

Laparoscopic splenectomy for treatment of splenic marginal zone lymphoma

Zhong Wu, Jin Zhou, Xin Wang, Yong-Bin Li, Ting Niu, Bing Peng

Zhong Wu, Xin Wang, Yong-Bin Li, Bing Peng, Department of Hepatopancreatobiliary Surgery, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China
Jin Zhou, Department of Gastrointestinal Surgery, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China

Ting Niu, Department of Hematology, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China
Author contributions: Wu Z and Zhou J contributed equally to this work; Wu Z and Zhou J made substantial contributions to the conception and design of the study, data acquisition, and data analysis and interpretation; Wu Z, Wang X and Li YB drafted the article and revised it critically for important intellectual content; Peng B and Niu T provided final approval of the version to be published.

Correspondence to: Bing Peng, MD, Department of Hepatopancreatobiliary Surgery, West China Hospital, Sichuan University, Guoxuexiang 37, Chengdu 610041, Sichuan Province, China. pengbing84@hotmail.com

Telephone: +86-28-85422474 Fax: +86-28-85422474

Received: January 10, 2013 Revised: April 28, 2013

Accepted: May 17, 2013

Published online: June 28, 2013

Abstract

AIM: To investigate the short-term and long-term efficacy and safety of laparoscopic splenectomy (LS) for treatment of splenic marginal zone lymphoma (SMZL).

METHODS: A total of 18 continuous patients who were diagnosed with SMZL and underwent LS in our department from 2008 to 2012 were reviewed. The perioperative variables and long-term follow-up were evaluated. To evaluate the efficacy and safety of this procedure better, we also included 34 patients with liver cirrhosis who underwent LS, 49 patients with immune thrombocytopenia (ITP) who underwent LS, and 20 patients with SMZL who underwent open splenectomy (OS). The results observed in the different groups were compared.

RESULTS: No differences were found in the sex and Child-Pugh class of the patients in SMZL-LS, SMZL-OS, ITP, and liver cirrhosis groups. The splenic length of the patients in the SMZL-LS group was similar to that in the SMZL-OS and liver cirrhosis groups but significantly longer than in the ITP group. The SMZL-LS group had a significantly longer operating time compared with the SMZL-OS, ITP, and liver cirrhosis groups, and the SMZL-LS group exhibited significantly less blood loss compared with the SMZL-OS group. No difference was found in the length of the postoperative hospital stay between the SMZL-LS, SMZL-OS, ITP, and liver cirrhosis-LS groups. After surgery, 6 (33.3%) SMZL-LS patients suffered slight complications. During mean follow-up periods of 13.6 and 12.8 mo, one patient from the SMZL-LS group and two from the SMZL-OS group died as a result of metastasis after surgery. None of the ITP and liver cirrhosis patients died.

CONCLUSION: LS should be considered a feasible and safe procedure for treatment of SMZL in an effort to improve the treatment options and survival of patients.

© 2013 Baishideng. All rights reserved.

Key words: Splenic marginal zone lymphoma; Laparoscopic splenectomy; Open splenectomy; Liver cirrhosis; Immune thrombocytopenia

Core tip: Laparoscopic splenectomy (LS) achieves excellent results for treatment of benign hematological diseases. The role of LS in treatment of splenic marginal zone lymphoma (SMZL) is difficult to define due to the associated splenomegaly, which may influence long-term outcomes. We investigated the perioperative variables and long-term follow-up of 18 SMZL patients who underwent LS and compared them with SMZL patients who underwent open splenectomy, immune thrombocytopenia patients who underwent LS, and liver cirrhosis patients who underwent LS. LS should be considered an appropriate treatment strategy for SMZL

patients in an effort to improve the treatment options and survival of these patients.

Wu Z, Zhou J, Wang X, Li YB, Niu T, Peng B. Laparoscopic splenectomy for treatment of splenic marginal zone lymphoma. *World J Gastroenterol* 2013; 19(24): 3854-3860 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v19/i24/3854.htm> DOI: <http://dx.doi.org/10.3748/wjg.v19.i24.3854>

INTRODUCTION

Due to their low incidence rate, it is difficult and often ambiguous to determine the appropriate strategy for the treatment/management of splenic masses, which are considered uncommon diseases^[1]. The most common splenic malignancy is lymphoma^[1]. Splenic marginal zone lymphoma (SMZL) with or without villous lymphocytes is a disorder that was recently recognized as a distinct pathological entity in the World Health Organization classification^[2]. This disease mainly affects elderly and middle-aged patients with a median age of 65 years^[3]. At diagnosis, SMZL presents as an indolent and disseminated disease that is originally recognized after histopathological examination of surgically removed spleens as SMZL itself, or by means of morphological and immunophenotypic characterization of circulating neoplastic lymphocytes as splenic lymphoma with villous lymphocytes^[4-6]. Cytopenia and lymphocytosis are frequently observed^[7]. To date, there is no definitive standard treatment for SMZL. Approximately 2/3 of the patients are asymptomatic at diagnosis, and as many as one third of the patients will never require therapy. The diagnosis of this disease in patients who do not undergo splenectomy involves the morphological and immunophenotypic analysis of the peripheral blood and bone marrow^[8].

