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Laparoscopic Splenectomy and Azygoportal Disconnection: a Systematic Review

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ABSTRACT

Background and Objectives: Given the technical difficulty of laparoscopic splenectomy and azygoportal disconnection (LSD), data are limited that compare the laparoscopic to the open procedure. As the technique becomes more widespread, questions regarding its safety, feasibility, and reproducibility must be addressed. This review assesses the current status of LSD.

Methods: We conducted our literature review with a search of the PubMed database. All published series of 5 or more laparoscopic splenectomy and azygoportal disconnection procedures were examined. The demographic, intraoperative, and postoperative data analyzed included number of ports, conversion rate, operative duration, estimated intraoperative blood loss, postoperative hospital stay, and complications.

Results: Fifteen articles met the review criteria. Of 412 laparoscopic procedures, traditional laparoscopic splenectomy and azygoportal disconnection (TLSD) was used in 322 patients (78.2%), a modified laparoscopic procedure (MLSD) in 79 (19.2%), and a single-incision laparoscopic procedure (SLSD) in 11 (2.7%). Compared with the traditional and single-incision laparoscopic procedures, the MLSD procedure was associated with shorter operative duration and less blood loss. Furthermore, although the incidence of postoperative portal vein system thrombosis was higher in the laparoscopic than in the open splenectomy with azygoportal disconnection (OSD) procedure, the LSD procedure was associated with less pulmonary infection and pleural effusion and fewer incisional and overall complications than the open procedure. The rate of conversion to an open procedure was 5.4%.

Conclusions: LSD is feasible and safe for selected patients when performed by an expert laparoscopic surgeon. It has perioperative advantages over OSD, but studies with longer follow-up periods and larger samples of patients are needed.

Key Words: Azygoportal disconnection, Hypertension, Laparoscopy, Portal, Splenectomy.

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INTRODUCTION

Because of the high incidence of chronic hepatitis B and C infections worldwide, a large number of patients, especially in China, have portal hypertension secondary to liver cirrhosis. Hypersplenism and esophagogastric varices, which are common major complications of liver cirrhosis, occur in approximately 24–80% of cases, and the mortality rate is high.[1–3] Esophageal variceal hemorrhage is a major cause of death in patients with portal hypertension due to liver cirrhosis. Furthermore, more than 70% of individuals with portal hypertension and a history of variceal internal bleeding experience recurrent bleeding.[4,5] Complications of hypersplenism, including reductions in white blood cells, platelets, and hemoglobin (Hb), can result in bleeding, infection, and anemia.[6]

Liver transplantation has become the most effective treatment for many patients with liver cirrhosis and decompensated liver function. However, 2 major obstacles are organ shortages and high transplantation-related medical costs, especially in China.

The transjugular intrahepatic portosystemic shunt (TIPSS) procedure may be one option for chronic liver disease with decompensated liver function; however, hepatic dysfunction may progress after TIPSS with radical portal diversion, and the failure rate of TIPSS includes those due not only to stent blockage, which is reported to be as high as 30–80% 1 year after TIPSS,[7,8] but also to frequent clinically significant variceal hemorrhage[9] and portosystemic encephalopathy.

In 1964, Hassab described splenectomy with pericardial devascularization (Hassab procedure), which is now com-

monly used to treat patients with esophageal varices and hypersplenism.[10] The procedure plays an important role in the treatment of portal hypertension in China. Although its negative impact on liver function is relatively small, disadvantages of the Hassab procedure include a large surgical incision and significant morbidity.

Recent advances in laparoscopic techniques and devices have led to laparoscopic approaches that replace conventionally open abdominal surgery. In 1997, Hong et al[11] first reported laparoscopic splenectomy and azygoportal disconnection (LSD). Four techniques are currently used: modified (MLSD), traditional (TLSD), and single-incision (SLSD) LSD and open splenectomy with azygoportal disconnection (OSD). No comparative study of the 4 techniques has yet been performed. For this article, we reviewed the literature, to provide a comprehensive understanding of the current status of LSD, focusing on technical challenges, feasibility, and complications specific to minimally invasive approaches.

METHODS

Literature Review

We searched the PubMed database using the search string "splenectomy and esophagogastric devascularization," "splenectomy and azygoportal disconnection," "splenectomy and pericardial devascularization," or "splenectomy and gastroesophageal devascularization," along with the search term "laparoscopic." The beginning date of the search was not limited; the ending date was December 31, 2014. Eighteen relevant articles by 10 surgical teams were retrieved. Articles containing more than 5 LSD procedures were selected. In case of multiple publications by the same surgical team, to prevent data overlap when different variables were compared within group in each publication, only the more informative comparison was considered. Three articles were excluded from our analysis: a case report of 1 child[12] (our study focused on adults 18–80 years old); another case report[13] that addressed only 1 postoperative complication, gastric perforation, which was also mentioned in another article,[14]; and a third article that did not report LSD.[15]

In March 2007, Hong et al[11] reported 23 patients who had undergone LSD. In February 2008, Wang et al[16] reported 25 cases. In July 2009, Jiang et al[17] reported 28 cases in their controlled study. In February 2009, Zheng et al[18] reported 7 cases in their controlled study. In January 2012, Wang et al[19] reported 20 cases of LSD with intraoperative splenic blood salvage. In February 2013, Zheng et al[20] reported 24 cases in their controlled study. In January 2013, Zhao et al[21] reported 42 cases. In January 2013, Cheng et al[22] reported 80 cases in their controlled study. In June 2013, Jiang et al[23] reported 10 cases. In September 2013, Bai et al[24] reported 37 cases in their controlled study. In June 2014, Cheng et al[25] reported 204 cases. In July 2014, Jiang et al[26] reported 44 cases in their controlled study. In December 2014, Jiang et al[27] reported 79 cases in another controlled study, among them, 33 cases of LSD with intraoperative splenic blood salvage. Furthermore, in October 2014, Xu et al[28] reported 5 cases of single-incision laparoscopy and, in December 2012, Wu et al[29] reported 6 cases (**Table 1**).

All the retrieved studies that met the inclusion criteria were independently reviewed by 2 authors (GQJ and PC). The 2 reviewers discussed any differences until a consensus was achieved.

Tables 1–7 present the data obtained from each study: first author, publication date, number of patients, number of ports, energy device used for dissection, device used for splenic hilus sectioning, instrument used for spleen extraction, extraction site, size of spleen extraction site, use of autologous blood transfusion, use of drains, operative duration, estimated blood loss, number of blood transfusions, conversion rate, time to first flatus, time until out-of-bed activity, postoperative hospital stay, morbidity, and mortality.

