DOI:10.34084/bshr.1126347 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

http://dergipark.org.tr/tr/pub/bshr

Liver Biopsy in Chronic Hepatitis Patients: Our Single Center Experience

Kronik Hepatit Hastalarında Karaciğer Biyopsisi: Tek Merkez Deneyimimiz

Seyhmus Kavak[1], Safak Kaya[2], Ayhan Senol[1]

[1] University of Health Sciences, Gazi Yaşargil Training and Research Hospital, Radiology Clinic, Diyarbakir, Turkey

[2] University of Health Sciences, Gazi Yaşargil Training and Research Hospital, Infectious Diseases and Clinical Microbiology Clinic, Diyarbakir, Turkiye

ORCID ID: Şafak Kaya https://orcid.org/0000-0001-9912-7340, Seyhmus Kavak https://orcid.org/0000-0002-5426-7478, Ayhan Senol https://orcid.org/0000-0001-5467-0307

***Sorumlu Yazar / Corresponding Author:** Şafak Kaya **e-posta / e-mail:** ksafak76@gmail.com

Geliş Tarihi / Received : 05-06-2022 **Kabul Tarihi / Accepted:** 13-07-2022 **Yayın Tarihi / Online Published:** 31-08-2022

Kavak S, Kaya S, Senol A. Liver Biopsy in Chronic Hepatitis Patients: Our Single Center Experience, J Biotechnol and Strategic Health Res. 2022;6(2):174-179

Abstract

Aim Liver biopsy, which is used to determine fibrosis in patients with chronic hepatitis B, is an invasive procedure and may have complications. In this study, we planned to evaluate blinded and ultrasonography (USG)-guided liver biopsies and compare complications.

Material and Method This is a retrospective study containing the data of a total of 436 chronic hepatitis B patients who underwent liver biopsy in our hospital.

Results 150 (34.4%) of the patients included in the study were female, and the mean age was 33.3±13.1/year. Complications developed in 174 (39.9%) of the patients. Of these, 110 (51.9%) developed in patients who underwent blind biopsy, 64 (28.6%) developed in patients who underwent USG guided biopsy, and the difference was statistically significant ($p<0.001$). Among the major complications, bleeding developed only in 2 (0.5%) patients who underwent blind biopsy, and bile leakage in 2 (0.5%) patients who underwent blind biopsy. No major complications were observed in any of the patients who underwent USG guidance. Minor complications were also detected predominantly in patients who underwent blind biopsy.

Conclusion Liver biopsy is still a reliable method in terms of complications in the evaluation of fibrosis in patients followed up with chronic hepatitis B. Minor complications are less common in USG-guided biopsies.

Keywords Chronic hepatitis B, liver biopsy, complication

Özet

Amaç *Kronik hepatit B hastalarında fibrozisin belirlenmesinde kullanılan karaciğer biyopsisi invaziv bir işlem olması nedeniyle beraberinde komplikasyonları da olabilmektedir. Biz bu çalışmada kör ve ultrasonografi (USG) eşliğinde yapılan karaciğer biyopsilerini değerlendirmeyi, komplikasyonları karşılaştırmayı planladık.*

Gereç ve Yöntem *Bu çalışma hastanemizde karaciğer biyopsisi yapılan toplam 436 kronik hepatit B hastasının verisini içeren bir çalışmadır.*

Bulgular *Çalışmaya alınan hastaların 150 (%34,4)si kadın, yaş ortalaması 33,3±13,1 /yıl idi. Hastaların 174 (%39,9)ünde komplikasyon gelişmişti. Bunların 110 (%51,9)u kör biyopsi yapılan hastalarda, 64 (%28,6)ü ise USG eşliğinde biyopsi yapılan hastalarda gelişmişti ve aradaki fark istatistiksel olarak anlamlıydı ($p<0.001$). Major komplikasyonlardan kanama sadece kör biyopsi yapılan 2 (%0,5) hastada yine safra kaçağı kör biyopsi yapılan 2 (%0,5) hastada gelişmişti. Ultrasonografi eşliğinde yapılan hiçbir hastada major komplikasyon görülmemişti. Minör komplikasyonlar da ağırlıklı olarak kör biyopsi yapılan hastalarda tespit edilmişti.*

