

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2023 July 27; 15(7): 1262-1558



REVIEW

- 1262 Pathophysiological consequences and treatment strategy of obstructive jaundice
Liu JJ, Sun YM, Xu Y, Mei HW, Guo W, Li ZL

MINIREVIEWS

- 1277 Carbon footprints in minimally invasive surgery: Good patient outcomes, but costly for the environment
Chan KS, Lo HY, Shelat VG

ORIGINAL ARTICLE**Basic Study**

- 1286 Primary animal experiment to test the feasibility of a novel Y-Z magnetic hepatic portal blocking band
Zhang MM, Li CG, Xu SQ, Mao JQ, Ren YX, Zhang YH, Ma J, Shi AH, Lyu Y, Yan XP
- 1294 Magnetic compression anastomosis for reconstruction of digestive tract after total gastrectomy in beagle model
Zhang MM, Li CG, Xu SQ, Mao JQ, Zhang YH, Shi AH, Li Y, Lyu Y, Yan XP
- 1304 Differences in metabolic improvement after metabolic surgery are linked to the gut microbiota in non-obese diabetic rats
Luo X, Tan C, Tao F, Xu CY, Zheng ZH, Pang Q, He XA, Cao JQ, Duan JY
- 1317 Intervention effects and related mechanisms of glycyrrhizic acid on zebrafish with Hirschsprung-associated enterocolitis
Liu MK, Chen YJ, Chen F, Lin ZX, Zhu ZC, Lin Y, Fang YF, Wu DM
- 1331 Histological study of the structural layers around the esophagus in the lower mediastinum
Saito T, Muro S, Fujiwara H, Umabayashi Y, Sato Y, Tokunaga M, Akita K, Kinugasa Y

Case Control Study

- 1340 Liver transplantation for combined hepatocellular carcinoma and cholangiocarcinoma: A multicenter study
Kim J, Joo DJ, Hwang S, Lee JM, Ryu JH, Nah YW, Kim DS, Kim DJ, You YK, Yu HC
- 1354 Optimal choice of stapler and digestive tract reconstruction method after distal gastrectomy for gastric cancer: A prospective case-control study
Wu Z, Zhou ZG, Li LY, Gao WJ, Yu T

Retrospective Cohort Study

- 1363 Impact of perioperative blood transfusion on oncological outcomes in ampullary carcinoma patients underwent pancreaticoduodenectomy
Fei H, Zhang XJ, Sun CY, Li Z, Li ZF, Guo CG, Zhao DB

Retrospective Study

- 1375 Nomogram based on clinical characteristics for predicting overall survival in gastric cancer patients with preoperative anemia
Long Y, Zhou XL, Zhang CL, Wang YN, Pan WS
- 1388 Major complications after ultrasound-guided liver biopsy: An annual audit of a Chinese tertiary-care teaching hospital
Chai WL, Lu DL, Sun ZX, Cheng C, Deng Z, Jin XY, Zhang TL, Gao Q, Pan YW, Zhao QY, Jiang TA
- 1397 Different percutaneous transhepatic biliary stent placements and catheter drainage in the treatment of middle and low malignant biliary obstruction
Yang YB, Yan ZY, Jiao Y, Yang WH, Cui Q, Chen SP
- 1405 Utilization of deep neuromuscular blockade combined with reduced abdominal pressure in laparoscopic radical gastrectomy for gastric cancer: An academic perspective
Zhang YW, Li Y, Huang WB, Wang J, Qian XE, Yang Y, Huang CS
- 1416 Efficacy of peritoneal drainage in very-low-birth-weight neonates with Bell's stage II necrotizing enterocolitis: A single-center retrospective study
Shen Y, Lin Y, Fang YF, Wu DM, He YB
- 1423 Emergency exploratory laparotomy and radical gastrectomy in patients with gastric cancer combined with acute upper gastrointestinal bleeding
Kuang F, Wang J, Wang BQ
- 1434 Correlation of serum albumin level on postoperative day 2 with hospital length of stay in patients undergoing emergency surgery for perforated peptic ulcer
Xie D, Lu PL, Xu W, You JY, Bi XG, Xian Y

Clinical Trials Study

- 1442 Laboratory scoring system to predict hepatic indocyanine green clearance ability during fluorescence imaging-guided laparoscopic hepatectomy
Chen ZR, Zeng QT, Shi N, Han HW, Chen ZH, Zou YP, Zhang YP, Wu F, Xu LQ, Jin HS

Observational Study

- 1454 Incidence, characteristics and risk factors for alveolar recruitment maneuver-related hypotension in patients undergoing laparoscopic colorectal cancer resection
Zhang NR, Zheng ZN, Wang K, Li H
- 1465 New classification system for radical rectal cancer surgery based on membrane anatomy
Jiang HH, Ni ZZ, Chang Y, Li AJ, Wang WC, Lv L, Peng J, Pan ZH, Liu HL, Lin MB

Randomized Controlled Trial

- 1474 Transcutaneous electrical acupoint stimulation in adult patients receiving gastrectomy/colorectal resection: A randomized controlled trial
Hou YT, Pan YY, Wan L, Zhao WS, Luo Y, Yan Q, Zhang Y, Zhang WX, Mo YC, Huang LP, Dai QX, Jia DY, Yang AM, An HY, Wu AS, Tian M, Fang JQ, Wang JL, Feng Y

