prompt anticoagulant therapy.^{33,34} From December 1998, we decided to apply a routine policy of ultrasound color Doppler examination of all patients undergoing LS to evaluate the real incidence of the splenoportal thrombosis in our patients. The incidence in the 41 patients studied was 9.7%, but all cases were asymptomatic. In this series, no characteristics identified preoperatively by ultrasound color Doppler of the splenic branches were correlated with the development of postoperative intraportal thrombosis. Postoperative ultrasound color Doppler examination allowed an early diagnosis, suggesting that it should be included in the routine postoperative management of

LS for hematological diseases for an early diagnosis and prompt initiation of anticoagulant therapy.

CONCLUSION

The results of the present study confirm that laparoscopy should be considered the preferential approach for splenectomy, even in patients with a diagnosis of malignant disease and splenomegaly. In experienced centers, LS may be considered safe and effective also in children with benign or malignant hematological diseases. The present series confirms that no specific condition can be considered an absolute contraindication to LS after the learning curve period.

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