When splenectomy is indicated, laparoscopic splenectomy (LS) is the favored approach for treatment of benign hematological disorders. The role of LS in the treatment of a variety of hematological diseases, such as immune thrombocytopenia (ITP) and thrombotic thrombocytopenia, for which all other medical therapies have been exhausted has been elaborately documented^[8]. The technical success, minimal morbidity, reduced disability, and high patient acceptance have resulted in the classification of LS as the gold standard for treatment of ITP^[9,10]. Although splenomegaly was once considered a contraindication for laparoscopy, an increasing number of studies have proven the efficacy and safety of LS in both the short-term and the long-term treatment of splenomegaly and hypersplenism^[11,12].

The role of LS in patients with hematological malignancies remains ambiguous due to the skepticism regarding the use of minimally invasive techniques for the management of malignant or potentially malignant splenic diseases^[12]. However, the increased incidence of patients with non-Hodgkin's lymphoma, particularly elderly pa-

tients, and the relative increase in the number of splenectomies performed in the treatment of hematological malignancies makes this issue particularly germane^[13]. To date, there are only a few case studies that have analyzed the use of LS in the treatment of SMZL^[1,4,8]. The present study aimed to reveal whether the surgical outcomes of LS are beneficial, safe, and/or secure for the treatment of SMZL to determine whether this procedure should be considered a standard protocol in the management of SMZL. To achieve the most meaningful comparison between patients with similar disease mechanisms, we analyzed 20 patients with SMZL that underwent open splenectomy (OS), 49 with ITP, and 34 with splenomegaly due to liver cirrhosis and portal hypertension who were treated with LS.

MATERIALS AND METHODS

Patients

Our retrospective comparative study was designed to determine the efficacy and surgical outcomes of SMZL patients who underwent LS (SMZL-LS group) and to compare the outcomes with those observed in SMZL patients who underwent OS (SMZL-OS group) and in ITP and liver cirrhosis patients who underwent LS in West China Hospital at Sichuan University in 2008-2012. We include our published report on the use of LS in the management of ITP and liver cirrhosis and compared these results with the outcomes obtained for LS in the management of SMZL.

The chief diagnostic indicator of SMZL was histological confirmation. The diagnosis of ITP was based on bone marrow aspirate that documented a sufficient number of megakaryocytes. All of the patients with liver cirrhosis underwent LS and subsequent liver biopsy. All of the patients were characterized by the principal indicators for splenectomy: diagnostic and therapeutic. The major anticipated therapeutic benefits were the relief of the local symptoms of splenomegaly and the correction of cytopenia.

The patients included in this study underwent a detailed demographic, clinical, and biochemical assessment. The hematological response and liver function were assessed before and 7 d after surgery using peripheral blood count (leukocytes, hemoglobin, and platelets) and total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and albumin assays. At the time of preoperative evaluation for splenectomy, all of the patients underwent a color Doppler ultrasonography (US) scan and computed tomography (CT) to calculate the length of the spleen and to determine the presence of any portal or splenic vein thrombosis (PSVT). Seven days after the operation, all of the patients underwent careful screening for thrombosis. The patients who showed evidence of splenic vein thrombosis by US underwent CT to confirm the extent of thrombosis.

Operative technique of LS

The operative techniques of OS, LS, and hand-assisted

Table 1 Demographic characteristics

Variable	SMZL		Liver cirrhosis	ITP	P value ¹	P value ²	P value ³
	LS	OS					
Cases	18	22	34	49			
Age, yr	56.4 ± 10.5	52.0 ± 10.8	47.7 ± 12.2	36.2 ± 15.9	0.191	0.013	0.000
Sex (M/F)	8/10	10/12	16/18	10/39	0.949	0.857	0.049
Child-Pugh class					0.336	0.522	0.282
A	16 (88.9)	17 (77.3)	27 (79.4)	47 (95.9)			
B	2 (11.1)	5 (22.7)	5 (14.7)	2 (4.1)			
C	0	0	2 (5.9)	0 (0)			
Comorbidity							
ITP	1	2					
SLE	1	0					
Pulmonary effusion	1	2					
Herpes zoster	1	1					

Data are presented as mean ± SD or *n* (%). ¹SMZL-LS vs SMZL-OS groups; ²SMZL-LS vs liver cirrhosis group; ³SMZL-LS vs ITP groups. SMZL: Splenic marginal zone lymphoma; OS: Open splenectomy; LS: Laparoscopic splenectomy; ITP: Immune thrombocytopenia; M: Male; F: Female; SLE: Systemic lupus erythematosus.

laparoscopic splenectomy (HALS) have been described previously by our group^[11,12]. In addition, we removed and biopsied a 1 cm × 1 cm piece of hepatic tissue from the left lobe of the liver of patients with liver cirrhosis.