SYSTEMATIC REVIEWS

- 1485 Combined and intraoperative risk modelling for oesophagectomy: A systematic review
Grantham JP, Hii A, Shenfine J
- 1501 Spleen-preserving distal pancreatectomy from multi-port to reduced-port surgery approach
Hsieh CL, Tsai TS, Peng CM, Cheng TC, Liu YJ
- 1512 Resection of isolated liver oligometastatic disease in pancreatic ductal adenocarcinoma: Is there a survival benefit? A systematic review
Halle-Smith JM, Powell-Brett S, Roberts K, Chatzizacharias NA

META-ANALYSIS

- 1522 Outcome of split liver transplantation *vs* living donor liver transplantation: A systematic review and meta-analysis
Garzali IU, Akbulut S, Aloun A, Naffa M, Aksoy F

CASE REPORT

- 1532 Idiopathic hypereosinophilic syndrome with hepatic sinusoidal obstruction syndrome: A case report and literature review
Xu XT, Wang BH, Wang Q, Guo YJ, Zhang YN, Chen XL, Fang YF, Wang K, Guo WH, Wen ZZ
- 1542 Reoperation for heterochronic intraductal papillary mucinous neoplasm of the pancreas after bile duct neoplasm resection: A case report
Xiao G, Xia T, Mou YP, Zhou YC
- 1549 Successful resection of colonic metastasis of lung cancer after colonic stent placement: A case report and review of the literature
Nakayama Y, Yamaguchi M, Inoue K, Hamaguchi S, Tajima Y

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Georgios Tsoulfas, AGAF, FACS, FICS, MD, PhD, Professor, Transplant Surgery, Aristotle University of Thessaloniki School of Medicine, Thessaloniki 54124, Greece. tsoulfas@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS, World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, etc.

INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJGS* as 2.0; IF without journal self cites: 1.9; 5-year IF: 2.2; Journal Citation Indicator: 0.52; Ranking: 113 among 212 journals in surgery; Quartile category: Q3; Ranking: 81 among 93 journals in gastroenterology and hepatology; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Rui-Rui Wu, Production Department Director: Xiang Li, Editorial Office Director: Jia-Ru Fan.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Peter Schemmer

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

July 27, 2023

COPYRIGHT

© 2023 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Retrospective Study

Major complications after ultrasound-guided liver biopsy: An annual audit of a Chinese tertiary-care teaching hospital

Wei-Lu Chai, Dan-Lei Lu, Zhong-Xia Sun, Chao Cheng, Zhuang Deng, Xin-Yan Jin, Tong-Long Zhang, Qiong Gao, Yu-Wei Pan, Qi-Yu Zhao, Tian-An Jiang

Specialty type: Gastroenterology and hepatology

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Gutierrez-Cuevas J, Mexico; Manesis EK, Greece

Received: February 11, 2023

Peer-review started: February 11, 2023

First decision: March 26, 2023

Revised: April 5, 2023

Accepted: May 6, 2023

Article in press: May 6, 2023

Published online: July 27, 2023



Wei-Lu Chai, Dan-Lei Lu, Zhong-Xia Sun, Xin-Yan Jin, Tong-Long Zhang, Qiong Gao, Yu-Wei Pan, Qi-Yu Zhao, Tian-An Jiang, Department of Ultrasonography, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, Zhejiang Province, China

Chao Cheng, Zhuang Deng, Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, Zhejiang Province, China

Corresponding author: Tian-An Jiang, PhD, Chief Doctor, Researcher, Teacher, Department of Ultrasonography, The First Affiliated Hospital, Zhejiang University School of Medicine, No. 79 Qingchun Road, Hangzhou 310003, Zhejiang Province, China. tiananjiang@zju.edu.cn

Abstract

BACKGROUND

As ultrasound-guided percutaneous liver biopsy (PLB) has become a standard and important method in the management of liver disease in our country, a periodical audit of the major complications is needed.

AIM

To determine the annual incidence of major complications following ultrasound-guided PLB and to identify variables that are significantly associated with an increased risk of major complications.

METHODS

A total of 1857 consecutive cases of PLB were included in our hospital from January 2021 to December 2021. The major complication rate and all-cause 30-d mortality rate were determined. Multivariate analyses were performed by logistic regression to investigate the risk factors associated with major complications and all-cause 30-d mortality following ultrasound-guided PLB.

RESULTS

In this audit of 1857 liver biopsies, 10 cases (0.53%) of major complications occurred following ultrasound-guided PLB. The overall all-cause mortality rate at 30 d after PLB was 0.27% (5 cases). Two cases (0.11%) were attributed to major hemorrhage within 7 d after liver biopsy. Fibrinogen less than 2 g/L [odds ratio (OR): 17.226; 95% confidence interval (CI): 2.647-112.102; $P = 0.003$], post-biopsy hemoglobin level (OR: 0.963; 95% CI: 0.942-0.985; $P = 0.001$), obstructive jaundice

(OR: 6.698; 95%CI: 1.133-39.596; $P = 0.036$), application of anticoagulants/antiplatelet medications (OR: 24.078; 95%CI: 1.678-345.495; $P = 0.019$) and age (OR: 1.096; 95%CI: 1.012-1.187; $P = 0.025$) were statistically associated with the incidence of major complications after PLB.