Statistical Analysis

Data are presented as the mean ± SD, median, and range, or number and percentage; when applicable, a weighted average (WA) was calculated to show the statistical sum of the means for each variable.[30] The χ^2 or Fisher's exact test was used to compare categorical variables among groups, as appropriate. Student's unpaired t test was used to compare continuous variables. Differences reaching $P < 0.05$ were statistically significant. All statistical analyses were performed with SPSS for Windows, Version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Fifteen articles, including 412 patients who underwent LSD, were included in this review (**Figure 1**). The first series was published in 2007 and the second in 2008. Four articles, reporting 81 cases (15.4%), were published between January 1, 2007, and December 31, 2009; no articles were published between January 1, 2010, and December

Table 1.
PubMed Literature Review With Comparison of Related Parameters of LSD and OSD

First Author (Ref.)	Publication Year	Cases (n)	Ports (n)	Operative time	Blood Loss (mL)	Transfusions % (n)	Conversion Rate % (n)	First Flatus	Out-of-Bed Activity (days)	Postoperative Stay (days)	Perioperative Deaths
Jiang (27)[a]	2014	33	5	209 ± 54	158 ± 220	0	0	2.6 ± 0.9 (d)	2.4 ± 0.7	11.3 ± 2.3	0
Jiang (27)[b]		46	5	221 ± 57	179 ± 158	2	0	2.4 ± 0.9 (d)	2.6 ± 0.7	10.7 ± 2.6	0
Jiang (26)[c]	2014	44	5	210 (140–390)*	150 (50–800)*	NA	0	2.4 ± 1.0 (d)*	2.59 ± 0.69*	10 (7–18)*	0
Jiang (26)[d]		71	5	180 (110–300)	300 (50–1200)	NA	–	3.2 ± 1.0 (d)	5.96 ± 0.93	15 (7–28)	0
Cheng (25)[c]	2014	204	5	232 ± 59	189 ± 137	19.6 (40/204)	7.8 (16/204)	3.5 ± 0.9 (d)	NA	8.7 ± 2.2	0
Bai (24)[c]	2014	37	5	210 (140–390)*	150 (50–800)*	NA	0	2.4 ± 1.0 (d)*	2.7 ± 0.7*	10 (7–18)*	0
Bai (24)[d]		70	–	175 (110–300)	300 (50–1200)	NA	–	3.2 ± 1.0 (d)	5.9 ± 0.9	15 (7–28)	0
Jiang (23)[c]	2014	10	5	288 ± 54	240 ± 217	NA	0	NA	NA	11.3 ± 3.2	0
Cheng (22)[c]	2013	80	5	254 ± 65	191 ± 163*	20.0 (16/80)	11.3 (9/80)	89.9 ± 24.5 (h)*	NA	10.1 ± 2.5*	NA
Cheng (22)[d]		73	–	235 ± 69	241 ± 209	26.0 (19/73)	–	98.4 ± 28.8 (h)	NA	14.4 ± 3.5	NA
Zhao (21)[c]	2013	26	5	145 ± 25	146 ± 109	0	NA	NA	NA	11.7 ± 2.2	0
Zheng (20)[c]	2013	24	4	210 (140–360)	90 (30–300)*	NA	0	72 (36–127) (h)*	NA	NA	0
Zheng (20)[d]		30	–	190 (150–270)	350 (150–800)	NA	–	117 (71–210) (h)	NA	NA	0
Wang (19)[a]	2012	20	4	3.1 ± 0.3	70.5 ± 32.5	0	0	NA	NA	8.4 ± 2.2	0
Zheng (18)[c]	2009	7	4	180 (160)	100 (220)	NA	NA	NA	NA	12(53)	0
Zheng (18)[d]		17	–	190 (120)	400 (500)	NA	–	NA	NA	15(70)	0
Jiang (17)[c]	2009	26	4	235 ± 36*	200 ± 30*	23.08 (6/26)*	7.14 (2/26)	NA	NA	6.5 ± 2.3*	0
Jiang (17)[d]		26	–	178 ± 47	420 ± 50	38.46 (10/26)	–	NA	NA	11.7 ± 4.5	0
Wang (16)[c]	2008	25	4	4.1 (3.0–5.5) (h)	(100–400)	NA	1	NA	NA	(6–15)	0
Hong (11)[c]	2007	23	4	235 (180–350)	520 (200–1600)	NA	3	NA	NA	8.5 (6–17)	0
Xu (28)[c]	2014	6	1	265	300	NA	0	NA	NA	13	0
Wu (29)[c]	2013	5	1	252 (220–270)	290 (250–350)	NA	0	NA	NA	8.2(7–9)	0

Data are expressed as the mean ± SD or median (range). Operative time is in minutes, unless stated otherwise. NA, not available.

[a] Autologous blood transfusion laparoscopic group.

[b] Without autologous blood transfusion laparoscopic group.

[c] LSD group.

[d] OSD group.

*$P < .05$.

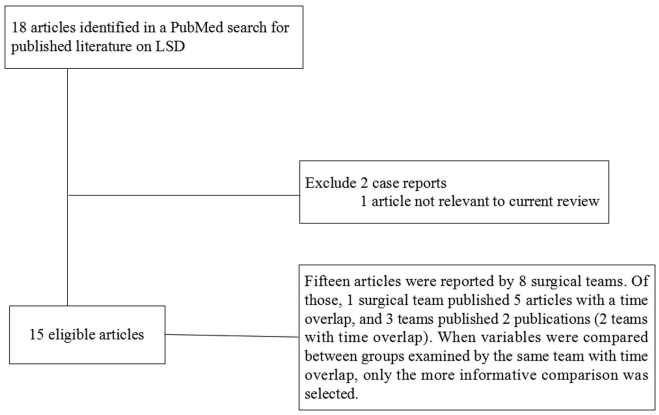

Figure 1. Flowchart showing selection of articles included in the review.

31, 2011; and 11 articles, reporting 444 cases (84.6%), were published between January 1, 2012, and December 31, 2014 (**Figure 2**). All LSD procedures were reported from institutions in China.

Surgical Techniques

Eleven patients (2.7%) underwent SLSD, 79 (19.2%) underwent MLSD, and 322 (78.2%) underwent TLSD (**Figure 3**). Since the first TLSD series was reported in 2007,[11] 5 surgical teams have reported on this technique. SLSD was first reported in 2013; since then, only 2 teams have reported using this technique. The first and only team to report MLSD published 4 articles in 2014 (**Table 1**).

All authors reported the use of ports (n = 412; 100%). Two teams (n = 283; 68.7%) reported the use of 5 ports, 3 teams (n = 92; 22.3%) reported the use of 4 ports, 1 team (n = 26; 6.3%) reported the use of 4 or 5 ports, and 2 teams (n = 11; 2.7%) reported the use of 1 port (**Table 1**).

Details on the device used for dissection were provided in all articles (n = 412 cases; 100%). In 4 surgical teams, a single device was used; in another 4 teams, 2 devices were used. The LigaSure Vessel Sealing device (Covidien, Minneapolis, Minnesota, USA) alone was used by 2 surgical teams (n = 85; 20.6%), and ultrasonic shears alone by 2 (n = 227; 55.1%). LigaSure (Covidien) and ultrasonic shears were used in combination by 4 teams (n = 100; 24.3%) (**Table 2**).

Details on the device used to divide the splenic hilum were provided in all articles (n = 412; 100%). A stapler alone was used by 5 teams (n = 179; 43.4%) and clips

