

Effectiveness and safety of minilaparoscopy-guided spleen biopsy: a retrospective series of 57 cases

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Abstract

Background Minilaparoscopy is an accepted method for liver biopsy. We report our experience with minilaparoscopy for splenic biopsy.

Methods We reviewed the records of all minilaparoscopy procedures performed from 1996 to 2004 at the University of Mainz Medical Center and from 2005 to mid-2011 at the University of Hamburg Medical Center to identify patients who underwent a minilaparoscopy-guided splenic biopsy. All procedures were performed using the previously described method (2.75-mm trocar, 2.3-mm Veress needle, 1.9-mm laparoscope) with the patient under conscious sedation (midazolam/meperidine/propofol). Splenic biopsies were performed using a second trocar with an 18-G Tru-Cut needle. Argon plasma coagulation (APC) and/or fibrin glue (FG) were used to control postbiopsy bleeding.

Results Fifty-seven patients underwent minilaparoscopy-guided biopsy of the spleen (27 females, 30 males; median age = 41 years, range = 16–76). A specimen suitable for histopathologic evaluation was obtained in all patients. Grouped by preprocedure indication, a definitive diagnosis was obtained in 70% (7/10) of patients who had splenic mass lesions in prior imaging (3 B-NHL, 2 hemangioma,

1 tuberculosis, 1 sarcoidosis; $p < 0.01$) compared to 29% (10/34) in the group with unexplained fever or suspected lymphoma (3 tuberculosis, 2 B-NHL, 1 hepatosplenic T-cell lymphoma, 1 sarcoidosis, 1 Still's disease, 1 EBV, 1 Q-fever) and 0/13 with unexplained splenomegaly. Focal lesions noted at laparoscopy yielded to a histologic diagnosis in 38% (11/29) of 42 patients compared to 21% (6/28) without laparoscopic abnormality ($p = 0.25$). Bleeding from the biopsy site was noted in 96.5% (55/57) and was classified as brisk in 9. Control of hemorrhage was achieved in all patients (APC: 47, FG: 1, APC/FG: 7). There was no postprocedure bleeding or other complications.

Conclusion Splenic biopsy guided by minilaparoscopy can be performed safely. Postprocedure bleeding is readily controlled with APC with or without fibrin glue. The highest diagnostic yield is in patients with focal splenic lesions.

Keywords Spleen biopsy · Minilaparoscopy · Focal spleen lesion

Abbreviations

APC	Argon plasma coagulation
B-NHL	B-cell non-Hodgkin's lymphoma
EBV	Epstein-Barr virus/infectious mononucleosis
INR	International normalized ratio
PCR	Polymerase chain reaction

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Splenic biopsy can be useful in establishing the diagnosis of malignancies (especially lymphoma) and certain systemic infectious diseases. In the 1970s, splenic biopsies were routinely performed for diagnosis and staging of Hodgkin's and non-Hodgkin's lymphomas. Initially, percutaneous biopsies were performed using a Menghini

needle and subsequent reports described standard laparoscopic biopsy [1–4]. In 1984, Dagnini et al. [5] reported the largest series to date of splenic biopsies for lymphoma staging, splenomegaly of unclear etiology, and “clinically suspected” splenic pathology. Improved imaging and laboratory techniques and the relatively invasive nature of conventional laparoscopy performed under general anesthesia have led to a decline in laparoscopic splenic biopsies. Since the late 1980s a few case series have described image-guided percutaneous splenic biopsies and intervention for diagnostic and therapeutic indications [6–13].

Minilaparoscopy performed with a 2-mm laparoscope and with the patient under conscious sedation has been accepted as a useful means of liver biopsy, especially for patients with impaired coagulation [14]. Our group reported our early experience with minilaparoscopy for splenic biopsy in four patients in 2002 [15]. Herein we report our cumulative experience over 15 years.