CONCLUSION

In conclusion, the results of this annual audit confirmed that ultrasound-guided PLB can be performed safely, with a major complication rate within the accepted range. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

Key Words: Liver; Percutaneous; Biopsy; Ultrasound; Complication

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Ultrasound-guided percutaneous liver biopsy has become a standard and important method in the management of liver disease. This annual audit confirmed that ultrasound-guided percutaneous liver biopsy is safely performed, with a major complication rate within the accepted range and in line with previously published data. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

Citation: Chai WL, Lu DL, Sun ZX, Cheng C, Deng Z, Jin XY, Zhang TL, Gao Q, Pan YW, Zhao QY, Jiang TA. Major complications after ultrasound-guided liver biopsy: An annual audit of a Chinese tertiary-care teaching hospital. *World J Gastrointest Surg* 2023; 15(7): 1388-1396

URL: <https://www.wjgnet.com/1948-9366/full/v15/i7/1388.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v15.i7.1388>

INTRODUCTION

Image-guided liver biopsy is a widely accepted technique and a standard diagnostic procedure that is usually performed to assess diffuse liver disease by nontargeted biopsy or to diagnose a specific hepatic abnormality by targeted biopsy[1, 2]. Ultrasound is the main imaging modality for percutaneous liver biopsy (PLB) because of its real-time multiplanar scanning capabilities and lack of radiation exposure. Generally, the most common type of liver biopsy is ultrasound-guided PLB, which is a safe and effective procedure; however, this procedure does have risks[1-3].

Complications following PLB vary widely and have been examined in both prospective and retrospective studies; the reported rate of PLB-related major adverse events was 0.70%-1.06%. The literature suggests that the mortality directly related to PLB ranges from 0.01% to 0.20%, and the all-cause mortality rate is approximately 0.2%[2-6]. The most commonly reported and concerning severe complication of PLB is hemorrhage, and the frequency of moderate to severe bleeding varies from 0% to 5.3%[7,8].

A recent investigation emphasized that coagulation status and patient-related factors contributed to a high risk of major complications following PLB[7]. The practice guidelines recommended that there should be local and national audits on liver biopsy to ensure that the complication rates were within the accepted range[3]. As ultrasound-guided PLB has become a standard and important method in the management of liver disease in our country, a periodical audit on its application and complications is needed to ensure that the complication rate is within the accepted range and to further optimize the procedure. Therefore, we carried out this study to determine the annual incidence of major complications following ultrasound-guided PLB in a Chinese tertiary-care teaching hospital and to identify significant variables associated with an increased risk of major complications.

MATERIALS AND METHODS

Patients and design

The Quality Management Division of our hospital initiated this retrospective annual audit of severe adverse events after ultrasound-guided PLB following the Standard Operating Procedure of Data Validation, which was certificated by Joint Commission International. Our institutional review board approved this audit and waived related informed consent according to the regulations of the ethics committee. A total of 1857 consecutive cases of ultrasound-guided PLB performed in a Chinese tertiary-care teaching hospital in a major metropolitan area from January 2021 to December 2021 were included. Cases of PLB combined with hepatic drainage or drug injection were also included, but cases involving targeted biopsies performed just before thermal ablation of hepatic tumors were excluded. Hematological tests, which included routine blood examination and coagulation tests within 7 d before PLB, were needed, and on the day after PLB, the level of hemoglobin was routinely examined. The data on patient demographics, laboratory tests, prebiopsy images,

PLB details (objectives, operators and techniques), pathology results, major complications and peri-biopsy management were collected from digital medical records and the picture archiving and communication system according to a predefined standardized protocol and entered into worksheets (Microsoft Office Excel 2007; Microsoft, Redmond, Wash) by ten radiology trainees.

Ultrasound-guided PLB

Ultrasound guidance was defined as the use of ultrasound or contrast-enhanced ultrasound to obtain real-time visualization of the whole course of PLB, which included prebiopsy imaging assessment, needle advancement and triggering and post-biopsy imaging assessment. In our center, all ultrasound-guided PLBs were performed as inpatient procedures by interventional radiologists with adequate training, and the patients were observed in the hospital overnight.

The indications for PLB in our center were as follows: (1) Determine the nature and/or grade of hepatic tumors; (2) Investigate the reason for abnormal liver function tests; (3) Determine the severity of liver damage; and (4) Obtain liver tissue for non-histological assessment (microbiology, biochemical, other).

Absolute contraindications for PLB were as follows: (1) International normal ratio (INR) > 1.5; (2) Prothrombin time (PT) prolonged 5 s; and (3) Platelet count < $50 \times 10^9/L$. Biliary dilatation, ascites and lack of cooperation of the patient were considered partial contraindications. Where a biopsy was performed outside guidelines or standardized protocols, multidisciplinary consultation was performed prior to biopsy, and decisions were reflected in medical records.

In our institution, discontinuation of antiplatelet medication or anticoagulants was requested (antiplatelet medication and warfarin: At least 5 d before PLB; heparin and related products: 12-24 h before PLB). After PLB, antiplatelet therapy was resumed after 2-3 d, and warfarin was restarted the following day. The risk of discontinuing anticoagulant/antiplatelet medication was strictly weighed against the potential risk of hemorrhage during PLB. Patients who used antiplatelet medications and anticoagulants were recorded, even though peri-biopsy administration strictly conformed to the above regulations.

Under local anesthesia, two passes by an 18-gauge (G) Tru-cut needle (Tru-cut; Angiotech, Gainesville, FL, United States) with a fully automatic device was the standard technique for targeted or nontargeted liver biopsy. Coaxial cutting needle biopsy with or without plugging by gelatin sponge while withdrawing the introduction was based on the clinical indication and operator's preference. Contrast-enhanced ultrasonography with SonoVue (contrast agent, Bracco, Milan, Italy) or Sonazoid (contrast agent, GE Healthcare, United States) was an important tool for evaluating the vascularization of target lesions or the patent biopsy method, differentiating necrotic tissue from tumorous tissue and identifying hemorrhage events during the whole course of PLB. SonoVue was supplied as lyophilized powder and reconstituted with 5 mL of saline to make a homogeneous microbubble suspension; 2.4 mL of this suspension was administered per bolus, followed by a 5-mL physiologic saline flush. The Sonazoid was supplied as 16 μ L perfluorobutane microspheres and reconstituted with 2 mL of distilled water to make a homogeneous microbubble suspension; 0.12 μ L (0.015 mL)/kg of this suspension was administered per bolus, followed by a 5-mL physiologic saline flush. A total of 18 operators in our center performed ultrasound-guided PLB, and 5 of them had more than 10 years of experience in abdominal intervention.