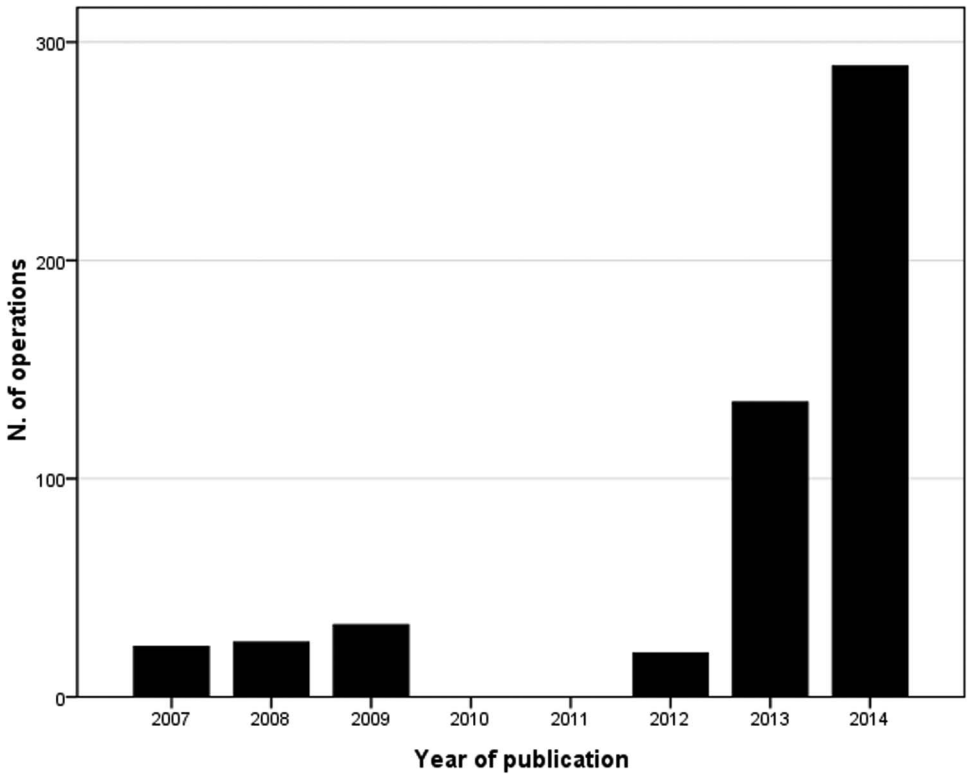

Figure 2. Number of operations in published studies by year.

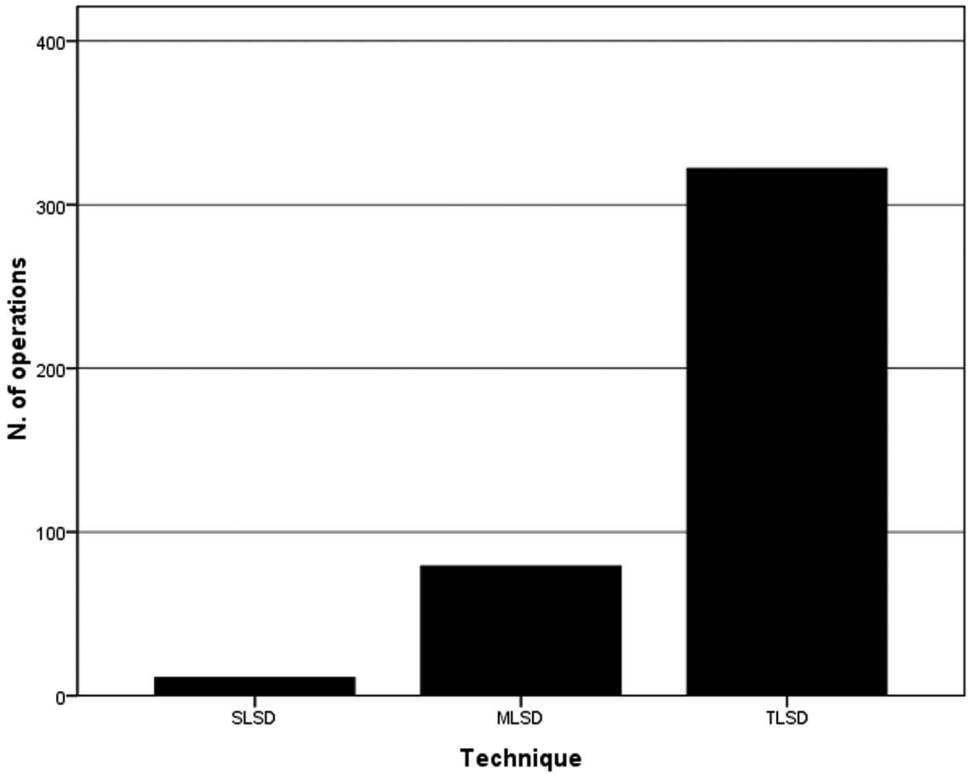

Figure 3. Number of LSD procedures by surgical technique.

alone by 1 team (n = 6; 1.5%). A stapler or cutter (n = 204; 49.5%) was used by 1 team, and a ligature or clip (n = 23; 5.6%) was used by 1 team (**Table 2**).

Details on spleen extraction site were provided by 7 teams (n = 389; 94.4%). In 5 teams (n = 378; 97.2%), the specimen was extracted through an incision in the left midclavicular line, halfway between the costal margin and the umbilicus. Specimens in SLSD (2 teams) were delivered through the single umbilical incision (n = 11; 2.8%) (**Table 2**).

Information on the instrument used to extract the spleen was available in all articles (n = 412; 100%). Seven teams extracted the spleen by using a large specimen bag (n = 333; 80.8%). Only in the MLSD team (n = 79; 19.2%) was the spleen specimen extracted by an electromechanical morcellator (**Table 2**).

Information on the size of the spleen extraction site was available from 3 teams (n = 90; 21.8%). Two SLSD teams reported that the sizes were 2 cm (n = 6; 6.7%) and 3 cm (n = 5; 5.6%). The MLSD team reported that the size was only 1.2 cm (n = 79; 87.8%) (**Table 2**).

Information on autologous blood transfusion was available from 4 teams (n = 84; 20.4%) (**Table 2**). Information on the use of drains was provided by only 7 teams (n = 45; 10.9%), but only Wang et al (n = 65; 8.9%) reported routinely avoiding the use of drains (**Table 2**).[16]

Outcomes

Conversion to Laparotomy

Information on conversion to open surgery was reported by 8 teams (n = 412; 100%). Overall, 22 LSD procedures were converted to open surgery. Wang et al[16] did not provide the reason for their single conversion, but reasons for the other 21 conversion were severe inflammation or dense adhesions around the spleen that hindered separation (n = 7; 33.3%) and uncontrollable bleeding at the surgical site (n = 14; 66.7%).

Massive, uncontrollable intraoperative bleeding is extremely dangerous and is the primary reason for conversion to laparotomy. Given the thrombocytopenia, massive splenomegaly, poor liver function, coagulopathy, and multiple collateral vessels in patients with liver cirrhosis, prevention and alleviation of bleeding and reducing the rate of conversion are challenging. Adequate preparation involves preoperative adjustment of coagulation function,

Table 2.
Technical Details of LSD Reported in the Literature

First Author (Ref.)	Energy Device	Device for Sectioning Splenic Hilus	Extraction Site	Instrument for Extracting Spleen	Size of Site (cm)	Autologous Blood Transfusion	Drains
Jiang (27)[a]	LigaSure	Stapler	Left midclavicular line	Electromechanical morcellator	1.2	Yes	Yes
Jiang (27)[b]	LigaSure	Stapler	Left midclavicular line	Electromechanical morcellator	1.2	No	Yes
Jiang (26)[c]	LigaSure	Stapler	Left midclavicular line	Electromechanical morcellator	1.2	No	Yes
Cheng (25)[c]	Ultrasonic shear	Cutter or Stapler	Left midclavicular line	Bag	NA	No	Yes
Bai (24)[c]	LigaSure	Stapler	Left midclavicular line	Electromechanical morcellator	1.2	No	Yes
Jiang (23)[c]	LigaSure	Stapler	Left midclavicular line	Electromechanical morcellator	1.2	No	Yes
Cheng (22)[c]	Ultrasonic shear	Cutter or Stapler	Left midclavicular line	Bag	NA	No	Yes
Zhao (21)[c]	LigaSure	Stapler	Left midclavicular line	Bag	NA	Yes	Yes
Zheng (20)[c]	LigaSure or ultrasonic shear	Stapler	Left midclavicular line	Bag	NA	No	Yes
Wang (19)[a]	LigaSure or ultrasonic shear	Stapler	NA	Bag	NA	Yes	NA
Zheng (18)[c]	LigaSure or ultrasonic shear	Stapler	Left midclavicular line	Bag	NA	No	Yes
Jiang (17)[c]	LigaSure or ultrasonic shear	Stapler	NA	Bag	NA	No	NA
Wang (16)[c]	LigaSure or ultrasonic shear	Stapler	Left axillary line	Bag	NA	No	No
Hong (11)[c]	Ultrasonic shear	Ligature or clips	NA	Bag	NA	No	Yes
Xu (28)[c]	LigaSure	Clips	Umbilicus	Bag	2.0	Yes	Yes
Wu (29)[c]	LigaSure or ultrasonic shear	Stapler	Umbilicus	Bag	3.0	No	Yes

NA, not available.