Patients and methods

Patients

All patients who were to undergo a minilaparoscopy for diagnostic evaluation from December 1996 to December 2004 (I. Department of Medicine, University of Mainz, Germany) and between March 2005 to June 2011 (I. Department of Medicine, University Hospital of Hamburg-Eppendorf, Germany) were registered in a prospective database (Microsoft Office Access). All patients in whom a minilaparoscopy-guided splenic biopsy was performed were identified in the database. The database was reviewed for patient age, gender, procedure indication, coagulation parameters, macroscopic findings of liver and spleen, postbiopsy bleeding, coagulation method used, complications, and histologic diagnosis. The analysis of the database was approved by the local Institutional Review Board.

This retrospective study investigated the diagnostic impact and complications of minilaparoscopy-guided splenic biopsy. Therefore, diagnostic yield was analyzed based on the clinical indication for splenic biopsy as follows: (1) focal splenic lesion detected in previous imaging method [computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound]; (2) unexplained fever according to the previously described clinical syndrome “fever of unknown/unexplained origin (FUO)” [16], or clinically suspected lymphoma (e.g., symptomatic patients with lymphadenopathy and splenomegaly or as a staging procedure for known lymphoma); and (3) splenomegaly in prior imaging without specific symptoms. In addition, the diagnostic impact of biopsies of focal lesions was analyzed, comparing lesions detected only laparoscopically and focal

lesions detected in prior imaging. Finally, the utility of a concomitant liver biopsy was assessed.

Methods

Written informed consent was obtained and current blood count and coagulation tests from every patient were reviewed before minilaparoscopy. There was no age restriction for the procedure. Exclusion criteria for the procedure were acute coronary syndrome, unstable congestive heart failure (NYHA III and IV), severe respiratory failure, and pregnancy. Patients with a coagulopathy (platelet count <50/nl or INR >1.5) routinely received platelet or fresh frozen plasma transfusions.

Minilaparoscopy was performed as previously described [14] using a 2.75-mm trocar, 2.3-mm Veress needle, 1.9-mm optic laparoscope (Fa. Wolf GmbH, Knittlingen, Germany), and nitrous oxide (N₂O) as insufflation gas. For conscious sedation, midazolam and meperidine were used in titrated doses, and after 2005 propofol was used concomitantly [17].

Splenic biopsy was performed with an automatic 18-G tissue core biopsy needle (Tru-Cut, Cardinal Health, Dublin, OH, USA and Bard monopty, Tempe/AZ, USA) using a separately placed trocar. Immediate postbiopsy bleeding was graded strong if it persisted longer than 5 min or was pulsatile. Postbiopsy bleeding was routinely treated using argon plasma coagulation (Arco, Söring GmbH, Quickborn, Germany) and/or fibrin glue (CSL Behring, Hattersheim, Main, Germany).

Monitoring during examination consisted of continuous pulse oximetry and blood pressure measurement every 5 min. Oxygen was provided as needed via a nasal probe to maintain oxygen saturation above 92%. After the procedure blood pressure and pulse rate were recorded every 30 min for 6 h. Postprocedure blood count and ultrasound were not routinely performed.

Statistics

Statistical analysis was performed using OpenOffice.org ver. 3.3.0. Fisher’s exact test was calculated with R ver. 2.13.1, with a $p \leq 0.05$ deemed significant. The p value due to clinical indication was calculated for each indication group against the others. The p value due to laparoscopic finding was calculated among the two groups (present vs. not present).

Results

Demographic data

A minilaparoscopy-guided splenic biopsy was performed in 57 patients over the 15-year period of this study. The

gender distribution was similar (27 women and 30 men) and the median age of the patients was 41 years (range = 16–76 years). INR was normal in all patients and two patients had a platelet count below 50/nl. A sufficient histologic sample was obtained in every patient. The biopsy yielded a definitive diagnosis in 17 of the 57 cases (30%). A concomitant laparoscopic liver biopsy was performed in 45 of the 57 patients (79%). Demographic details are listed in Table 1.

Diagnostic yield classified by clinical indication for splenic biopsy

The highest diagnostic yield was observed in patients with focal splenic lesions detected in prior imaging studies (Table 2). A definitive diagnosis was obtained in 7 of 10 patients (70%; $p < 0.01$): B-cell non-Hodgkin's lymphoma ($n = 3$), hemangioma ($n = 2$), tuberculosis ($n = 1$), and sarcoidosis ($n = 1$).