Follow-up

The mean follow-up time of SMZL patients who underwent LS was 13.6 mo. US and CT studies were performed at 1-mo intervals for 6 mo and at 3-mo intervals thereafter to determine whether the patients relapsed or developed PSVT. Upon the detection of PSVT by CT, we initiated anticoagulation therapy, which consisted of heparin (10000 U/d, intravenously), followed by warfarin. The dose of warfarin was adjusted to achieve an international normalized ratio (INR) of 1.5-2.0. Warfarin was administered until the disappearance of PSVT was confirmed by CT. All of the tests and examinations were repeated depending on the clinical condition of the patient.

Statistical analysis

The continuous variables are expressed as the mean ± SD. The statistical analyses were performed using the SPSS for Windows version 16.0 (SPSS, Chicago, IL, United States). The differences between the variables were compared using Student's *t* test and the χ^2 test. Differences with *P* < 0.05 were considered statistically significant.

RESULTS

Demographic characteristics

No differences were found between the demographic characteristics of the SMZL-LS and SMZL-OS groups. The SMZL-LS patients were significantly older than the liver cirrhosis and ITP patients. In addition, women tend to suffer from ITP, and thus there were significant sex differences between the ITP group and both the SMZL-LS and the liver cirrhosis groups (Table 1). There were no differences in the Child-Pugh class between the SMZL-LS group and the SMZL-OS and the liver cir-

rhosis groups, whereas the ITP patients had normal liver function. The comorbidity of the SMZL patients in both groups is shown in Table 1.

Perioperative outcomes

No patients in the ITP group exhibited conversion, but one patient from the liver cirrhosis group underwent conversion due to bleeding during the operation. In addition, one SMZL-LS patient underwent conversion because the harmonic was unable to stop the bleeding from the VASA during the operation. The SMZL-LS group had a significantly longer operation time compared with the SMZL-OS, ITP and liver cirrhosis groups. The EBL of the SMZL-OS group exhibited the most established blood loss, whereas the estimated blood loss (EBL) of the SMZL-LS and liver cirrhosis groups was not significantly different from that of the ITP group (Table 2). The SMZL-OS group exhibited a higher transfusion rate compared with the SMZL-LS group, whereas the transfusion rates of the other three types of patients were not significantly different. The spleen length of the SMZL-LS group was similar to that of the SMZL-OS and liver cirrhosis groups and longer than that of the ITP patients. The spleens of SMZL and liver cirrhosis patients usually exhibit splenomegaly or massive splenomegaly. The operation methods for the treatment of SMZL were LS (*n* = 8) or HALS (*n* = 10), whereas LS was used for the treatment of patients with liver cirrhosis and ITP.

Postoperative results

No difference was found in the length of postoperative hospital stay between the SMZL-LS, liver cirrhosis and ITP groups, whereas the SMZL-OS group experienced a significantly longer stay (Table 3). Six SMZL-LS, 10 SMZL-OS, 5 liver cirrhosis, and three ITP patients suffered complications. Patients with pulmonary effusion, pancreatic leakage, and abdominal cavity effusion were all cured through conservative treatment, such as somatostatin and drainage. One liver cirrhosis patient experienced

Table 2 Comparison of intraoperative details

Variable	SMZL		Liver cirrhosis	ITP	P value ¹	P value ²	P value ³
	LS	OS					
Conversion	1	-	1	0			
Operation time (min)	238.4 ± 37.9	185.9 ± 54.9	210.1 ± 48.5	163.9 ± 67.2	0.001	0.037	0.000
EBL	171.9 ± 228.4	310.0 ± 192.0	150.0 ± 146.1	65.7 ± 114.0	0.045	0.675	0.014
Transfusion	4/18 (22.2)	9/13 (69.0)	3/34 (8.8)	8/49 (16.3)		0.178	0.577
Spleen length (cm)	22.8 ± 5.5	23.7 ± 5.6	23.9 ± 3.9	12.1 ± 3.2	0.624	0.408	0.000
Additional operation							
Liver biopsy	0	0	34	0			
Lymph node biopsy	3	5		0			
LC	1	-	2	5			
Operation Method							
LS	8	-	34	49			
HALS	10	-	0	0			

Data are presented as mean ± SD or *n* (%). ¹SMZL-LS vs SMZL-OS groups; ²SMZL-LS vs liver cirrhosis groups; ³SMZL-LS vs ITP groups. SMZL: Splenic marginal zone lymphoma; OS: Open splenectomy; LS: Laparoscopic splenectomy; ITP: Immune thrombocytopenia; HALS: Hand-assisted laparoscopic splenectomy; EBL: Estimated blood loss; LC: Laparoscopic cholecystectomy.