The following pertinent variables were investigated and collected: platelet count; PT; fibrinogen; prebiopsy hemoglobin level; comorbidity; application of anticoagulant/antiplatelet medication; operator's experience; biopsy technique; objective of biopsy; number of passes to obtain adequate tissue specimens; post-biopsy application of hemostatic medication; location of target; multilesion; maximum diameter of target; post-biopsy hemoglobin level; repeat biopsy; and histological diagnosis. Exploratory analyses were conducted to identify any statistically significant variables that might be implicated in major complications.

Definitions

This audit focused on the identification of major complications, especially mortality directly related to ultrasound-guided PLB. The major complication in this study was defined according to the Quality Improvement Guidelines for Percutaneous Needle Biopsy of the Society of Interventional Radiology, including bleeding requiring transfusion or intervention, prolonged hospitalization, requiring major therapy, unplanned increase in level of care and permanent adverse sequelae or death. The main complications following PLB are liver hematoma (symptomatic or asymptomatic), pain, vasovagal reactions, hemothorax, hemoperitoneum, pneumothorax, hemobilia, bile leakage, organ perforation (gallbladder, colon) and arteriovenous fistula. Clinically significant hemorrhage is the most common and is defined as a decrease in hemoglobin level of more than 2.0 g/dL and a change in vital signs with radiologic evidence of bleeding necessitating blood transfusion. An acute major complication was defined as one that occurred less than 24 h after PLB, and a delayed major complication was defined as one that occurred more than 24 h after PLB. Overall all-cause mortality was also calculated by 30 d after PLB. All the included factors of both the major complication group and the no major complication group were compared, and the independent predictors for the occurrence of major complications after PLB were identified. Clinical, radiological and technical variables were investigated statistically for their association with all-cause 30-d mortality following PLB.

Data analysis

The differences in categorical variables between the major complication group and the no major complication group were presented as percentages and were compared using the χ^2 or Fisher's exact test, as appropriate. Normally distributed variables were expressed as the mean \pm standard deviation and were compared with the Student's *t* test. Nonnormally distributed variables were expressed as medians (quartile 1, quartile 3) and were compared by nonparametric tests (Mann-Whitney *U* test). Multivariate analyses were performed by a forward step (likelihood ratio) multivariable logistic regression model to investigate the risk factors associated with major complications and all-cause 30-d mortality

following ultrasound-guided PLB. All statistical tests were two-sided. A *P* value less than 0.05 was considered statistically significant. All analyses were performed using SPSS software (version 20.0, SPSS Inc., Chicago, IL, United States).

RESULTS

A total of 1857 biopsies were performed and included; 1108 (59.7%) patients were male. The mean age of the patients was 55.1 ± 17.8 years. Biopsy pathology revealed hepatocellular carcinoma (278, 15.0%), intrahepatic cholangiocarcinoma (225, 12.1%), secondary hepatic tumors (518, 27.9%), liver abscesses (91, 4.9%), chronic liver disease (393, 21.2%) and others (352, 18.9%). Demographic, clinical, procedural and pathological characteristics of the patients in the major complication and no major complication groups are listed in [Table 1](#).

In this audit of 1857 liver biopsies, 10 cases (0.53%) of major complications occurred following ultrasound-guided PLB, 9 of which were associated with clinically severe hepatic hemorrhage and 1 of which was associated with hemothorax. More than one complication might occur in 1 patient. Among 9 cases of severe hepatic hemorrhage, 1 case was combined with severe infection, 2 cases with hemoperitoneum and 1 case with hemothorax. The overall all-cause mortality rate at 30 d after PLB was 0.27% (5 cases), and 2 cases (0.11%) were attributed to major hemorrhage within 7 d after liver biopsy. No patients experienced pneumothorax. Eight of ten major complications (80%) occurred acutely within 24 h.

Except for blood transfusion, 4 patients received emergency laparotomy, 1 patient who had delayed artery pseudoaneurysm after liver biopsy required transcatheter embolization, 2 patients who had post-biopsy active bleeding underwent ultrasound-guided microwave ablation and local thrombin injection, and 1 patient who had hemoperitoneum underwent percutaneous drainage of fluid collection.