In patients with unexplained fever or clinically suspected lymphoma, biopsy resulted in a definitive diagnosis in 10 of 34 patients (29%; $p < 1.00$): tuberculosis ($n = 3$), B-cell non-Hodgkin's lymphoma ($n = 2$), hepatosplenic T-cell lymphoma ($n = 1$), sarcoidosis ($n = 1$), Still's disease ($n = 1$), infectious mononucleosis ($n = 1$), and Q-fever (positive PCR) ($n = 1$).

Biopsy in patients with splenomegaly and no symptoms ($n = 13$; $p < 0.01$) did not provide any definitive diagnostic results. In these patients minilaparoscopy was undertaken primarily for evaluation of liver diseases, namely, hepatopathy of unknown origin ($n = 11$), staging of HCV ($n = 1$), and splenomegaly after recovery from leishmaniasis ($n = 1$). In four patients, focal lesions of the spleen were noted laparoscopically which led to guided biopsy. The histologic examination found normal splenic tissue ($n = 8$) and nonspecific inflammatory changes ($n = 5$).

Laparoscopic signs of portal hypertension with ascites and/or dilated peritoneal vessels were present in 4 of 57 patients (7%), of which 3 were in the indication group splenomegaly.

Table 1 Demographic data

Demographic data		N (%)
Sex	Male	30 (53)
	Female	27 (47)
Age	Median (years)	41
	Range (years)	16–76
Indication for spleen biopsy	Focal lesions in prior imaging	10 (17)
	Unexplained fever/suspected lymphoma	34 (60)
	Splenomegaly	13 (23)

Diagnostic yield due to laparoscopic diagnosis of focal splenic lesions

Focal lesions of the spleen were detected during laparoscopy in 29 of 51 patients (51%). Laparoscopy-guided biopsy of these lesions provided a definitive histologic diagnosis in 11 of 29 patients (38%). Biopsies in patients with no focal lesion noted on laparoscopy provided a diagnosis in only 6 of 28 patients (21%), although this difference was not statically significant ($p = 0.25$).

Diagnostic yield of additional liver and peritoneal biopsies

An additional laparoscopic liver biopsy was performed in 45 of 57 patients (79%). Liver biopsy confirmed the results of the splenic biopsy in 7 of 45 patients: tuberculosis ($n = 4$), sarcoidosis ($n = 1$), hepatosplenic T-cell lymphoma ($n = 1$) and Q-fever (positive PCR) ($n = 1$). In one of the patients with tuberculosis, the diagnosis was also confirmed by peritoneal biopsy.

In 3 of 45 patients without a definitive splenic biopsy, an additional liver biopsy explained the presence of splenomegaly as due to portal hypertension resulting in previously unknown liver cirrhosis in two patients and extramedullary hematopoiesis with osteomyelofibrosis in one patient. The histologic findings of the other liver biopsies showed normal liver tissue, nonspecific inflammation, or toxic alterations and added no additional diagnostic information.

Management of postbiopsy bleeding, coagulation methods, and complications

Initial bleeding from the splenic puncture site occurred in 55 of 57 patients (96%). The bleeding was laparoscopically graded as strong in 9 patients. Bleeding was controlled in all patients with either APC ($n = 47$), APC in combination with fibrin glue ($n = 7$), or fibrin glue alone ($n = 1$). Neither clinical indication nor histologically proven malignancy nor laparoscopically identified splenic lesions were associated with a statistically significant increased bleeding rate.

There were no minor or major postprocedure complications, specifically, no delayed biopsy bleeding, blood transfusions required, no infection, no prolonged hospitalization, and no deaths.