Table 3 Comparison of postoperative details

Variable	SMZL		Liver cirrhosis	ITP	P value ¹	P value ²	P value ³
	LS	OS					
PHS (d)	8.17 ± 3.7	10.8 ± 4.2	7.5 ± 2.0	7.6 ± 2.1	0.044	0.378	0.389
Complication							
Pulmonary effusion	3	5	1	0			
Pancreatic leakage	1	2	1	1			
Abdominal cavity effusion	1	1	0	0			
Postoperative bleeding	0	0	1	2			
Portal/splenic vein thrombosis	1	2	2	0			
Total	6 (33.3)	10 (45)	5 (14.7)	3 (6.1)			

Data are presented as mean ± SD or *n* (%). ¹SMZL-LS vs SMZL-OS groups; ²SMZL-LS vs liver cirrhosis groups; ³SMZL-LS vs ITP groups. SMZL: Splenic marginal zone lymphoma; OS: Open splenectomy; LS: Laparoscopic splenectomy; ITP: Immune thrombocytopenia; PHS: Postoperative hospital stay.

postoperative bleeding. As a result, an emergency laparotomy and blood transfusion were performed, and the patient was discharged 14 d after LS. Two ITP patients suffered postoperative bleeding and received blood transfusion and conservative medical treatment. Both of these patients recovered 10 d after surgery. Patients were diagnosed with portal splenic vein thrombosis by postoperative dynamic CT. These patients received anticoagulation therapy consisting of heparin (10000 U/d *iv*) followed by warfarin. The dose of warfarin was adjusted to achieve an INR of 2. The administration of warfarin was continued every 3 mo until thrombosis disappeared.

After surgery and during follow-up, almost no significant differences in the hematological parameters and liver function outcomes were observed between the SMZL-LS and SMZL-OS groups. Total bilirubin of the liver cirrhosis group was much higher than that of the SMZL-LS and ITP groups because liver cirrhosis usually causes liver damage. The same result was observed in the analysis of the ALT and AST of the three groups of patients. The SMZL-LS and liver cirrhosis patients had a low white blood cell count (WBC) compared with the ITP patients ($P = 0.000$), and the WBCs of the SMZL-LS and liver cirrhosis groups were the same. The platelet counts of

the three types of patients were all different. The platelet count of the SMZL-LS group was higher than that of the liver cirrhosis group ($P = 0.000$), and the platelet count of the liver cirrhosis group was higher than that of the ITP group ($P = 0.000$). Postoperative comparison revealed that the liver cirrhosis patients had a higher level of total bilirubin and albumin than the SMZL patients. The ALT and AST levels in these patients were equal. The WBC of the ITP group was higher than that of the lymphoma and liver cirrhosis patients, but the WBC of the lymphoma and liver cirrhosis patients did not differ significantly. The platelet count of the three types of patients exhibited no significant differences (Table 4).

Follow-up outcomes

The SMZL-LS and SMZL-OS groups had a mean follow-up of 13.6 and 12.8 mo, respectively. At these times, none of the patients became septic or experienced wound complications following LS. One SMZL-LS and 2 SMZL-OS patients died as a result of metastasis following surgery. The other 17 patients experienced disease-free survival. None of the patients in the ITP and liver cirrhosis groups died.

Table 4 Comparison of the preoperative and postoperative hematological parameters and liver function variables