[a] Autologous blood transfusion laparoscopic group.

[b] Without autologous blood transfusion laparoscopic group.

[c] LSD group.

[d] OSD group.

appropriate platelet supplementation, and a high level of technical skill of the surgical team. The ability to control bleeding and the speed with which hemostasis is achieved depend on the laparoscopic skills of the surgeon and first assistant and on their cooperation with each other. To some extent, accurate and rapid cooperation determine the rate of conversion. Furthermore, intraoperative cell salvage and autologous blood transfusion may also decrease the rate of conversion because of preservation of blood volume and increased self-confidence of the surgeon with the use of an autologous blood-recovery system. To date, none of our 65 MLSD procedures with

autologous blood transfusion has required conversion to an open procedure.

Data on intra- and postoperative outcome variables are presented in **Tables 1** and **3**.

Operative Time

The mean operative duration of OSD was reported by 4 teams (n = 200; 100%; WA 201.3 minutes) (**Table 4**). The mean operative time of LSD was reported by all teams (n = 412; 100%); WA was 221.7 min. Mean operative durations of MLSD, TLSD, and SLSD were reported by 1 (n = 79; 100%; WA 216.0 minutes), 5 (n = 322; 100%; WA 221.8 minutes) and 2 (n = 11; 100%; WA 259.1 minutes) teams, respectively (**Table 5**).

Intraoperative Blood Loss

Estimated mean volume of intraoperative blood loss for LSD was reported by all but 1 team (Wang et al,[16] who did not report the mean volume) (n = 387; 93.9%), with a WA of 192.7 mL (**Table 4**). Specifically, mean blood loss for MLSD, TLSD, and SLSD was reported by 1 (n = 79; 100%; WA 170.2 mL), 5 (n = 297; 92.2%; WA 194.9 mL), and 2 (n = 11; 100%; WA 295.5 mL) teams, respectively. Mean estimated operative blood loss for OSD was reported by 4 teams (n = 200; 100%), with a WA of 301.6 mL (**Table 5**).

Postoperative Hospital Stay

The mean length of postoperative hospital stay was reported by 7 teams (n = 370; 89.8%; WA 9.5 d). Mean hospital stay for MLSD, TLSD, and SLSD were reported by 1 (n = 79; 100%; WA 11.0 d), 4 (n = 280; 87.0%; WA 9.0 d) and 2 (n = 11; 100%; WA 10.8 d) teams, respectively. Mean length stay for OSD was reported by 4 teams (n = 187; 93.5%) (**Table 4**), with a WA of 14.3 d (**Table 5**).

Postoperative Complications

Six teams (n = 401; 97.3%) provided information on incidence of postoperative complications of LSD. Morbidity ranged between 12.1 and 56.3%. In all, 123 postoperative complications were reported, for a total morbidity rate of 29.9%. Complications of OSD were reported by 4 teams (n = 200; 100%). Morbidity ranged between 33.3 and 79.5%. In all, 91 postoperative complications were reported for OSD, for a morbidity rate of 45.5% (**Table 6**).

Portal Venous System Thrombosis

Data on portal venous system thrombosis (PVST) associated with LSD were reported by 3 teams (n = 309; 75%). The incidence of PVST ranged between 3.8 and 38.2% (n = 87; 28.1%). PVST associated with OSD was reported by 3 teams (n = 170; 85%), with an incidence between 0 and 30.1%. PVST developed in 30 patients with OSD, for an incidence of OSD-associated PVST of 17.6% (**Table 6**).

Gastric Perforation

Data on gastric perforation during LSD were reported by 6 teams (n = 417; 97.4%). Two patients experienced gastric perforation. Information on gastric perforation during OSD was reported by 4 teams (n = 200; 100%). One patient who underwent OSD experienced gastric perforation (**Table 6**).

Gastric perforations were mainly due to thermal injury from harmonic shears and healed in approximately 2 months, with sufficient abdominal drainage.[18,20] Gastric perforation is a rare complication of LSD. However, if abdominal drainage is insufficient, it may be life-threatening for a patient with liver cirrhosis. It can be avoided by proper attention to surgical technique.[24]

Pancreatic Fistula

Information on pancreatic fistula in LSD, although not always recorded according to standardized methodology, was reported by 3 teams (n = 309; 75%). Incidence ranged between 0.9 and 3.8%. Overall, pancreatic fistula developed in 5 patients who underwent LSD. Pancreatic fistula in OSD was reported by 3 teams (n = 170; 85%). The incidence ranged between 0 and 2.7%. Three patients who had OSD had pancreatic fistula (**Table 6**).

Pancreatic fistula is most often caused by a massively enlarged spleen. The more enlarged the spleen, the more difficult it is to separate the tail of the pancreas from it, but one aspect of the situation that can be controlled is avoiding, as much as possible, injuring the tail of the pancreas. Because the tail of the pancreas can be easily scratched by forceps, pushing aside the tail pancreas with unopened forceps can protect the pancreas and decrease the rate of pancreatic fistula.

Pulmonary Infection

Information on LSD-associated pulmonary infection was reported by 6 teams (n = 333; 77.8%). Pulmonary infection developed in 3 patients who underwent LSD. Information on OSD-related pulmonary infection was reported by 4 teams (n = 200; 100%). Thirteen OSD patients had a pulmonary infection (**Table 6**).

Pleural Effusion

Data on pleural effusion with LSD were reported by 4 teams (n = 273; 63.8%). In 12 LSD cases, the patients had