Discussion

Diagnostic laparoscopy has been proven to be accurate and safe for evaluation of liver diseases [2, 4, 5, 14, 18–20] and

Table 2 Results

	Diagnostic histology	Diagnosis	%	<i>p</i> *
<i>Due to clinical indication (n = 57)</i>				
Focal splenic lesions in prior imaging methods	7/10	B-NHL (3) Hemangioma (2) Tuberculosis (1) Sarcoidosis (1)	70	<0.01
Unexplained fever or clinical suspicion of lymphoma	10/34	Tuberculosis (3) B-NHL (2) Hepatosplenic T-cell lymphoma (1) Sarcoidosis (1) Still's disease (1) EBV (1) Q-fever (1)	29	1.00
Splenomegaly	0/13	–	0	<0.01
<i>Due to laparoscopic finding (n = 57)</i>				
Laparoscopic spleen lesion present	11/29	B-NHL (4) Tuberculosis (2) Sarcoidosis (2) Hemangioma (2) Hepatosplenic T-cell lymphoma (1)	38	0.25
Laparoscopic spleen lesion not present	6/28	B-NHL (1) Tuberculosis (2) Still's disease (1) EBV (1) Q-fever (1)	21	
<i>Results of additional liver biopsy (n = 45)</i>				
Confirmation of spleen biopsy	7/45	Tuberculosis (4) Sarcoidosis (1) Hepatosplenic T-cell lymphoma (1) Q-fever (1)	15	
Additional findings	30/45	Unspecific inflammation (12) Toxic changes (9) Cirrhosis (4) Viral inflammation (3) Hemophagocytosis (1) Extramedullary hematopoiesis (1)	67	
Normal liver tissue	8/45		18	

B-NHL B-cell non-Hodgkin's lymphoma, *EBV* Epstein-Barr virus/infectious mononucleosis

* Due to indication: group versus all others; due to laparoscopic finding: present versus not present

peritoneal pathologies of infectious or malignant origin [21]. This case series shows minilaparoscopy to be feasible and safe for obtaining a guided splenic biopsy. The highest diagnostic yield was observed in patients with focal lesions seen either in prior imaging studies (70%) or during laparoscopy itself (38%). The next highest yield was observed from splenic biopsy for unexplained fever or clinical suspicion of lymphoma (29%). Isolated splenomegaly without

other specific clinical symptoms did not result in any definitive diagnosis and was related mostly to another clinical disease, e.g., portal hypertension with liver cirrhosis.

Comparison with surgical laparoscopy

Before the availability of modern imaging techniques, several studies assessed the impact of diagnostic

conventional laparoscopy with splenic biopsy for staging of proven or suspected lymphoma. A smaller series of laparoscopic biopsies in the 1970s detected splenic lymphoma in only 14 of 37 (38%) cases, with confirmed splenic infiltration noted after surgical splenectomy [4]. Dagnini et al. [5] reported the most extensive series of 1,243 laparoscopic splenic biopsies in 779 patients using a Menghini needle (1.8 mm), a bio-cut needle, or Palmer's forceps. Indications were staging of Hodgkin's disease and non-Hodgkin's lymphoma ($n = 453$), evaluation of splenomegaly of unknown etiology ($n = 163$), and clinical suspicion of splenopathy ($n = 163$). Diagnostic yield of staging for Hodgkin's and non-Hodgkin's lymphoma was greatest in the group with laparoscopic visible lesions [diagnosis of lymphoma in 28 of 64 (44%)] followed by splenomegaly [diagnosis of lymphoma in 20 of 104 (19%)] and normal spleen size [diagnosis of lymphoma in 5 of 234 (2%)]. Evaluation of splenomegaly and clinical suspicion of splenopathy resulted in a higher rate of definitive histologic diagnosis, with a splenic lesion present laparoscopically (58% compared to 10%). This supports the use of biopsy of focal spleen lesions found at the time of laparoscopy or in imaging to gain a definitive diagnosis. In the case of splenomegaly without clinical symptoms, splenic biopsy should be discussed carefully; the reported poor diagnostic yield was comparable to our series.

Comparison with image-guided procedures

Case series of ultrasound-guided spleen biopsy also support a higher diagnostic yield for underlying focal splenic lesions. A series of ultrasound-guided fine needle biopsies (Chiba-type needle, 22 G) yielded a definitive diagnosis in 8 of 22 patients with focal splenic lesions [6]; the diagnoses were cysts ($n = 3$), non-Hodgkin's lymphoma ($n = 2$), and hemangioma, hemangiosarcoma, and metastatic spread ($n = 3$). On the other hand, another small series [8] reported ultrasound-guided spleen biopsy using the Surecut needle (21 G) for staging of non-Hodgkin's lymphoma in eight patients without focal lesions and a normal or slightly enlarged spleen. A lymphomatous infiltration was detected histologically in only two of the eight cases.