Variable	SMZL		Liver cirrhosis	ITP	P value ¹	P value ²	P value ³
	LS	OS					
Preoperation							
TBIL (mmol/L)	15.7 ± 8.5	23.3 ± 11.2	28.3 ± 17.2	13.3 ± 6.5	0.023	0.005	0.231
ALT (U/L)	25.1 ± 17.6	30.6 ± 11.1	54.7 ± 44.0	36.2 ± 33.6	0.237	0.009	0.187
AST (U/L)	25.7 ± 16.9	33.9 ± 16.9	59.3 ± 40.1	25.9 ± 21.9	0.133	0.001	0.956
Albumin (g/L)	36.8 ± 6.6	35.1 ± 8.4	37.6 ± 5.7	40.7 ± 5.3	0.478	0.653	0.015
HGB (g/L)	102.7 ± 26.1	106.3 ± 30.3	112.2 ± 22.5	123.7 ± 23.1	0.687	0.175	0.002
WBC (× 10 ⁹ /L)	4.2 ± 3.3	4.0 ± 3.2	3.2 ± 2.6	11.3 ± 6.7	0.867	0.255	0.000
PLT (× 10 ⁹ /L)	65.8 ± 35.6	56.1 ± 30.5	38.1 ± 15.7	20.6 ± 20.2	0.359	0.000	0.000
Postoperation							
TBIL (mmol/L)	11.9 ± 6.7	16.2 ± 7.8	19.4 ± 11.3		0.078	0.014	
ALT (U/L)	23.4 ± 12.9	28.1 ± 13.9	32.0 ± 25.9		0.279	0.192	
AST (U/L)	27.4 ± 17.7	29.5 ± 14.7	28.6 ± 9.7		0.682	0.753	
Albumin (g/L)	31.2 ± 5.5	33.7 ± 3.9	34.5 ± 3.9		0.114	0.017	
HGB (g/L)	101.1 ± 15.1	99.2 ± 15.1	138.6 ± 172.1	117.3 ± 20.4	0.699	0.362	0.003
WBC (× 10 ⁹ /L)	9.9 ± 6.7	11.3 ± 6.5	7.9 ± 1.8	14.4 ± 4.9	0.481	0.122	0.003
PLT (× 10 ⁹ /L)	298.8 ± 304.1	318.1 ± 211.1	237.2 ± 165.0	287.8 ± 140.1	0.814	0.346	0.840

Data are presented as mean ± SD. ¹SMZL-LS vs SMZL-OS groups; ²SMZL-LS vs liver cirrhosis groups; ³SMZL-LS vs ITP groups. HGB: hemoglobin; PLT: platelet count; TBIL: Total bilirubin; WBC: White blood cell count; SMZL: Splenic marginal zone lymphoma; OS: Open splenectomy; LS: Laparoscopic splenectomy; ITP: Immune thrombocytopenia; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase.

DISCUSSION

SMZL is globally deemed a low-grade lymphoma with an indolent clinical course. Numerous cases exhibit a protracted straightforward progression, an excellent response to splenectomy or chemotherapy treatment, and sometimes an unmodified clinical picture in the absence of any treatment. The 5-year survival rate ranges from 65% to 78%^[14,15]. Retrospective studies have shown that patients who underwent splenectomy exhibited a significantly improved survival rate compared with those patients who underwent chemotherapy^[14]. Splenectomy is the generally preferred treatment for SMZL. Although this process is not preventive, splenectomy offers superior swift relief of symptoms and often completely modifies any affiliated cytopenia. Additionally, this surgical procedure offers excellent disease management, which usually makes it possible for individuals to avoid systemic therapy^[14]. Although the advantages of LS, such as shorter hospital stay, less scarring, earlier return to activity, and less inflammatory responses^[16], have been documented previously, the residual tumor and tumor recurrence should be taken into account in the consideration of LS as an appropriate procedure for the treatment of a potentially malignant lesion.

Extensive experience with LS at many centers has led to its use in the treatment of a wide variety of benign hematological diseases. Furthermore, our previous results demonstrated that LS is an efficient and safe strategy for the treatment of hypersplenism secondary to liver cirrhosis^[11]. Our current data suggest that the results of LS for treatment of SMZL are comparable with the results for treatment of ITP and liver cirrhosis, which confirms the safety of this procedure for these diseases. Although the SMZL group included a significantly older patient population compared with the ITP group and exhibited

a spleen length comparable to that of the liver cirrhosis patients, the SMZL patients underwent successful operations with low morbidity and no mortality. The significantly longer operating time and the significantly higher blood loss in the SMZL patients compared with the ITP and liver cirrhosis groups were expected but did not correlate with adverse outcomes^[9].

The ability to achieve a satisfactory outcome in this difficult patient group is probably related to the technical expertise of the surgeon^[9]. It has been shown that splenic size is an independent predictor of postoperative complications^[14]. Yano *et al*^[17] reported their experience with HALS for the treatment of splenic tumors in 10 patients. They have recommended the HALS approach because it allows easier mobilization of the spleen (particularly with splenomegaly) and easier resection of the adjacent organs or tissue if necessary. However, Makrin *et al*^[18] concluded that most splenic tumors can be treated using a completely laparoscopic approach. This total laparoscopic approach may be unsuitable when the tumor is associated with massive splenomegaly; in these cases HALS may be considered. In our study, eight patients underwent total LS, whereas 10 patients underwent HALS. We performed LS on patients with splenic length > 20 cm. To ensure sufficient space throughout the surgical procedure, additional movements of the spleen were required, which escalated the blood loss and the chance of perisplenic organ injury. In contrast, the majority of our patients with splenomegaly underwent LS effectively^[19]. In this particular analysis, we attempted to appraise the intraoperative and postoperative consequences with respect to substantial splenomegaly, utilizing LS and HALS for the treatment of SMZL. Of the 81 patients studied by Thieblemont *et al*^[20], 44 exhibited spleen lymphoma and anemia, and 13 of these had Coombs-positive hemolytic anemia. Of our 18 patients, 38.9% exhibited Coombs-