Table 3.
Complications of LSD and OSD

First Author (Ref.)	Cases (n)	Complications % (n)	PVST % (n)	Gastric perforation (n)	Pancreatic fistula (n)	Refractory ascites (n)	Abdominal infection (n)	pulmonary infection (n)	Pleural effusion (n)	Incision complications (n)	Follow-up time (months)	EGVB % (n)	Encephalopathy
Jiang (27)[a]	33	12.1 (4/33)	9.1 (3/33)	0	1	NA	0	0	NA	0	NA	NA	NA
Jiang (27)[b]	46	13.0 (6/46)	10.9 (5/46)	0	1	NA	0	0	NA	0	NA	NA	NA
Jiang (26)[c]	44	15.9 (7/44)*	11.4 (5/44)	0	2	NA	0	0	NA	0*	NA	NA	NA
Jiang (26)[d]	71	36.6 (26/71)	11.3 (8/71)	0	1	NA	2	3	NA	9	NA	NA	NA
Cheng (25)[c]	204	49 (100/204)	38.2 (78/204)	0	1	5	0	3	5	NA	2–65	3.7 (7/189)Tc1.1 (2/189)	
Bai (24)[c]	37	13.5 (5/37)*	10.8 4/37)	0	1	NA	0	0	NA	0*	NA	NA	NA
Bai (24)[d]	70	35.7 (25/70)	10.0 (7/70)	0	1	NA	2	3	NA	9	NA	NA	NA
Jiang (23)[c]	10	NA	NA	NA	NA	NA	NA	NA	NA	NA	3.5	0	0
Cheng (22)[c]	80	56.3 (45/80)*	50.0 (40/80)*	0	1	3	0	2	4	0	2–50	6.3 (5/80	1 (1.3)
Cheng (22)[d]	73	79.5 (58/73)	30.1 (22/73)	1	2	4	1	6	12	2	2–50	8.2 (6/73)	0
Zhao (21)[c]	42	14.3 (6/42)	0	1	NA	5	NA	NA	NA	NA	26 (2–46)	2	1
Zheng (20)[c]	24	16.7 (4/24)	NA	1	NA	2	NA	0	NA	0	3–36	0	0
Zheng (20)[d]	30	33.3 (10/30)	NA	0	NA	5	NA	2	NA	3	3–36	0	0
Wang (19)[a]	20	10.0 (2/20)	NA	0	NA	NA	NA	NA	2	NA	18.0 ± 9.0	0	0
Zheng (18)[c]	7	14.3 (1/7)	NA	1	NA	0	NA	0	NA	NA	NA	NA	NA
Zheng (18)[d]	17	23.5 (4/17)	NA	0	NA	3	NA	1	NA	NA	NA	NA	NA
Jiang (17)[c]	26	19.2 (5/26)*	3.8 (1/26)	0	1	NA	NA	0	2	1	1–34	0	0
Jiang (17)[d]	26	42.3 (11/26)	0	0	0	NA	NA	2	1	5	1–34	0	0
Wang (16)[c]	25	NA	NA	0	NA	NA	NA	NA	NA	NA	3–60	0	0
Hong (11)[c]	23	30.4 (7/23)	NA	0	NA	2	1	NA	3	1	9	0	NA
Xu (28)[c]	6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Wu (29)[c]	5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA, not available.

[a] Autologous blood transfusion laparoscopic group

[b] Without autologous blood transfusion laparoscopic group.

[c] LSD group.

[d] OSD group.

Table 4.
Comparison of Outcomes Between LSD and OSD

Outcome	LSD	OSD	P
WA of operative time (min)	221.7 (412)	201.3 (200)	<.001
WA of blood loss (mL)	192.7 (387)	301.6 (200)	<.001
WA of hospital stay (days)	9.5 (375)	14.3 (187)	<.001

Data are WA (n).

a postoperative pulmonary infection. Information on pleural effusion with OSD was reported by 2 teams (n = 99; 23.1%). Thirteen patients who underwent OSD had a pulmonary infection (**Table 6**).

Incisional Complications

Information on incisional complications associated with LSD was reported by 4 teams (n = 228; 53.3%). Compared with 19 incisional complications in 200 cases of OSD, there were 2 incisional complications in 228 cases of LSD, suggesting an advantage of LSD over OSD with regard to incision healing ($P < .001$) (**Table 6**).

Incisional complications involve incisional hernia, superficial incisional infections, and deep incisional infections. MLSD, requiring even smaller incisions, does not require enlargement of any incision to extract the enlarged spleen. For this reason, MLSD leads only rarely to postoperative abdominal pain and ensures better incisional cosmesis and fewer incisional complications. In the present review, no incisional complications were reported in the 79 patients who underwent MLSD.

DISCUSSION

The evolution of LSD, according to the studies reported, comprises 3 stages. The first stage was laparoscopic splenectomy (LS) for hematologic spleen. LS was first described in 1991. Since then, many surgeons have performed LS in patients with a normal-sized spleen who have hematologic disorders —mainly, idiopathic thrombocytopenic purpura.[31–36] During the second stage, LS for splenomegaly due to liver cirrhosis was developed and became widely accepted. Splenomegaly was initially a contraindication for LS[37]; however, experienced surgeons with exceptional laparoscopic skill performed LS successfully to treat splenomegaly secondary to liver cirrhosis. For the most part, however, LS in patients with liver cirrhosis remains technically challenging and a hand-assisted procedure is employed by some surgeons. The third stage saw the development of LSD for patients with liver cirrhosis who had portal hypertensive bleeding and hypersplenism, with thrombocytopenia, massive splenomegaly, poor liver function, impaired coagulation factors, and multiple collateral vessels.[38,39] Traditional OSD is often associated with high risk. As the technology of LS for splenomegaly secondary to liver cirrhosis has matured, TLSD has gradually developed and become more accepted as a treatment for patients with cirrhosis, bleeding portal hypertension, and secondary hypersplenism. Similarly, early in the third stage, a hand-assisted procedure was put to use.[40] A variety of surgical techniques are currently used to extract the spleen during LSD, including cumbersome intracorporeal bags to withdraw massively enlarged spleens, creation of enlarged incisions to morcellate and withdraw splenic tissue, and hand-assisted laparoscopy.[11,16–20,40–43] The year 2012 saw the introduction of an MLSD technique that greatly reduces impairments,[23,24,26,27] in which a massively enlarged spleen is removed from the abdominal cavity through the existing incision using an electromechanical morcellator. MLSD is an even less invasive laparoscopic technique that will extend the advantages of laparoscopic surgery to patients likely to benefit the most: those with cirrhosis with bleeding portal hypertension and hypersplenism. Recently, SLSD was reported by 2 surgical teams, 1 performing 5 and 1 performing 6 procedures. No perioperative complications were recorded, perhaps because of small sample sizes. Surgeons must possess considerable laparoscopic skill to perform SLSD because of the challenge of the unavoidable contact between instruments.

Robotic surgery may develop into a fourth stage. Currently, there is no report of robotic splenectomy and azygoportal disconnection (RSD), but Giza et al[44] reported on robotic splenectomy in 2014, demonstrating that a robotic system is beneficial in difficult splenectomies, particularly where there is hypersplenism secondary to liver cirrhosis. Given the difficulty and risk of surgery in patients with cirrhosis, portal hypertensive bleeding, and secondary hypersplenism, RSD should provide some geneogenous advantages over LSD, as well as benefits in cosmesis and pain reduction, among others.

Comparison with Traditional Open Surgery

Compared with traditional open surgery, the minimally invasive nature of laparoscopic surgery makes it feasible, effective, and safe and results in less pain, fewer complications, and more rapid recovery.[45–47]

Table 5.
Comparison of Perioperative Variables Among the 4 Surgical Techniques

Variable	MLSD	TLSD	SLSD	OSD	*P*					
					MLSD vs TLSD	MLSD vs SLSD	MLSD vs OSD	TLSD vs SLSD	TLSD vs OSD	SLSD vs OSD
WA of operative time (min)	216.0 (79)	221.8 (322)	259.1 (11)	201.3 (200)	<.001	<.001	<.001	<.001	<.001	<.001
WA of blood loss (mL)	170.2 (79)	194.9 (297)	295.5 (11)	301.6 (200)	<.001	<.001	<.001	<.001	<.001	.175
WA of hospital stay (days)	11.0 (79)	9.0 (280)	10.8 (11)	14.3 (187)	<.001	.865	<.001	.039	<.001	.001

Data are WA (n).