Univariate correlates of the occurrence of major complications following ultrasound-guided PLB were age, patients with obstructive jaundice, prebiopsy hemoglobin level, fibrinogen less than 2 g/L, prebiopsy application of anticoagulants/antiplatelet medications, post-biopsy application of hemostatic medication and post-biopsy hemoglobin level. The objective of PLB, operator experience, biopsy technology, characteristics of targets, number of specimens and histological diagnosis were not contributing factors for major complications ([Table 1](#)). Multivariable analysis revealed that obstructive jaundice [odds ratio (OR): 6.698; 95% confidence interval (CI): 1.133-39.596; *P* = 0.036], fibrinogen less than 2 g/L (OR: 17.226; 95%CI: 2.647-112.102; *P* = 0.003), prebiopsy application of anticoagulants/antiplatelet medication (OR: 24.078; 95%CI: 1.678-345.495; *P* = 0.019), post-biopsy hemoglobin level (OR: 0.963; 95%CI: 0.942-0.985; *P* = 0.001) and age (OR: 1.096; 95%CI: 1.012-1.187; *P* = 0.025) were statistically associated with an increased risk of major complications after PLB ([Table 2](#)). The patients with obstructive jaundice had a 6.7-fold increased risk of major complications. The patients with a fibrinogen level less than 2 g/L had a 2.1% risk of major complications compared with 0.3% for the patients with a fibrinogen level greater than 2 g/L. Although strictly followed by the recommendations on the peri-biopsy administration of anticoagulants or antiplatelet medications, the risk of major complications was also significantly increased compared with the patients who had not used anticoagulants or antiplatelet medications. The post-biopsy hemoglobin level was a meaningful indicator for the occurrence of major complications, and the older patients were more likely to develop major complications following PLB. For all-cause 30-d mortality after PLB, the prebiopsy hemoglobin level (OR: 0.963; 95%CI: 0.928-0.999; *P* = 0.042) and post-biopsy hemoglobin level (OR: 0.958; 95%CI: 0.930-0.987; *P* = 0.005) were deemed statistically meaningful predictors ([Table 2](#)).

DISCUSSION

Ultrasound-guided PLB plays an increasingly important role in the management of liver disease or abnormal liver function tests[1-3] as well as in patients with a diagnostic dilemma[9]. It is important to maintain the safety of liver biopsy and control the potential risks as the volume of liver biopsies increases worldwide. The results of this annual audit of 1857 liver biopsies in Chinese tertiary-care teaching hospitals confirmed that the incidence of major complications (0.53%) following ultrasound-guided PLB was low and in line with published data from other parts of the world[2-8].

The reported morbidity and mortality associated with PLB varies extensively[10]. An American multicenter study included 2740 liver biopsies for patients with advanced chronic liver disease. The rate of serious adverse events was 1.1%, and the bleeding rate was 0.58%[4]. The analysis of elective PLBs collected from the National Health Service of England showed that death within 7 d directly related to liver biopsy occurred in approximately 1 in 10000 biopsies, and the major hemorrhage rate was 0.6%[5]. From Australian audits on percutaneous core liver biopsies, major complications occurred in 12 patients (1.0%); 7 patients had an abnormal baseline coagulation profile[11]. A systematic review concluded that the rate of major bleeding after liver biopsy ranged from 0.1% to 4.6%[7]. In accordance with these previous large-scale reports, the major complication rate, the overall all-cause 30-d mortality and the biopsy-related mortality from our study were within the expected parameters, and post-biopsy hemorrhage accounted for the main source of adverse events.

The risk factors for complications in the published literature vary considerably. In this audit, the factors influencing the incidence of major complications and mortality following ultrasound-guided PLB were explored. Patient-related factors primarily influenced the occurrence of major complications, but operator-related or procedure-related factors were not found, even though needle size and hepatic malignancy were identified as risk factors in the published literature[3,4,6-8,12,13]. Older age was deemed to be associated with a significantly higher likelihood of post-biopsy major complications. This finding was supported by several studies, which noted that patient age > 50 years or < 2 years significantly increased the risk[3,7,14].

Table 1 Demographic, clinical, procedural and pathological characteristics of patients in the major complication and no major complication groups

Variables	Major complication, <i>n</i> = 10, %	No major complication, <i>n</i> = 1847, %	<i>P</i> value
Sex			
Male	8, 80.0	1100, 59.6	0.189
Female	2, 20.0	747, 40.4	
Age, median (Q1, Q3)	65.0 (54.5, 76.3)	58.0 (47.0, 67.0)	0.156
Comorbidity			
Cardiovascular and cerebrovascular diseases	2, 20.0	238, 12.9	0.504
Extensive ascites	0, 0	35, 1.9	0.660
Obstructed jaundice	3, 30.0	137, 7.4	0.007
Laboratory test			
Platelet count < 50 × 10 ⁹ /L	0, 0	15, 0.8	0.922
Prebiopsy hemoglobin level, median (Q1, Q3)	112.5 (76.5, 126.3)	125.0 (112, 139)	0.027
Fibrinogen < 2 g/L	5, 50.0	228, 12.3	< 0.001
PT prolonged 5 s	1, 10.0	63, 3.4	0.255
Objectives of PLB			
Focal liver lesions	8, 80.0	1346, 72.9	0.336
Diffuse liver disease	2, 20.0	501, 27.1	
Prebiopsy application of anticoagulants/antiplatelet medication/Y	2, 20.0	79, 4.5	0.02
Postbiopsy application of hemostatic medication/Y	9, 90.0	462, 26.6	< 0.001
Operator/10-yr experience	6, 60.0	665, 36.0	0.115
Biopsy technique			
Bare introduction Tru-cut (18G)	6, 60.0	922, 49.9	0.525
Coaxial introduction Tru-cut (18G)	4, 40.0	925, 50.1	
Location of targets			
Right	6, 75.0	1046, 73.0	0.659
Left	1, 12.5	301, 21.0	
Hilar	1, 12.5	86, 6.0	
The maximum diameter of targets, median (Q1, Q3)	2.8 (1.7, 6.3)	3.3 (2.1, 5.9)	0.514
Multilesion/Y	4, 44.0	848, 60.2	0.336
Post-biopsy hemoglobin level, median (Q1, Q3)	81.0 (65.3, 107.8)	114.7 (109.0, 126.0)	0.001
Repeat biopsy/Y	0, 0	30, 1.6	0.685
Number of specimens, median (Q1, Q3)	2 (2.0, 2.3)	2 (2.0, 2.0)	0.553
Histological analysis			
HCC	0, 0	278, 15.1	0.094
ICC	3, 30.0	222, 12.0	
Secondary hepatic tumor	2, 20.0	516, 27.9	
Liver abscess	1, 10.0	90, 4.9	
Chronic liver disease	0, 0	393, 21.3	
Others	4, 40.0	348, 18.8	

HCC: Hepatocellular carcinoma; ICC: Intrahepatic cholangiocarcinoma; PLB: Percutaneous liver biopsy; PT: Prothrombin time; Q: Quartile; Y: Yes.