positive hemolytic anemia. A study of 309 patients revealed the 50% of the patients remained anemic^[21]. However, our comparative study is unique because it analyzed the effectiveness of LS in the treatment of an assortment of diseases, particularly SMZL. Our outcomes demonstrate that, regardless of the numerous strategies for the treatment of SMZL, LS might prove advantageous for a number of reasons, including its significantly shorter hospital stay and low postoperative stress; these findings have been confirmed by several other investigators. Splenectomy frequently contributes to somatic compensation of patients, which results in local relapse in the spleen, prevents continuing dissemination of the primary tumor site, and mostly corrects cytopenia, thereby creating better conditions for chemotherapy^[22]. One of the patients enrolled in our study died as a result of metastasis several weeks after surgery; the patient's death was therefore unrelated to our treatment approach.

The sex of the different groups differed significantly, mainly because of the characteristics and epidemiology of SMZL and ITP. The splenic size was an important indicator of the conversion rate, the operation time, and the blood loss. The SMZL and the liver cirrhosis patients had significantly longer spleens. The operation time of the SMZL group was significantly longer than that of the liver cirrhosis and ITP groups, which implies that surgery for lymphoma is more difficult than for liver cirrhosis and ITP. We found that the spleen of the lymphoma patients usually adhered to the greater omentum or intestine. It therefore requires a longer time to separate these tissues and organs. LS is the gold standard for the treatment of ITP. Compared with LS for the treatment of ITP, LS for liver cirrhosis may be more difficult because the blood vessels are thick and varicose. The EBL of the SMZL and the liver cirrhosis groups was higher than that of the ITP group, whereas there was no significant difference between the EBL of the SMZL group and that of the liver cirrhosis group. This finding indicates that LS exhibits similar outcomes in the treatment of both types of patients.

Fine-needle aspiration (FNA) was used in the diagnosis of the splenic mass with a high positive rate of approximately 80%-88.9%^[23,24]. Previous studies reported a low morbidity rate and no biopsy-site seeding of the tumor. However, the incidentally discovered lesions comprised the minority of the lesions (20%-27%)^[1]. Furthermore, this technique may be associated with bleeding complications and the risk of tumor dissemination^[21]. Tessier *et al*^[1] demonstrated that FNA biopsy is unnecessary unless the patient cannot tolerate splenectomy, that is, in the setting of a solitary splenic mass with no history of malignancy. Based on the results of Tessier *et al*^[1], the SMZL patients in our study did not undergo FNA.

In conclusion, we evaluated the safety and efficacy of LS for the treatment of SMZL and compared these results with the outcome of LS for treatment of ITP and liver cirrhosis, and from the use of OS for the treatment of SMZL. Our findings show that LS is usually safe and effective for the treatment of SMZL. Although the

SMZL patients who underwent LS required a significantly longer operation time than those with ITP and liver cirrhosis, no significant differences were observed in the transfusion requirements, postoperative complications, or length of postoperative hospital stay. LS might be a favored procedure for the treatment of SMZL. However, further research is required to determine more definitely its effectiveness in the treatment of SMZL. Furthermore, the role of HALS as a first-choice approach or an alternative approach for the treatment of massive splenomegaly needs to be investigated.

COMMENTS

Background

Laparoscopic splenectomy (LS) is the favored operative approach for the treatment of benign hematological disorders that require splenectomy. Although splenomegaly was once considered a contraindication for laparoscopy, an increasing number of studies have proven the efficacy and safety of the use of LS for both the short-term and long-term treatment of splenomegaly. However, the role of LS in the treatment of patients with hematological malignancies remains ambiguous due to skepticism regarding the use of minimally invasive techniques for the treatment of malignant or potentially malignant splenic diseases.

Research frontiers

To date, there is no definitive standard for the treatment of splenic marginal zone lymphoma (SMZL). Approximately two-thirds of patients are asymptomatic at the time of diagnosis, and as many as one-third of the patients will never require therapy. However, the incidence of patients with SMZL is increasing, especially in the elderly population. The use of LS for the treatment of hematological malignancy has gradually improved. In this study, the authors demonstrated that LS might be a feasible and safe treatment option for SMZL.

Innovations and breakthroughs

To date, there are only a few case studies that have analyzed the use of LS for the treatment of SMZL. In addition, only a few studies have compared LS and open splenectomy (OS) for the treatment of SMZL. Furthermore, no study has shown differences in the perioperative and long-term outcomes between SMZL, immune thrombocytopenia (ITP), and splenomegaly. This study demonstrated that LS is a feasible and safe procedure for the treatment of SMZL.