Sonuç *Kronik hepatit B ile takip edilen hastaların fibrozisinin değerlendirilmesinde karaciğer biyopsisi komplikasyonlar açısından hala güvenilir bir yöntemdir. Minör komplikasyonlar USG eşliğinde yapılan biyopsilerde daha az görülmektedir.*

Anahtar Kelimeler *Kronik hepatit B, karaciğer biyopsi, komplikasyon*

INTRODUCTION

Chronic hepatitis B (CHB) is an important problem that concerns the world population. The World Health Organization reported that there were approximately 257 million people infected with hepatitis B virus (HBV) in the world in 2015, and an estimated 887,000 people died from HBV-related complications in the same year[1-3]. The effective vaccination programs in many countries have resulted in a significant reduction in the incidence of HBVinfection. Despite this, it is still an important cause of morbidity and mortality[4].

The age, comorbidity, and family history should be taken into account when making a treatment decision in a patient followed up for CHB. The level of HBV DNA and alanine aminotransferase (ALT) and the degree of liver disease are the most important criteria in making this decision. Although the use of non-invasive tests has increased recently in defining the degree of liver disease and determining fibrosis, liver biopsy is still used[5]. Liver biopsy can be performed percutaneously, transjugularly, laparoscopically and intraoperatively. Percutaneous biopsy can also be performed with palpation/percussion, accompanied by blind biopsy and ultrasonography (USG)[6,7]. However, biopsy is an invasive procedure and it should be kept in mind that minor/major complications may develop. In this study, we aimed to evaluate blinded and USG-guided liver biopsies and to compare complications.

METHODS

This study includes the data of a total of 436 patients who were hospitalized in the Infectious Diseases Clinic of our hospital between 2011-2019 and underwent liver biopsy. The ethics committee approval for the study was obtained from the Medical Ethics Committee of our hospital (Date/Number: 02.07.2021/821). The consent was obtained from all patients before biopsy was performed. Anticoagulant drugs were discontinued 7 days before. Platelet count, prothrombin and partial thromboplastin times were studied before biopsy. Blind biopsy was performed in 212 (48.6%) patients, and ultrasound guided biopsy was performed in 224 (51.4%) patients. Epidemiological data such as age, gender, underlying diseases and complications of the patients were obtained from the hospital database and files. The data of patients who underwent blind biopsy and those who underwent USG guided biopsy were compared.

Biopsy procedures

Blind biopsy was performed by an infectious diseases specialist in the infectious diseases service, using a single-use (Hepafix®, B.Braun Melsungen AG, Germany) set containing Menghini type needle. The patients were fasted for at least 8 hours before the procedure. The patient was placed in the supine position and the right hand was placed under the head. Starting from under the right clavicle with percussion, the liver dullness was determined and the area to be entered was marked. The biopsy site was wiped with 1% povidone iodine and then cleaned with alcohol. The area was covered with a sterile drape. In the marked interval, local anesthesia was performed with 2-4 ml of lidocaine over the lower rib. An incision was made above the lower rib. Progress was made by entering through the incision with a biopsy needle. The needle was entered towards the xiphoid and parallel to the ground. After passing the skin and subcutaneous tissues, the plunger was held back while the needle was advanced. Then, a small amount of saline was poured to clear the occlusive tissues in the needle without entering the liver capsule. At the same time, the patient was asked to fully exhale and remain in expiration. The plunger of the injector was retracted. The needle was pushed into the liver and then quickly removed. The biopsy material taken was placed in formol solution.