Table 2 Risk factors related to increased risk of major complications and all-cause 30-d mortality

	β	OR (95%CI)	P value
Risk factors for major complication			
Obstructed jaundice	1.902	6.698 (1.133-39.596)	0.036
Fibrinogen < 2 g/L	2.846	17.226 (2.647-112.102)	0.003
Prebiopsy application of anticoagulants/antiplatelet medications	3.181	24.078 (1.678-345.495)	0.019
Postbiopsy hemoglobin level	-0.037	0.963 (0.942-0.985)	0.001
Age	0.091	1.096 (1.012-1.187)	0.025
Risk factors for all-cause 30-d mortality			
Prebiopsy hemoglobin	-0.038	0.963 (0.928-0.999)	0.042
Postbiopsy hemoglobin	-0.043	0.958 (0.930-0.987)	0.005

CI: Confidence interval; OR: Odds ratio.

Practice guidelines recommend that liver biopsy should be performed for biliary obstruction only when there is doubt about the diagnosis and the benefit to the patient outweighs the risk, such as biliary peritonitis, septicemic shock and death[3]. Our study also demonstrated that the risk of major complications was significantly higher in patients with obstructive jaundice. This may be ascribed to the nature and location of the biopsy targets; they were more likely to be tumors of biliary origin and developed adjacent to the hepatic vessels. Therefore, it should be carefully assessed during the liver biopsy procedure to prevent adjacent vessel puncture.

As the level of prebiopsy platelet count and PT/INR were strictly evaluated and controlled, the level of fibrinogen appeared to be more of a limiting issue for the following major complications. In the majority of studies, the hemorrhagic complication rates increased as the INR increased and platelet counts decreased[2,3,15-17]. A previous study suggested that the fibrinogen level, platelet count < 30 × 10⁹/L and elevated INR were the best routine coagulation parameters for the prediction of new onset of major bleeding[7,17,18]. The function of fibrinogen has not been verified in the cohort of liver biopsies in situations where the platelet count and PT/INR were within the recommended range. The cutoff level of fibrinogen in this analysis was the lower limit of the reference value of fibrinogen tested in our hospital, which varied between different laboratories. Therefore, patients with consumptive coagulopathy and low fibrinogen are at high risk of post-biopsy bleeding.

Although we strictly followed the recommendations on the peri-biopsy administration of anticoagulants or antiplatelet medications, the patients with a history of anticoagulants or antiplatelet medications had a major complication rate that was comparable to that of patients who had not received these drugs. For anticoagulants or antiplatelet medications interfering with coagulation status or platelet function, especially under the development of new relevant drugs, a predominantly increased frequency of bleeding was identified and demonstrated by several large-scale reports[3,19]. As with all clinical decisions, the risks of discontinuing the coagulants or antiplatelet medications should be carefully balanced with the benefit of liver biopsy. If appropriate, consultant advice may be needed.

The post-biopsy hemoglobin level was associated with major complications and all-cause 30-d mortality following ultrasound-guided PLB. Major hemorrhage, which is the most common severe complication of liver biopsy, is defined as a decrease in hemoglobin level of more than 2.0 g/dL and a change in vital signs with radiologic evidence of bleeding[7, 20]. Therefore, the change in hemoglobin strongly predicts ongoing blood loss. The risk of all-cause mortality at 30 d after PLB increased as the prebiopsy hemoglobin level decreased, which has not been reported before. By case review, the deaths were combined with hematological disease, autoimmune disease or late malignancy; the level of hemoglobin was much lower compared with controls. Whether these comorbidities influenced the incidence of post-biopsy all-cause mortality was understudied.

There are important limitations to our study. First, this was a single-center, annual audit initiated by the Quality Management Division of our hospital. The adverse events after PLB were retrospectively examined by reviewing the electronic medical records. The documentation was incomplete if the patient left our hospital, and the incidence may be inaccurate. A large-scale, multicenter and prospective study is warranted to validate the findings of our study, especially the administration of peri-biopsy coagulants/antiplatelet medications and the assessment of the baseline coagulation profile. Second, under the introduction of a coaxial system, the use of biopsy track plugging by gelatin sponges was based on the operator's preference in our hospital. Therefore, the impact of this technique was unclear and under investigated. Third, the diagnostic yield of ultrasound-guided PLB in this audit was not obtained and analyzed.

CONCLUSION

The results of this annual audit confirmed that ultrasound-guided PLB can be safely performed in our hospital, with a major complication rate within the accepted range and in line with previously published data. This study highlighted the

administration of peri-biopsy coagulants/antiplatelet medications and coagulation parameters, especially fibrinogen levels. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

ARTICLE HIGHLIGHTS

Research background

As ultrasound-guided percutaneous liver biopsy (PLB) has become a standard and important method in the management of liver disease in our country, a periodical audit of the major complications is needed.

Research motivation

As ultrasound-guided PLB has become a standard and important method in the management of liver disease in our country, a periodical audit on its application and complications is needed to ensure that the complication rate is within the accepted range and to further optimize the procedure. Therefore, we carried out this study to determine the annual incidence of major complications following ultrasound-guided PLB in a Chinese tertiary-care teaching hospital and to identify significant variables associated with an increased risk of major complications.