Applications

To achieve the most meaningful comparison between patients with similar disease mechanisms, the authors included patients with SMZL who underwent OS, patients with ITP, and patients with splenomegaly due to liver cirrhosis and portal hypertension who were treated with LS. The study revealed that LS is safe for the treatment of SMZL and should be considered in its management.

Terminology

SMZL with or without villous lymphocytes is a disorder that was recently recognized as a distinct pathological entity in the World Health Organization classification. SMZL was originally recognized either after histopathological examination of surgically removed spleens as SMZL itself, or by means of morphological and immunophenotypic characterization of circulating neoplastic lymphocytes as splenic lymphoma with villous lymphocytes.

Peer review

This was an interesting study in which the authors analyzed the perioperative and long-term variables in the use of LS for the treatment of lymphoma. This study shows that the morbidity associated with treatment of SMZL is no more than expected compared with the outcomes obtained for LS treatment of other diseases. The results are instructive and suggest that LS is a feasible and safe procedure for the treatment of SMZL.

REFERENCES

- 1 Tessier DJ, Pierce RA, Brunt LM, Halpin VJ, Eagon JC, Frisella MM, Czerniejewski S, Matthews BD. Laparoscopic splenectomy for splenic masses. *Surg Endosc* 2008; **22**: 2062-2066 [PMID: 18246392 DOI: 10.1007/s00464-008-9748-8]
- 2 Dogan A, Isaacson PG. Splenic marginal zone lymphoma.