Ultrasonography-guided liver biopsy was performed by an expert radiologist in the interventional radiology unit. All patients were processed in the supine position. Before the biopsy procedure, the biopsy area was prepared under standard sterile conditions and the patient was covered with a sterile drape, except for the biopsy area. A sterile sheath was placed on the USG probe. Local anesthesia was

applied to the skin first, then to the subcutaneous tissues and liver capsule in the planned transition line. After local anesthesia, a small incision was made on the skin and under the guidance of USG, vascular structures were avoided and a 17G coaxial needle was inserted into the liver parenchyma. The co-axial system consists of an outer cannula and an inner needle (Stile) system. It provides the opportunity to take more than one tissue sample with a single parenchymal passage and to apply embolizing material through the system in case of possible bleeding. The inner needle (stylet) was removed and the 18G needle automatic biopsy gun (Tru-Core™ II) was inserted into the cannula. And biopsy samples were taken. If there was arterial or disturbing amount of venous bleeding before the cannula was removed, a bioabsorbable sponge plug was applied through the cannula and hemostasis was achieved throughout the trace. After the biopsy, the patients were placed on the right side and pressure was applied to the biopsy area. Blood pressure and heart rate were monitored every 15 minutes for the first two hours, and every 30 minutes for the next four hours, by administering intravenous fluids.

Statistical analysis

Data analysis was done in SPSS's Windows 22.0 package program. Whether the distribution of continuous variables was close to normal was investigated using the Shapiro Wilk test. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables, and frequency analysis and percentage (%) for categorical variables. The significance of the difference between the groups in terms of means was investigated using the Mann-Whitney U test. Categorical variables were analyzed with Pearson's Chi-Square test. For $p<0.05$, the results were considered statistically significant.

RESULTS

Of the 436 patients included in the study, 150 (34.4%) were female, and the mean age was 33.3±13.1/year (min-max: 15-78). Forty-nine (11.2%) patients had comorbidities [diabetes mellitus: 16 (3.7%), hypertension: 15 (3.4%), coronary artery disease: 10 (2.3%), rheumatic disease: 3 (0.7%), chronic lung disease: 5 (1.1%)]. Blind biopsy was performed in 212 (48.6%) patients (group 1), and USG guided biopsy was performed in 224 (51.4%) patients (group 2). Evaluation could not be made because insufficient material was taken in 12 (2.8%) of the patients. Complications developed in 174 (39.9%) patients (Table 1).

Table 1. Characteristics of patients with CHB who underwent liver biopsy

Variable	n (%)
Age±SD	33.3±13.1
Gender	
Female	150 (34.4)
Male	286 (65.6)
Biopsy size, mm ± SD	11.8±5.8
Comorbidity	
Diabetes mellitus	16 (3.7)
Hypertension	15 (3.4)
Coronary artery disease	10 (2.3)
Rheumatic disease	3 (0.7)
Chronic lung disease	5 (1.1)
Complication	174
Pain	135 (31)
Nausea	58 (13.3)
Vomiting	28 (6.4)
Bleeding	2 (0.5)
Bile leakage	2 (0.5)
Insufficient sample	12 (2.8)

Of these, 110 (51.9%) developed in group 1 patients, 64 (28.6%) developed in group 2 patients, and the difference was statistically significant ($p<0.001$). Pain was present in 135 (31%) patients, nausea in 58 (13.3%), vomiting in 28 (6.4%), intra-abdominal bleeding in 2 (0.5%), and bile leakage in 2 (0.5%). Of the patients in group 1, 86 (40.6%) had pain, 35 (16.5%) nausea, 16 (7.5%) vomiting, 2 (0.9%) bleeding, 2 (0.9%) bile leakage was available. In Group 2 patients, 49 (21.9%) had pain, 23 (10.3%) had nausea, 12 (5.4%) had vomiting, and no bleeding or bile leakage was observed. There was a significant difference in pain be-

tween the two groups (p<0.001). (Table 2).