In 1992 Cavanna et al. [9] described results of ultrasound-guided tissue core biopsies (Surecut needle, 21–22 G) in 48 patients for staging of an underlying lymphoma. In 12 of the 48 patients (25%), lymphomatous infiltration of the spleen was detected, 8 of which had focal lesions visualized sonographically. Ultrasound showed splenomegaly in three patients and a normal spleen in only one. The same group [13] reported 160 ultrasound-guided spleen biopsies for diagnosis of metastatic spread between 1993 and 2003. The results were lymphoma in 122 cases and metastatic spread in 13 cases.

Modern imaging and laboratory diagnostics have reduced the need for spleen biopsy, especially for staging of lymphomatous diseases. This led to a shift to therapeutic spleen interventions, e.g., CT-guided abscess drainage [11, 12].

Technical aspects

Diagnostic minilaparoscopy does not always enable visualization of the entire spleen. This may be especially difficult in patients with a normal spleen size or who are obese. Use of additional instruments such as a probe or forceps can be helpful for mobilization of the omentum and spleen. We analyzed the yield of all splenic biopsies but we do not know the potential failure rate of minilaparoscopic spleen visualization. Dagnini et al. [5] reported failure of spleen visualization in 4% of diagnostic laparoscopies. Because diagnostic minilaparoscopy is a comparable technique, a similar failure rate can be assumed.

Minilaparoscopy enables one-step guided biopsies of liver, peritoneum, and spleen in patients with suspicious focal lesions or systemic diseases such as fever of unknown origin. In our series infiltration of both liver and spleen could be detected in seven patients due to tuberculosis, sarcoidosis, lymphoma, and Q-fever, and in one patient tuberculosis was also diagnosed in a peritoneal biopsy.

Ultrasound-guided biopsy using the fine-needle aspiration technique yields rather small cytologic samples, whereas laparoscopy-guided tissue core biopsy yields histologic specimens using Menghini or the automatic Tru-Cut needle with a minimum diameter of 18 G. This is beneficial for an exact histologic examination, especially when lymphoma is suspected, where immunohistochemical analysis is essential [10]. Moreover, sufficient biopsy material allows an additional microbiological culture or diagnostic PCR tests.

Complications

Bleeding was laparoscopically seen immediately after spleen biopsy in almost every case. It was stopped effectively using APC or fibrin glue and no delayed bleeding complication occurred. This is in accordance with a series of laparoscopic spleen biopsies that reported sufficient hemostasis using a compression technique via a probe or application of fibrin glue [5].

An early review of 11,700 abdominal fine-needle biopsies (intra- and extraperitoneal, mainly ultrasound guided, 20–23 G) reported an overall complication rate of 0.55%, with one death due to necrotizing pancreatitis after biopsy of a enlarged normal pancreas; a major complication rate of 0.05% (two cases of biliary peritonitis, two tumor seedings, one intrahepatic hematoma, and one peritonitis); and a minor complication rate of 0.49% (mainly moderate hemorrhage, pain, and fever) [22].

Another small series [11] described strong bleeding after spleen biopsy with the need to perform a splenectomy in three cases (8%): two were found to have a vascularized splenic tumor upon histology, and one patient had a splenic abscess.

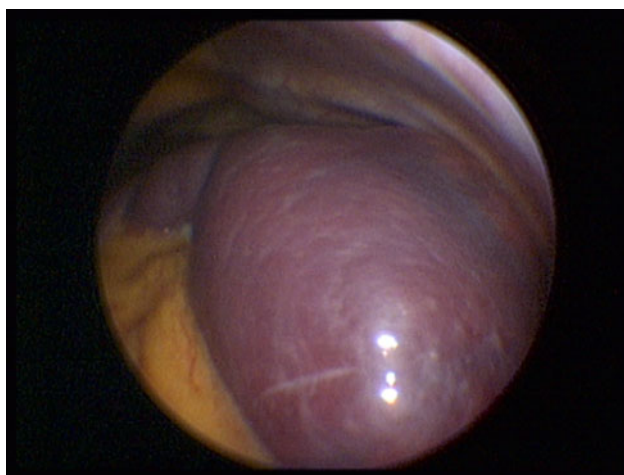
An Italian multicenter study [10] analyzing 398 ultrasound-guided fine-needle biopsies of the spleen reported a total complication rate of 5%. Severe complications such as bleeding or pneumothorax occurred in 1% and there were no procedure-related deaths. Similar to our study, other case series have reported no minor or severe complications [8, 9, 13, 23]. To prevent delayed bleeding complications, laparoscopic hemostasis of the puncture site seems to be beneficial. Notably in our study two patients with splenic hemangioma and two patients with a low platelet count below 50/nl were biopsied without complications.