- Semin Diagn Pathol* 2003; **20**: 121-127 [PMID: 12945935 DOI: 10.1016/S0740-2570(03)00012-1]
- 3 **Kalpadakis C**, Pangalis GA, Angelopoulou MK, Sachanas S, Kontopidou FN, Yiakoumis X, Kokoris SI, Dimitriadou EM, Dimopoulou MN, Moschogiannis M, Korkolopoulou P, Kyrtsonis MC, Siakantaris MP, Papadaki T, Tsaftaris P, Plata E, Papadaki HE, Vassilakopoulos TP. Treatment of splenic marginal zone lymphoma with rituximab monotherapy: progress report and comparison with splenectomy. *Oncologist* 2013; **18**: 190-197 [PMID: 23345547]
 - 4 **Schmid C**, Kirkham N, Diss T, Isaacson PG. Splenic marginal zone cell lymphoma. *Am J Surg Pathol* 1992; **16**: 455-466 [PMID: 1599024 DOI: 10.1097/00000478-199205000-00004]
 - 5 **Thieblemont C**, Davi F, Noguera ME, Briere J, Bertoni F, Zucca E, Traverse-Glehen A, Felman P, Berger F, Salles G, Coiffier B. Splenic marginal zone lymphoma: current knowledge and future directions. *Oncology (Williston Park)* 2012; **26**: 194-202 [PMID: 22489356]
 - 6 **Isaacson PG**, Piris MA, Berger F, Swerdlow SH, Thieblemont C, Pitaluga S, Harris NL. Splenic B-cell marginal zone lymphoma. In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW, Editors. WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon: International Agency for Research on Cancer, 2008: 185-187
 - 7 **Matutes E**, Oscier D, Montalban C, Berger F, Callet-Bauchu E, Dogan A, Felman P, Franco V, Iannitto E, Mollejo M, Papadaki T, Remstein ED, Salar A, Solé F, Stamatopoulos K, Thieblemont C, Traverse-Glehen A, Wotherspoon A, Coiffier B, Piris MA. Splenic marginal zone lymphoma proposals for a revision of diagnostic, staging and therapeutic criteria. *Leukemia* 2008; **22**: 487-495 [PMID: 18094718 DOI: 10.1038/sj.leu.2405068]
 - 8 **Pich A**, Fraire F, Fornari A, Bonino LD, Godio L, Bortolin P, Chiusa L, Palestro G. Intrasinusoidal bone marrow infiltration and splenic marginal zone lymphoma: a quantitative study. *Eur J Haematol* 2006; **76**: 392-398 [PMID: 16480431 DOI: 10.1111/j.1600-0609.2005.00624.x]
 - 9 **Walsh RM**, Brody F, Brown N. Laparoscopic splenectomy for lymphoproliferative disease. *Surg Endosc* 2004; **18**: 272-275 [PMID: 14691699 DOI: 10.1007/s00464-003-8916-0]
 - 10 **Habermalz B**, Sauerland S, Decker G, Delaitre B, Gigot JF, Leandros E, Lechner K, Rhodes M, Silecchia G, Szold A, Targarona E, Torelli P, Neugebauer E. Laparoscopic splenectomy: the clinical practice guidelines of the European Association for Endoscopic Surgery (EAES). *Surg Endosc* 2008; **22**: 821-848 [PMID: 18293036 DOI: 10.1007/s00464-007-9735-5]
 - 11 **Cai YQ**, Zhou J, Chen XD, Wang YC, Wu Z, Peng B. Laparoscopic splenectomy is an effective and safe intervention for hypersplenism secondary to liver cirrhosis. *Surg Endosc* 2011; **25**: 3791-3797 [PMID: 21681623 DOI: 10.1007/s00464-011-1790-2]
 - 12 **Zhou J**, Wu Z, Pankaj P, Peng B. Long-term postoperative outcomes of hypersplenism: laparoscopic versus open splenectomy secondary to liver cirrhosis. *Surg Endosc* 2012; **26**: 3391-3400 [PMID: 22648114 DOI: 10.1007/s00464-012-2349-6]
 - 13 **Rose AT**, Newman MI, Debelak J, Pinson CW, Morris JA, Harley DD, Chapman WC. The incidence of splenectomy is decreasing: lessons learned from trauma experience. *Am Surg* 2000; **66**: 481-486 [PMID: 10824750]
 - 14 **Wall LL**. Reproductive health in developing countries: a new initiative. *Br J Obstet Gynaecol* 1995; **102**: 1017-1018 [PMID: 8652473 DOI: 10.1046/j.1365-2141.1996.d01-1711.x]
 - 15 **Chacón JI**, Mollejo M, Muñoz E, Algara P, Mateo M, Lopez L, Andrade J, Carbonero IG, Martínez B, Piris MA, Cruz MA. Splenic marginal zone lymphoma: clinical characteristics and prognostic factors in a series of 60 patients. *Blood* 2002; **100**: 1648-1654 [PMID: 12176884]
 - 16 **Wu Z**, Zhou J, Pankaj P, Peng B. Laparoscopic and open splenectomy for splenomegaly secondary to liver cirrhosis: an evaluation of immunity. *Surg Endosc* 2012; **26**: 3557-3564 [PMID: 22710653 DOI: 10.1007/s00464-012-2366-5]
 - 17 **Yano H**, Nakano Y, Tono T, Ohnishi T, Iwazawa T, Kimura Y, Kanoh T, Monden T. Hand-assisted laparoscopic splenectomy for splenic tumors. *Dig Surg* 2004; **21**: 215-222 [PMID: 15237254 DOI: 10.1159/000079395]
 - 18 **Makrin V**, Avital S, White I, Sagie B, Szold A. Laparoscopic splenectomy for solitary splenic tumors. *Surg Endosc* 2008; **22**: 2009-2012 [PMID: 18594922]
 - 19 **Zhou J**, Wu Z, Cai Y, Wang Y, Peng B. The feasibility and safety of laparoscopic splenectomy for massive splenomegaly: a comparative study. *J Surg Res* 2011; **171**: e55-e60 [PMID: 21885066 DOI: 10.1016/j.jss.2011.06.040]
 - 20 **Thieblemont C**, Felman P, Callet-Bauchu E, Traverse-Glehen A, Salles G, Berger F, Coiffier B. Splenic marginal-zone lymphoma: a distinct clinical and pathological entity. *Lancet Oncol* 2003; **4**: 95-103 [PMID: 12573351]
 - 21 **Arcaini L**, Lazzarino M, Colombo N, Burcheri S, Boveri E, Paulli M, Morra E, Gambacorta M, Cortelazzo S, Tucci A, Ungari M, Ambrosetti A, Menestrina F, Orsucci L, Novero D, Pulsoni A, Frezzato M, Gaidano G, Vallisa D, Minardi V, Tripodo C, Callea V, Baldini L, Merli F, Federico M, Franco V, Iannitto E. Splenic marginal zone lymphoma: a prognostic model for clinical use. *Blood* 2006; **107**: 4643-4649 [PMID: 16493005 DOI: 10.1182/blood-2005-11-4659]
 - 22 **Musteata VG**, Corcimaru IT, Iacovleva IA, Musteata LZ, Suharschii IS, Antoci LT. Treatment options for primary splenic low-grade non-Hodgkin's lymphomas. *Clin Lab Haematol* 2004; **26**: 397-401 [PMID: 15595997]
 - 23 **Kocjan G**, Smith AN. Bile duct brushings cytology: potential pitfalls in diagnosis. *Diagn Cytopathol* 1997; **16**: 358-363 [PMID: 9143832]
 - 24 **Keogan MT**, Freed KS, Paulson EK, Nelson RC, Dodd LG. Imaging-guided percutaneous biopsy of focal splenic lesions: update on safety and effectiveness. *AJR Am J Roentgenol* 1999; **172**: 933-937 [PMID: 10587123 DOI: 10.2214/ajr.172.4.10587123]

P- Reviewer Rizzieri DA S- Editor Huang XZ
L- Editor Kerr C E- Editor Ma S