Table 2. Comparison of complications in patients who underwent blind liver biopsy (group 1) and USG guided biopsy (group 2).

Variable	Group 1 (N=212)	Group 2 (N=224)	P value
Pain	86 (40.6 %)	49 (21.9 %)	<0.001
Vomiting	16 (7.5 %)	12 (5.4 %)	0.351
Nausea	35 (16.5 %)	23 (10.3 %)	0.055
Bile leakage	2 (0.9 %)	0 (0 %)	<0.001
Bleeding	2 (0.9 %)	0 (0 %)	<0.001
Insufficient material	12 (5.7 %)	0 (0 %)	<0.001

DISCUSSION

Liver biopsy is considered the gold standard for evaluating fibrosis due to CHB. Liver biopsy is a method that still maintains its importance in the diagnosis of liver diseases, although imaging methods have been developed and used frequently[8]. Since it is an invasive procedure, complications observed during and after the procedure can sometimes be serious. Factors such as biopsy technique and the experience of the physician who performed the biopsy affect the development of complications. Liver biopsy can be performed in three ways: percutaneous, transvenous, and laparoscopic[9,10]. Percutaneous liver biopsies can be performed in two different ways as fine needle aspiration biopsy (FNAB) or cutting needle biopsy (tru-cut). In our study, biopsies performed with blinded FNAB and ultrasonography-guided cutting needle biopsy were taken. The complication rate due to percutaneous liver biopsy is 1-5% and the mortality rate is 0.01-0.009%. Percutaneous biopsies using imaging modalities have largely prevented the complications of blind biopsy[11]. Pain may develop at the biopsy site or in the right shoulder. The most common complication is pain and is seen in 25-30% of patients[12]. It is thought that the negative pressure created in blind biopsies performed with the menghini method causes more pain after biopsy[13]. In the study of Weigand et al., in which 715 patients were evaluated, pain complications developed in 40 (5.6%) patients that did not require analgesics and in 13 (1.8%) patients that required analgesics[14]. Pain developed in a total of 31% of our patients. Most of these developed after blind biopsy and the difference between the two methods was significant. In the study of Vivas et al., 18% of patients developed pain, and the majority were women (30% vs. 15%)[15]. It was determined by Onay et al. that severe pain developed in 2.9% of patients with CHB who underwent USG-guided biopsy[16]. Pain developed in 21.9% of our patients who underwent biopsy with USG. Medication was required in only 9.3% (n=21) of these patients. In the our study, other minor complications such as nausea and vomiting were also at a lower rate after USG-guided biopsy. Bleeding is the most common cause of mortality in patients undergoing biopsy. Therefore, bleeding parameters should be closely monitored before and after biopsy. While intra or perihepatic bleeding can be seen in 20% of cases after percutaneous biopsy, blood transfusion may be required in approximately 1 in 500 biopsies[17-18]. Bleeding developed in only 0.5% of our patients, and these patients were patients who underwent blind biopsy. The incidence of biliary peritonitis is less than 2%. In our patients, bile leakage developed only in 2 patients who underwent blind biopsy.No major complications were observed after the USG-guided biopsy. None of the patients developed exitus. The size of the material obtained in the biopsy is important for the diagnosis. It is widely believed that if the biopsy material is 15 mm long, it will contain at least 6-8 portal areas and this will be sufficient[19]. The average size of the biopsy material we obtained from our patients was 11.8 mm. Twelve patients with insufficient material were those who underwent blind biopsy. In the study of Flemming et al., which included 100 chronic hepatitis C patients, it was reported that higher quality samples were obtained than blind biopsy in liver biopsies performed under USG guidance[20].

CONCLUSION

Liver biopsy is still a reliable method in terms of complications in the evaluation of fibrosis in patients followed up with CHB. In our study, it was found that minor com-

plications were seen less frequently when performed with USG. Although major complications in blind biopsy are very rare, they were not seen in patients who underwent USG-guided biopsy.