Research objectives

The aim of this study was to determine the annual incidence of major complications following ultrasound-guided PLB and to identify variables that were significantly associated with an increased risk of major complications.

Research methods

A total of 1857 consecutive cases of PLB were included in our hospital from January 2021 to December 2021. The major complication rate and all-cause 30-d mortality rate were determined. Multivariate analyses were performed by logistic regression to investigate the risk factors associated with major complications and all-cause 30-d mortality following ultrasound-guided PLB.

Research results

In this audit of 1857 liver biopsies, 10 cases (0.53%) of major complications occurred following ultrasound-guided PLB. The overall all-cause mortality rate at 30 d after PLB was 0.27% (5 cases), and 2 cases (0.11%) were attributed to major hemorrhage within 7 d after liver biopsy. Fibrinogen less than 2 g/L [odds ratio (OR): 17.226; 95% confidence interval (CI): 2.647-112.102; $P = 0.003$], post-biopsy hemoglobin level (OR: 0.963; 95% CI: 0.942-0.985; $P = 0.001$), obstructive jaundice (OR: 6.698; 95% CI: 1.133-39.596; $P = 0.036$), application of anticoagulants/antiplatelet medications (OR: 24.078; 95% CI: 1.678-345.495; $P = 0.019$) and age (OR: 1.096; 95% CI: 1.012-1.187; $P = 0.025$) were statistically associated with the incidence of major complications after PLB.

Research conclusions

In conclusion, the results of this annual audit confirmed that ultrasound-guided PLB can be performed safely, with a major complication rate within the accepted range. Strict patient selection and peri-biopsy laboratory assessment are more important than procedural factors for optimizing the safety outcomes of this procedure.

Research perspectives

A large-scale, multicenter and prospective study is warranted to validate the findings of our study, especially the administration of peri-biopsy coagulants/antiplatelet medications and the assessment of the baseline coagulation profile.

FOOTNOTES

Author contributions: Jiang TA and Chai WL contributed to conceptualization; Chai WL, Lu DL and Jiang TA contributed to data curation; Chai WL and Sun ZX contributed to formal analysis; Jiang TA contributed to funding acquisition and resources; Chai WL, Cheng C, Jin XY, Deng Z, Zhang TL, Zhao QY and Jiang TA contributed to investigation; Chai WL and Gao Q contributed to methodology; Jiang TA, Sun ZX, Zhao QY, Lu DL and Pan YW contributed to project administration; Chai WL and Lu DL contributed software; Zhao QY, Jiang TA and Sun ZX contributed to supervision; Chai WL and Jiang TA contributed to validation; Chai WL contributed to writing the original draft; Zhao QY and Jiang TA contributed to reviewing and editing.

Institutional review board statement: Ethical approval was obtained from the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine before the study.

Informed consent statement: The requirement for informed consent was waived due to the retrospective nature of the study.

Conflict-of-interest statement: All the authors report having no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Tian-An Jiang 0000-0002-7672-8394.