Table 6.
Perioperative Complications of LSD and OSD Procedures Reported in the Literature

Complication	Cases (n)	LSD (%)	Cases (n)	OSD (%)	*P*
PVST	87/309	24.3	30/170	17.6	.010
Gastric perforation	2/417	0.4	1/200	0.5	.99
Pancreatic fistula	5/309	1.6	3/170	1.8	.99
Refractory ascites	12/216	5.6	9/103	8.7	.284
Abdominal infection	1/306	0.3	3/144	2.1	.189
Pulmonary infection	3/333	0.9	13/200	6.5	<.001
Pleural effusion	12/273	4.4	13/99	13.1	.003
Incision complications	2/228	0.9	19/200	9.5	<.001
Total complications	123/412	29.9	91/200	45.5	<.001

Surgical trauma results in the activation of inflammatory and systemic immunologic responses, a process called surgical stress. Acute inflammatory responses are switched on by direct tissue trauma, such as incision, dissection, organ manipulation, and vascular compromise.[48–51] Laparoscopic surgery, with its minimal manipulation of organs, as well as smaller surgical incisions, is thought to create less severe systemic immune and inflammatory responses than traditional open surgery.

Other types of laparoscopic surgical techniques have shown immunologic advantages over traditional open surgery,[48,50,52] including lower concentrations of interleukin-6 and C-reactive protein.[53–56]

In 2012, we developed MLSD, a new technique that greatly reduces impairments.[23,24,26,27] To date, we have performed MLSD in more than 100 patients with liver cirrhosis, portal hypertensive bleeding, and secondary hypersplenism. To the best of our knowledge, ours was the first report of the use of an electromechanical morcellator to draw a massive amount of splenic tissue completely from the abdominal cavity during LSD.[23] Our study suggested that, compared with OSD, MLSD is associated, not only with the above-mentioned advantages, but also with many other advantages, including better liver and renal function,[26] lower inflammatory immune responses with fewer postoperative days of elevated temperature (>38.0°C), lower white blood cell counts,[24] and lower concentrations of C-reactive protein, interleukin-6,-and procalcitonin.[26]

As demonstrated by this review, the WA of the operative duration of LSD was longer than that of OSD. However, volume of estimated blood loss was less, and hospital stay was shorter, in LSD than in OSD (both $P < .05$) (**Table 4**). Among the 3 LSD techniques, MLSD is associated with shorter operative duration and less estimated blood loss than either TLSD ($P < .05$) or SLSD ($P < .05$) (**Table 5**).

Complications

Two studies[18,22] reported that there was no significant difference in perioperative complications between LSD and OSD, whereas others[17,20,24,26,27] reported lower complication rates for LSD.

Three things may explain these conflicting results: first, inconsistent inclusion criteria with regard to definitions of

Table 7.
Intraoperative Autologous Blood Transfusion

First Author (Ref.)	Cases (n)	Preoperative Hb (g/L)	Postoperative Hb (g/L)	*P*
Jiang (33)[a]	33	107.0 ± 15.4	118.5 ± 15.8[C]	<.05
Jiang (33)[b]	46	112.5 ± 15.2	102.7 ± 15.6	<.05
Wang (22)[a]	20	93 ± 8	115 ± 11[C]	<.01
Wang (22)[b]	20	95 ± 10	92 ± 9	>.05

[a]Autologous blood transfusion LSD group.

[b] Without autologous blood transfusion LSD group.

[c] *a* vs. *b*; $P < .05$.

complications by different studies; second, surgical teams with various levels of technical skill in performing laparoscopic procedures; and finally, small sample sizes of the studies.

Many studies[17,18,20,22,24,26,27] have demonstrated that the short-term effects, including smaller volumes of both estimated intraoperative blood loss and intraoperative blood transfusion; less postoperative pain; shorter times to first oral intake, earlier passage of flatus and time until out-of-bed activity; shorter postoperative hospital stay; and lower rates of incisional complications, were better for LSD than for OSD. The medium-term effects, including esophagogastric variceal rebleeding, encephalopathy, secondary liver cancer, and death, during a follow-up of 2–50 months did not differ significantly between the 2 surgical procedures.[22]

The present review found rates of gastric perforation, pancreatic fistula, and refractory ascites to be similar between LSD and OSD, but found the PVST rate to be higher for LSD than for OSD. However, rates of pulmonary infection, pleural effusion, incisional complications, and all other complications were all lower for LSD than for OSD (**Table 6**).

Portal Vein System Thrombosis

PVST is a common and potentially life-threatening complication of splenectomy.[57,58] Severe PVST (Yerdel grade IV) can lead to aggravated portal hypertension, recurrent esophagogastric variceal bleeding, fatal bowel ischemia, or intestinal infarction,[59] and can significantly reduce a patient's life expectancy.[60] It is noteworthy that PVST is a more frequent complication of LS than of OS[61]; similarly, more patients experience PVST after LSD than after OSD,[22] but PVST may be the only disadvantage of LSD among many medium- and long-term results. The mechanism of the higher rate of PVST in LSD is not yet clear. The CO_2 used to create pneumoperitoneum and the intra-abdominal pressure produced by pneumoperitoneum, may be contributors to PVST. LSD differs from OSD in that, during LSD, the splenic hilar vessels are divided with an endoscopic vascular stapler, and perisplenic ligaments and azygoportal disconnection are accomplished mainly with the LigaSure device (Covidien) or harmonic shears. The effects of these processes on vessels and tissues may be causes of PVST. Ikeda et al[61] showed that the incidence of PVST in patients with cirrhosis and portal hypertension was significantly higher in those who received LS (12/22, 55%) than in those who underwent OS (4/21, 19%). Cheng et al[22] found that PVST occurred more frequently after LSD (40/80, 50%) than after OSD (22/73, 30.1%).

In terms of prevention, the routine use of aspirin and dipyridamole has not been shown to reduce the incidence of PVST. The use of postoperative prophylaxis, such as heparin for high-risk patients, has been recommended.[62,63]

It is possible that the lack of heparin use in many studies contributed to the high incidence of PVST. A small randomized controlled trial[64] evaluated the safety and efficacy of enoxaparin, a low-molecular-weight heparin, in preventing PVST in patients with advanced cirrhosis. A 12-month course of enoxaparin 4000 IU/d was demonstrated to be safe and effective in preventing PVST in patients with advanced cirrhosis, and it appeared to delay the occurrence of hepatic decompensation and to improve survival.

Enoxaparin may also be effective in preventing postoperative PVST after LS or LSD. Compliance may be an issue, however, as subcutaneous injection of enoxaparin over a long period is not well tolerated by some patients. We believe the administration of oral vitamin K antagonists

may be another effective way to prevent and treat postoperative PVST. We have conducted a small randomized controlled trial to determine whether warfarin anticoagulation is safe and effective in preventing PVST after MLSD in patients with liver cirrhosis (ClinicalTrials.gov ID: NCT02247414). More prospective studies are needed to investigate how to decrease the incidence of PVST after LSD or LS.

Autologous Blood Transfusion

Since 2013, Jiang et al[27] have used intraoperative cell salvage and autologous blood transfusion during MLSD to minimize intraoperative blood loss, exploit the large volume of blood sequestered in the enlarged spleen, and decrease the need for allogeneic blood transfusion. Before the publication of that report, only 1 other study had examined the use of intraoperative splenic blood salvage during LSD, reporting that cell salvage significantly increased postoperative Hb concentration and minimized the risks and complications of perioperative allogeneic transfusion.[19] There are important differences between these 2 studies, however. In the study by Wang et al,[19] the blood sequestered in the enlarged spleen was not salvaged until the end of the operation, and intraoperative blood was not collected; in our study, both the blood sequestered in the enlarged spleen and intraoperative blood were collected, and splenic blood was salvaged on 2 different occasions. After laparoscopic mobilization of the spleen and disconnection of the hilus lienis vessels, sequestered blood released from the spleen was collected from the left subphrenic space. This method avoiding clot formation within the spleen allows sequestered blood to be collected earlier and the volume maximized. After morcellation and extraction of the entire spleen, a small quantity of blood released from splenic tissue was also collected.