Conflict of interest

There is no person/organization that financially supports the work and the authors have no conflict of interest.

References

1. Maynard JE. Hepatitis B: global importance and need for control. Vaccine. 1990 Mar;8 Suppl:S18-20
2. Ott JJ, Stevens GA, Groeger J,et al. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine. 2012;30(12):2212-2219.
3. World Health Organization. Global hepatitis report, 2017. [Updated 2017]. [Accessed December18, 2020].https://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455- eng.pdf;jsessionid=DC3616B5BDF94FA8B6AC2FDBC71E5B51?sequence=1.
4. World Health Organization. Hepatitis B. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b (Accessed on March 13, 2022).
5. Yapali S, Talaat N, Lok AS. Management of hepatitis B: our practice and how it relates to the guidelines. Clin Gastroenterol Hepatol. 2014; 12:16-26.
6. Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology. 2009;49:1017-44.
7. Khalifa A, Rockey DC. The utility of liver biopsy in 2020. Curr Opin Gastroenterol. 2020;36:184-191.
8. Büyükkaya R, Oktay M, Büyükkaya A, ve ark. Kronik Viral Hepatitli Hastalarda Ultrasonografi Eşliğinde Kesici İğne İle Yapılan Perkutan Karaciğer Biyopsilerinin Değerlendirilmesi. Abant Med J. 2014; 3(2): 112-115.
9. İnci MF, Özkan F, Balaban O. Ultrasonografi Eşliğinde 18 G Kesici İğne İle Yapılan Perkütan Karaciğer Kitle Biyopsileri: Klinik Tecrübemiz. Abant Med J. 2012; 1(3):140-143.
10. Ahn HS, Kim SM, Jang M, et al. Comparison of sonography with sonographically guided fineneedle aspiration biopsy and core-needle biopsy for initial axillary staging of breast cancer. J Ultrasound Med. 2013; 32(12): 2177-2184.
11. Güner R, Baykam N. Which one should be prefered: liver biopsy or non-invasive procedures? Viral Hepat J. 2017;23:63-64.
12. Filingeri V, Sforza D, Tisone G. Complications and risk factors of a large series of percutaneous liver biopsies in patients with liver transplantation or liver disease. Eur Rev Med Pharmacol Sci. 2015;19 (9):1621-1629.
13. Karacaer Z, Yılmaz Karadağ F, Durmuş G, et al. Percutaneous liver needle biopsy methods can be safe and effective in patients with viral hepatitis. Viral Hepat J. 2017;23:65-70.
14. Weigand K, Weigand K. Percutaneous liver biopsy: retrospective study over 15 years comparing 287 inpatients with 428 outpatients. J Gastroenterol Hepatol. 2009;24(5):792-799.
15. Vivas S, Palacio MA, Rodríguez M, et al. Ambulatory liver biopsy: complications and evolution in 264 cases. Rev Esp Enferm Dig. 1998;90(3):175-182.
16. Onay M, Altay ÇM, Binboğa AB. Ultrason Kılavuzluğunda Karaciğer Biyopsisi. Ankara Üniversitesi Tıp Fakültesi Mecmuası. 2022;75(1):97-102
17. Firpi RJ, Soldevila–Pico C, Abdelmalek MF, et al. Short recovery time after percutaneous liver biopsy: should we change our current practices? Clin Gastroenterol Hepatol. 2005;3(9):926-929.
18. Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology. 2009;49(3):1017-1044.
19. Colloredo G, Guido M, Sanzogni A, et al. Impact of liver biopsy size on histo-logical evaluation of cronic viral hepatitis: the smaller the sample, the milder the disease. J Hepatol. 2003;39: 239-244.
20. Flemming JA, Hurlbut DJ, Mussari B, et al. Liver biopsies for chronic hepatitis C: should nonultrasound-guided biopsies be abandoned?. Can J Gastroenterol. 2009;23(6):425-430.