Conclusion

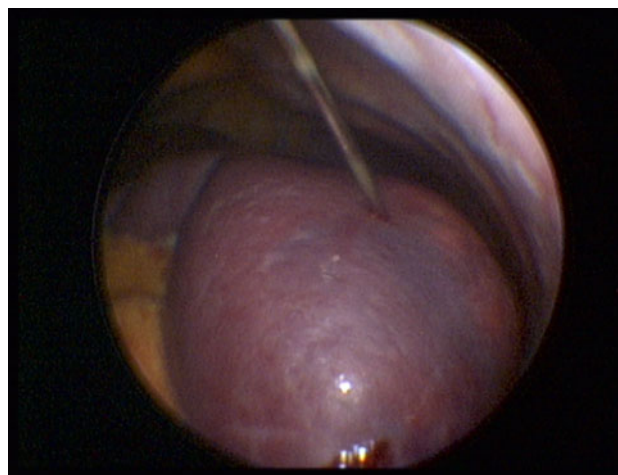
Although modern imaging and laboratory diagnostics often obviate the need for histologic confirmation, splenic biopsy may be useful for achieving a definitive diagnosis in selected patients. Minilaparoscopic splenic biopsy performed outside the operating room with the patient under conscious sedation is a safe technique with a high diagnostic yield, especially in patients with focal splenic lesions. Laparoscopic hemostasis after biopsy prevents delayed bleeding complications.

Case report

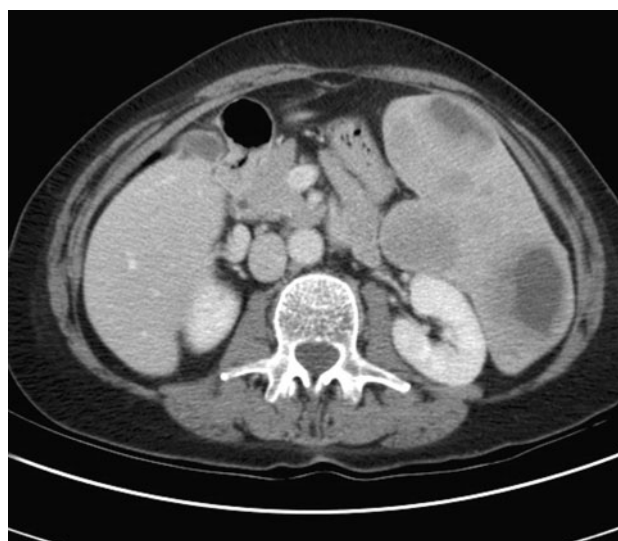
A 60-year-old woman was referred to our department for evaluation of splenic mass lesions and night sweats after



Picture 1 Lower spleen pole



Picture 2 Splenic puncture with Bard needle 18 G



Picture 3 Abdomen CT with mass lesions in the spleen

her primary-care physician noted multiple splenic mass lesions on routine abdominal ultrasound. We performed a minilaparoscopy-guided splenic biopsy. The histologic examination defined (confirmed) a B-cell non-Hodgkin's lymphoma. To date, the patient has received eight cycles of chemotherapy (R-CHOEP) with a complete response and she is doing well (Pictures 1, 2, 3).

Disclosures Dr. Tobias Werner, Dr. Johannes Koch, Dr. Christian Frenzel, Prof. Dr. Ansgar W. Lohse, and PD Dr. Ulrike W. Denzer have no conflicts of interest or financial ties to disclose.

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