Our study found that a significant increase in Hb concentration (11.2 ± 4.8 g/L; $P < .05$) was observed in those receiving salvaged autologous blood before surgery to postoperative day 1, and that a significant decrease (9.8 ± 6.45 g/L; $P < .05$) was observed in the group without cell salvage during the same time frame. Preoperative Hb concentrations were similar between groups with and without autologous blood transfusion, but Hb concentration on postoperative day 1 was significantly higher in the autologous blood transfusion group (**Table 7**). Furthermore, autologous blood transfusion was associated with a postoperative body temperature within the normal range.[27]

Because of its many advantages, MLSD with intraoperative cell salvage and autologous blood transfusion may become the gold standard for treating patients who have cirrhosis with portal hypertensive bleeding and secondary hypersplenism.

CONCLUSION

LSD is feasible and safe, with lower mortality and complication rates than OSD. The major drawback of all reviewed series examining LSD was the small number of cases and limited follow-up, which do not permit strong conclusions to be drawn. Specifically designed prospective studies with much larger cohorts, including randomized comparisons with open procedures, should be performed.

References:

1. Schiedermaier P. Splanchnic hemodynamics: cirrhotic versus non-cirrhotic portal hypertension. *J Gastroenterol Hepatol.* 2004;19:S150–S154.

2. Hong WD, Zhu QH, Huang ZM, et al. Predictors of esophageal varices in patients with HBV-related cirrhosis: a retrospective study. *BMC Gastroenterol.* 2009;9:11.

3. Jensen DM. Endoscopic screening for varices in cirrhosis: findings, implications, and outcomes. *Gastroenterology.* 2002; 122:162–1630.

4. Grace ND, Groszmann RJ, Garcia-Tsao G, et al. Portal hypertension and variceal bleeding: an AASLD single topic symposium. *Hepatology.* 1998;28:86–880.

5. Gotoh Y, Iwakiri R, Sakata Y, et al. Evaluation of endoscopic variceal ligation in prophylactic therapy for bleeding of oesophageal varices: a prospective controlled trial compared with endoscopic injection sclerotherapy. *J Gastroenterol Hepatol.* 1999; 14:241–244.

6. Sibulesky L, Nguyen JH, Paz-Fumagalli R, Taner CB, Dickson RC. Treatment modalities for hypersplenism in liver transplant recipients with recurrent hepatitis C. *World J Gastroenterol.* 2009; 15:5010–5013.

7. LaBerge JM, Somberg KA, Lake JR, et al. Two-year out-come following transjugular intrahepatic portosystemic shunt for variceal bleeding: results in 90 patients. *Gastroenterology.* 1995; 108:1143–1151.

8. Casado M, Bosch J, Garciaa-Pagan JC, et al. Clinical events after transjugular intrahepatic portosystemic shunt: correlation with hemodynamic findings. *Gastroenterology.* 1998;114:1296–1303.

9. Sanyal AJ, Freedman AM, Luketic VA, et al. The natural history of portal hypertension after transjugular intrahepatic portosystemic shunts. *Gastroenterology.* 1997;112:889–898.

10. Liu N, Liu B, Xu RY, Fang HP, Deng MH. Splenectomy with endoscopic variceal ligation is superior to splenectomy with pericardial devascularization in treatment of portalhy pertension. *World J Gastroenterol*. 2006;12:7375–7379.

11. Hong DF, Zheng XY, Peng SY, Gao M, Wu JG, Cao Q. Laparoscopic splenectomy and pericardial devascularization for treatment of portal hypertension due to liver cirrhosis. *Zhonghua Yi Xue Za Zhi*. 2007;87:820–822.

12. Vasilescu C, Stanciulea O, Popa M, Colita A, Arion C. Subtotal laparoscopic splenectomy and esophagogastric devascularization for the thrombocytopenia because of portal cavernoma–case report. *J Pediatr Surg*. 2008;43:1373–1375.

13. Zheng X, Yao Y, Liu Q. Gastric perforation after laparoscopic splenectomy and esophagogastric devascularization for portal hypertension: report of a case. *Surg Laparosc Endosc Percutan Tech*. 2011;21:e209–212.

14. Zheng X, Liu Q, Yao Y. Laparoscopic Splenectomy and Esophagogastric Devascularization Is a Safe, *Effective, Minimally Invasive Alternative for the Treatment of Portal Hypertension With Refractory Variceal Bleeding Surg Innov*. 2013;20:32–39.

15. Zhou J, Wu Z, Wu J, Peng B, Wang X, Wang M. Laparoscopic splenectomy plus preoperative endoscopic variceal ligation versus splenectomywith pericardial devascularization (Hassab's operation) for control of severe varices due to portal hypertension. *Surg Endosc*. 2013;27:4371–4377.

16. Wang YD, Ye H, Ye ZY, et al. Laparoscopic splenectomy and azygoportal disconnection for bleeding varices with hypersplenism. *J Laparoendosc Adv Surg Tech A*. 2008;18:37–41.

17. Jiang XZ, Zhao SY, Luo H, et al. Laparoscopic and open splenectomy and azygoportal disconnection for portal hypertension. *World J Gastroenterol*. 2009;15:3421–3425.

18. Zheng X, Liu Q, Yao Y. Total laparoscopic versus open splenectomy and esophagogastric devascularization in the management of portal hypertension: a comparative study. *Dig Surg* 2009;26:499–505.

19. Wang Y, Ji Y, Zhu Y, Xie Z, Zhan X. Laparoscopic splenectomy and azygoportal disconnection with intraoperative splenic blood salvage. *Surg Endosc*. 2012;26:2195–2201.

20. Zheng X, Liu Q, Yao Y. Laparoscopic splenectomy and esophagogastric devascularization is a safe, effective, minimally invasive alternative for the treatment of portal hypertension with refractory variceal bleeding. *Surg Innov*. 2013;20:32–39.

21. Zhao S, Lv T, Gong G, Wang C, Huang B, Zhou W. Outcome of laparoscopic splenectomy with sandwich treatment including pericardial devascularization and limited portacaval shunt for portal hypertension due to liver cirrhosis. *J Laparoendosc Adv Surg Tech A*. 2013;23:43–47.

22. Cheng Z, Li J-W, Chen J, et al. Laparoscopic versus open splenectomy and esophagogastric devascularization for bleeding varices or severe hypersplenism: a comparative study. *J Gastrointest Surg*. 2013;17:654–659.

23. Jiang G, Qian J, Yao J, Wang X, Jin S, Bai D. A new technique for laparoscopic splenectomy and azygoportal disconnection. *Surg Innov*. 2014;21:256–262.

24. Bai DS, Qian JJ, Chen P, et al. Modified laparoscopic and open splenectomy and azygoportal disconnection for portal hypertension. *Surg Endosc*. 2014;28:257–264.

25. Cheng Z, Li JW, Chen J, Fan YD, Guo P, Zheng SG. Therapeutic effects of laparoscopic splenectomy and esophagogastric devascularization on liver cirrhosis and portal hypertension in 204 cases. *J Laparoendosc Adv Surg Tech A*. 2014;24:612–616.

26. Jiang GQ, Chen P, Qian JJ, et al. Perioperative advantages of modified laparoscopic vs open splenectomy and azygoportal disconnection. *World J Gastroenterol*. 2014;20:9146–9153.

27. Jiang GQ, Bai DS, Chen P, et al. Modified laparoscopic splenectomy and azygoportal disconnection combined with cell salvage is feasible and might reduce the need for blood transfusion. *World J Gastroenterol*. 2014;20:18420–18426.