S-Editor: Gao CC

L-Editor: Filipodia

P-Editor: Wu RR

REFERENCES

- 1 **Khalifa A**, Rockey DC. The utility of liver biopsy in 2020. *Curr Opin Gastroenterol* 2020; **36**: 184-191 [PMID: 32097176 DOI: 10.1097/MOG.0000000000000621]
- 2 **Sidhu PS**, Brabrand K, Cantisani V, Correas JM, Cui XW, D'Onofrio M, Essig M, Freeman S, Gilja OH, Gritzmann N, Havre RF, Ignee A, Jenssen C, Kabaalioglu A, Lorentzen T, Mohaupt M, Nicolau C, Nolsøe CP, Nürnberg D, Radzina M, Saftoiu A, Serra C, Spàrchez Z, Sporea I, Dietrich CF. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part II. Diagnostic Ultrasound-Guided Interventional Procedures (Long Version). *Ultraschall Med* 2015; **36**: E15-E35 [PMID: 26669871 DOI: 10.1055/s-0035-1554036]
- 3 **Neuberger J**, Patel J, Caldwell H, Davies S, Hebditch V, Hollywood C, Hubscher S, Karkhanis S, Lester W, Roslund N, West R, Wyatt JJ, Heydtmann M. Guidelines on the use of liver biopsy in clinical practice from the British Society of Gastroenterology, the Royal College of Radiologists and the Royal College of Pathology. *Gut* 2020; **69**: 1382-1403 [PMID: 32467090 DOI: 10.1136/gutjnl-2020-321299]
- 4 **Seeff LB**, Everson GT, Morgan TR, Curto TM, Lee WM, Ghany MG, Shiffman ML, Fontana RJ, Di Bisceglie AM, Bonkovsky HL, Dienstag JL; HALT-C Trial Group. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. *Clin Gastroenterol Hepatol* 2010; **8**: 877-883 [PMID: 20362695 DOI: 10.1016/j.cgh.2010.03.025]
- 5 **West J**, Card TR. Reduced mortality rates following elective percutaneous liver biopsies. *Gastroenterology* 2010; **139**: 1230-1237 [PMID: 20547160 DOI: 10.1053/j.gastro.2010.06.015]
- 6 **Boyum JH**, Atwell TD, Schmit GD, Poterucha JJ, Schleck CD, Harmsen WS, Kamath PS. Incidence and Risk Factors for Adverse Events Related to Image-Guided Liver Biopsy. *Mayo Clin Proc* 2016; **91**: 329-335 [PMID: 26837481 DOI: 10.1016/j.mayocp.2015.11.015]
- 7 **Midia M**, Odedra D, Shuster A, Midia R, Muir J. Predictors of bleeding complications following percutaneous image-guided liver biopsy: a scoping review. *Diagn Interv Radiol* 2019; **25**: 71-80 [PMID: 30644369 DOI: 10.5152/dir.2018.17525]
- 8 **Howlett DC**, Drinkwater KJ, Lawrence D, Barter S, Nicholson T. Findings of the UK national audit evaluating image-guided or image-assisted liver biopsy. Part II. Minor and major complications and procedure-related mortality. *Radiology* 2013; **266**: 226-235 [PMID: 23143026 DOI: 10.1148/radiol.12120224]
- 9 **Rockey DC**, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. *Hepatology* 2009; **49**: 1017-1044 [PMID: 19243014 DOI: 10.1002/hep.22742]
- 10 **Tian G**, Kong D, Jiang T, Li L. Complications After Percutaneous Ultrasound-Guided Liver Biopsy: A Systematic Review and Meta-analysis of a Population of More Than 12,000 Patients From 51 Cohort Studies. *J Ultrasound Med* 2020; **39**: 1355-1365 [PMID: 31999005 DOI: 10.1002/jum.15229]
- 11 **van der Poorten D**, Kwok A, Lam T, Ridley L, Jones DB, Ngu MC, Lee AU. Twenty-year audit of percutaneous liver biopsy in a major Australian teaching hospital. *Intern Med J* 2006; **36**: 692-699 [PMID: 17040353 DOI: 10.1111/j.1445-5994.2006.01216.x]
- 12 **Chi H**, Hansen BE, Tang WY, Schouten JN, Sprengers D, Taimr P, Janssen HL, de Knegt RJ. Multiple biopsy passes and the risk of complications of percutaneous liver biopsy. *Eur J Gastroenterol Hepatol* 2017; **29**: 36-41 [PMID: 27556687 DOI: 10.1097/MEG.0000000000000731]
- 13 **Fotiadis N**, De Paepe KN, Bonne L, Khan N, Riddell A, Turner N, Starling N, Gerlinger M, Rao S, Chau I, Cunningham D, Koh DM. Comparison of a coaxial vs non-coaxial liver biopsy technique in an oncological setting: diagnostic yield, complications and seeding risk. *Eur Radiol* 2020; **30**: 6702-6708 [PMID: 32666317 DOI: 10.1007/s00330-020-07038-7]
- 14 **Mueller M**, Kratzer W, Oetzuerk S, Wilhelm M, Mason RA, Mao R, Haenle MM. Percutaneous ultrasonographically guided liver punctures: an analysis of 1961 patients over a period of ten years. *BMC Gastroenterol* 2012; **12**: 173 [PMID: 23216751 DOI: 10.1186/1471-230X-12-173]
- 15 **Atwell TD**, Smith RL, Hesley GK, Callstrom MR, Schleck CD, Harmsen WS, Charboneau JW, Welch TJ. Incidence of bleeding after 15,181 percutaneous biopsies and the role of aspirin. *AJR Am J Roentgenol* 2010; **194**: 784-789 [PMID: 20173160 DOI: 10.2214/AJR.08.2122]
- 16 **Sag AA**, Brody LA, Maybody M, Erinjeri JP, Wang X, Wimmer T, Silk M, Petre EN, Solomon SB. Acute and delayed bleeding requiring embolization after image-guided liver biopsy in patients with cancer. *Clin Imaging* 2016; **40**: 535-540 [PMID: 27133700 DOI: 10.1016/j.clinimag.2015.11.004]
- 17 **Drolz A**, Horvatits T, Roedl K, Rutter K, Staufner K, Kneidinger N, Holzinger U, Zauner C, Schellongowski P, Heinz G, Perkmann T, Kluge S, Trauner M, Fuhrmann V. Coagulation parameters and major bleeding in critically ill patients with cirrhosis. *Hepatology* 2016; **64**: 556-568 [PMID: 27124745 DOI: 10.1002/hep.28628]
- 18 **Hung A**, Garcia-Tsao G. Acute kidney injury, but not sepsis, is associated with higher procedure-related bleeding in patients with decompensated cirrhosis. *Liver Int* 2018; **38**: 1437-1441 [PMID: 29393567 DOI: 10.1111/liv.13712]
- 19 **Strobel D**, Bernatik T, Blank W, Will U, Reichel A, Wüstner M, Keim V, Schacherer D, Barreiros AP, Kunze G, Nürnberg D, Ignee A, Burmester E, Bunk AA, Friedrich-Rust M, Froehlich E, Schuler A, Jenssen C, Bohle W, Mauch M, Dirks K, Kaemmer J, Pachmann C, Stock J, Hocke M, Kendel A, Schmidt C, Jakobeit C, Kinkel H, Heinz W, Hübner G, Pichler M, Müller T. Incidence of bleeding in 8172 percutaneous ultrasound-guided intraabdominal diagnostic and therapeutic interventions - results of the prospective multicenter DEGUM interventional ultrasound study (PIUS study). *Ultraschall Med* 2015; **36**: 122-131 [PMID: 25876060 DOI: 10.1055/s-0034-1399282]

- 20 **Maheux A**, Purcell Y, Harguem S, Vilgrain V, Ronot M. Targeted and non-targeted liver biopsies carry the same risk of complication. *Eur Radiol* 2019; **29**: 5772-5783 [PMID: [31076864](#) DOI: [10.1007/s00330-019-06227-3](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