28. Xu J, Zhao L, Wang Z, Zhai B, Liu C. Single-incision laparoscopic splenectomy for massive splenomegaly combininggastroesophageal devascularization using conventional instruments. *Surg Laparosc Endosc Percutan Tech*. 2014;24:e183.

29. Wu SD, Fan Y, Kong J, Su Y. Transumbilical single-incision laparoscopic splenectomy plus pericardial devascularizationusing conventional instruments: initial experience of 5 cases. *J Laparoendosc Adv Surg Tech A*. 2013;23:150–153.

30. Gumbs AA, Rodriguez Rivera AM, Milone L, Hoffman JP. Laparoscopic pancreatoduodenectomy: a review of 285 published cases. *Ann Surg Oncol*. 2011;18:1335–1341.

31. Hashizume M, Sugimachi K, Ueno K. Laparoscopic splenectomy with an ultrasonic dissector. *N Engl J Med*. 1992;327:438.

32. Delaitre B, Maignien B, Icard P. Laparoscopic splenectomy. *Br J Surg*. 1992;79:1334.

33. Hashizume M, Sugimachi K, Kitano S, et al. Laparoscopic splenectomy. *Am J Surg*. 1994;167:611–614.

34. Flowers JL, Lefor AT, Steers J, Heyman M, Graham SM, Imbembo AL. Laparoscopic splenectomy in patients with hematologic diseases. *Ann Surg*. 1996;224:19–28.

35. Katkhouda N, Hurwitz MB, Rivera RT, et al. Laparoscopic splenectomy: outcome and efficacy in 103 consecutive patients. *Ann Surg*. 1998;228:568–578.

36. Schlinkert RT, Teotia SS. Laparoscopic splenectomy. *Arch Surg*. 1999;134:99–103.

37. Habermalz B, Sauerland S, Decker G, et al. Laparoscopic splenectomy: the clinical practice guide lines of the European

Association for Endoscopic Surgery (EAES). *Surg Endosc*. 2008; 22:821–848.

38. Kawanaka H, Akahoshi T, Kinjo N, et al. Technical standardization of laparoscopic splenectomy harmonized with handassisted laparoscopic surgery for patients with liver cirrhosis and hypersplenism. *J Hepatobiliary Pancreat Surg*. 2009;16:749–757.

39. Klingler PJ, Tsiotos GG, Glaser KS, Hinder RA. Laparoscopic splenectomy: evolution and current status. *Surg Laparosc Endosc*. 1999;9:1–8.

40. Yamamoto J, Nagai M, Smith B, et al. Hand-assisted laparoscopic splenectomy and devascularization of the upper stomach in the management of gastric varices. *World J Surg*. 2006;30: 1520–1525.

41. Helmy A, Abdelkader Salama I, Schwaitzberg SD. Laparoscopic esophagogastric devascularization in bleeding varices. *Surg Endosc*. 2003;17:1614–1619.

42. Wang Y, Zhan X, Zhu Y, Xie Z, Zhu J, Ye Z. Laparoscopic splenectomy in portal hypertension: a single-surgeon 13-year experience. *Surg Endosc*. 2010;24:1164–1169.

43. Li SL, Li YC, Xu WL, Shi BJ. Laparoscopic splenectomy and periesophagogastric devascularization with endoligature for portal hypertension in children. *J Laparoendosc Adv Surg Tech A*. 2009;19:545–550.

44. Giza DE, Tudor S, Purnichescu-Purtan RR, Vasilescu C. Robotic splenectomy: what is the real benefit? *World J Surg*. 2014; 38:3067–3073.

45. Ricci C, Casadei R, Taffurelli G, et al. Laparoscopic Versus Open Distal Pancreatectomy for Ductal Adenocarcinoma: A Systematic Review and Meta-Analysis. *J Gastrointest Surg*. 2015;19: 770–781.

46. Masoomi H, Buchberg B, Nguyen B, Tung V, Stamos MJ, Mills S. Outcomes of laparoscopic versus open colectomy in elective surgery for diverticulitis. *World J Surg* 2011;35:2143–2148.

47. Xiong JJ, Altaf K, Javed MA, et al. Meta-analysis of laparoscopic vs open liver resection for hepatocellular carcinoma. *World J Gastroenterol*. 2012;18:6657–6668.

48. Novitsky YW, Litwin DE, Callery MP. The net immunologic advantage of laparoscopic surgery. *Surg Endosc*. 2004;18:1411–1419.

49. Biffl WL, Moore EE, Moore FA, Peterson VM. Interleukin-6 in the injured patient. Marker of injury or mediator of inflammation? *Ann Surg*. 1996;224:647–664.

50. Sylla P, Kirman I, Whelan RL. Immunological advantages of advanced laparoscopy. *Surg Clin North Am*. 2005;85:1–18, vii.

51. Buunen M, Gholghesaei M, Veldkamp R, Meijer DW, Bonjer HJ, Bouvy ND. Stress response to laparoscopic surgery: a review. *Surg Endosc*. 2004;18:1022–1028.

52. Vittimberga FJ Jr., Foley DP, Meyers WC, Callery MP. Laparoscopic surgery and the systemic immune response. *Ann Surg*. 1998;227:326–334.

53. Schwenk W, Jacobi C, Mansmann U, Böhm B, Müller JM. Inflammatory response after laparoscopic and conventional colorectal resections results of a prospective randomized trial. *Langenbecks Arch Surg*. 2000;385:2–9.

54. Sietses C, Wiezer MJ, Eijsbouts QA, et al. A prospective randomized study of the systemic immune response after laparoscopic and conventional Nissen fundoplication. *Surgery*. 1999; 126:5–9.

55. Scheepers JJ, Sietses C, Bos DG, et al. Immunological consequences of laparoscopic versus open transhiatal resection for malignancies of the distal esophagus and gastroesophageal junction. *Dig Surg*. 2008;25:140–147.

56. Grande M, Tucci GF, Adorisio O, et al. Systemic acute-phase response after laparoscopic and open cholecystectomy. *Surg Endosc*. 2002;16:313–316.

57. Pietrabissa A, Moretto C, Takiguchi S, et al. Thrombosis in the portal venous system after elective laparoscopic splenectomy. *Surg Endosc*. 2004;18:1140–1143.

58. Targarona EM. Portal vein thrombosis after laparoscopic splenectomy: The size of the risk. *Surg Innov*. 2008;15:266–270.

59. Machado NO, Chopra PJ, Sankhla D. Portal vein thrombosis postlaparoscopic splenectomy presenting with infarction of gut: review of risk factors, investigations, postoperative surveillance, and management. *Surg Laparosc Endosc Percutan Tech*. 2010; 20:273–277.

60. Cohen J, Edelman RR, Chopra S. Portal vein thrombosis: a review. *Am J Med*. 1992;92:173–182.

61. Ikeda M, Sekimoto M, Takiguchi S, et al. High incidence of thrombosis of the portal venous system after laparoscopic splenectomy: a prospective study with contrast-enhanced CT scan. *Ann Surg*. 2005;241:208–216.

62. Winslow ER, Brunt LM, Drebin JA, Soper NJ, Klingensmith ME. Portal vein thrombosis after splenectomy. *Am J Surg*. 2002; 184:631–636.

63. Skarsgard E, Doski J, Jaksic T, et al. Thrombosis of the portal venous system after splenectomy for pediatric hematologic disease. *J Pediatr Surg*. 1993;28:1109–1112.

64. Villa E, Cammà C, Marietta M, et al. Enoxaparin prevents portal vein thrombosis and liver decompensation in patients with advanced cirrhosis. *Gastroenterology*. 2012;143:1253–1260.