Percutaneous Liver Biopsies: Safety and Efficacy

Perkütan Karaciğer Biyopsileri: Güvenilirlik ve Etkinlikleri

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ABSTRACT Objective: The aim of this study was to evaluate effecacy and safety of percutaneous liver biopsy performed under the assistance of ultrasonography in diffuse liver disease. **Material and Methods:** This was a retrospective study. We evaluated the ultrasound-assisted liver biopsy procedures of 784 patients which were performed in an outpatient setting between October 2001 and July 2008. The liver biopsies were performed following one-night fasting using disposable Menghini-type suction needles (16 gauge) after marking the best seen part of the best-thickest liver part distant from the adjacent organs. Liver portion suitable for biopsy was marked in the intercostal area by the use of ultrasonography and performed by an experienced gastroenterologist. After the biopsies, the vital signs of all patients were monitored for 6-8 hours. The patients without any problems were discharged on the same day. The shapes, sizes and number of the biopsy specimens were recorded, and then they were sent to the pathology department for histolopathological examination. The next day, control ultrasounds of all patients were performed. **Results:** Macroscopically adequate tissue was obtained in 780 cases (99.5%) with a mean tissue length of 15.5 mm. In 755 patients (96.4%), adequate tissue sample was obtained after one pass. After the procedure, severe pain requiring analgesia was seen in 13 patients (1.6%). There was no complication requiring hospitalisation. Major complication requiring intervention occurred in only one patient with chronic renal failure undergoing hemodialysis (0.12%). There were no deaths resulting from liver biopsies. **Conclusion:** According to the results of our series, we conclude that routine ultrasound of the puncture site is a quick, effective and, safe procedure. The complication rate is very low. The ultrasound assisted percutaneous liver biopsy modality should be used to all cases.

Key Words: Liver; biopsy, needle; ultrasonography; complications

ÖZET Amaç: Diffüz karaciğer hastalıklarında perkütan karaciğer biyopsilerinin ultrasonografi kılavuzluğunda yapılması durumunda, etkinliğinin ve güvenilirliğinin değerlendirilmesidir. **Gereç ve Yöntemler:** Bu geriye dönük çalışmada 2001 Ekim ile 2008 Temmuz ayları arasında, ayakta takip edilen 784 hastanın ultrasonografi kılavuzluğunda yaptığımız karaciğer biyopsisi işlemini değerlendirdik. Biyopsiler, bir gecelik açlığı takiben, ultrasonografi deneyimi olan gastroenterologlar tarafından karaciğerin en iyi-kalın ve komşu organlardan uzak kısmının en iyi görüldüğü yerin interkostal alanda işaretlenmesinden sonra, tek kullanımlık Menghini tipi biyopsi iğneleri (16 gauge) kullanılarak yapıldı. Biyopsilerden sonra, 6-8 saat boyunca, tüm hastaların yaşamsal bulguları takip edildi. Herhangi bir sorun gelişmeyen hastalar aynı gün taburcu edildi. Biyopsi örneklerinin şekilleri, büyüklükleri ve parçaların sayıları kaydedilerek histopatolojik inceleme için patoloji bölümüne gönderildi. Bir sonraki gün tüm hastaların kontrol ultrasonografileri yapıldı. **Bulgular:** Yedi yüz seksen hastada (%99.5), ortalama 15.5 mm uzunluğunda yeterli doku elde edildi. Yediyüzellibeş hastada (%96.4) yeterli doku örneği, ilk girişte elde edildi. İşlemden sonra, karaciğer biyopsisi yapılan 13 hastada (%1.6) analjezi gerektiren ciddi ağrı oldu. Hastaneye yatış gerektiren komplikasyon olmadı. Müdahale gerektiren ciddi komplikasyon, hemodiyalize giren kronik böbrek yetmezliği olan bir hastada gelişti (%0.12). Biyopsilerden kaynaklanan ölüm olmadı. **Sonuç:** Çalışmamızın sonuçlarına göre, biyopsi giriş yerinin rutin ultrasonu ardından yapılan perkütan karaciğer biyopsisinin, hızlı, etkili ve güvenilir bir işlem olduğunu söyleyebiliriz. Komplikasyon oranı çok düşüktür. Tüm olgularda karaciğer biyopsisinin ultrasonografi kılavuzluğunda yapılması gerektiğini düşünüyoruz.

Anahtar Kelimeler: Karaciğer; biyopsi, iğne; ultrasonografi; komplikasyonlar

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Despite the advances in imaging techniques and serological investigations, in many liver diseases, liver biopsy is still a gold standart to diagnose, prognosticate, and help to determine the treatment.[1-10] Although liver biopsy has been accepted as a safe procedure, some complications may occur in up to 5% of the patients, including pain requiring hospital admissions (1-5%), failure to obtain tissue (2%), bleeding requiring transfusion (0.3%), bleeding requiring surgery (0.04%), pneumothorax (0.35%), and obtaining other tissues (0.5%).[1,2,5,11] The complications of percutaneous liver biopsy have been classified as minor (pain, transient hypotension) and major (significant hypotension, pneumothorax, hemothorax, hemoperitoneum, hemobilia, intrahepatic hematoma, cardiac arrhythmia, gallbladder perforation, puncture of the kidney, colon or pancreas) complications.[2,3,5] Overall mortality rate is less than 0.1% and death is usually due to bleeding or to biliary peritonitis secondary to puncture of gallbladder.[2] For this reason, many physicians avoid liver biopsy as an invasive procedure, and seek alternative methods. However, liver biopsy gives valuable information about many conditions. Therefore, attempts to increase safety and decrease complications of liver biopsy should be made.

There are several approaches for liver biopsy, and several techniques have been suggested to decrease the complication rates of the procedure and to increase its diagnostic accuracy.[2] While the majority of liver biopsies are still performed blindly by transcostal approach using an aspiration or cutting-type needle, there is an increasing use of ultrasound assistance to establish most suitable access to the thicker liver parenchyma (assessing the most favorable angulation of the needle too), avoiding the puncture of adjacent organs.[1,12,13] Liver biopsy seems safer when performed by the assistance of ultrasound.[2,11] Nevertheless, routine use of ultrasound assistance for liver biopsies has not gained widespread acceptance, and it accounted for only one third of all biopsies performed.[14] Ultrasound is helpful for the localization of liver, especially in obese individuals, patients with chronic obstructive lung disease or when ascites is present.[3,5,12] There is also a statistically significant decrease in the complication rates of liver biopsies when performed under ultrasound guidance.[1,3,5,8-10,15-18] The major complication rates such as gallbladder puncture and pneumothorax are seen more with blinded percutaneous biopsies when compared to the ultrasound guidance.[3,6,18] Ultrasonography aids directing the biopsy needle away from the other tissues and large blood vessels, additionally the operator can choose the correct depth of the needle.[2] The complication rates differ in the literature according to different reports. Major complication rate of biopsies under ultrasound guidance ranges between 0.25-1.28% (mean, 0.86%), while this ratio reaches to 5.4% when the biopsys is performed blindly.[2]

Although several studies have examined the efficacy and complication rates of percutaneous liver biopsy performed by the assistance of ultrasound, these studies are not enough to predict the ultrasonography as a selected method for percutaneous liver biopsy. Moreover, as far as we know, thereno studies have reported the results of the ultrasound-assisted liver biopsies from Turkey. Therefore, we performed this study to reveal the efficacy and safety of the liver biopsy under the assistance of ultrasonography, performed in a long time in a large patient population.

MATERIAL AND METHODS

We reviewed 784 ultrasound-assisted percutaneous liver biopsy procedures retrospectively which were performed between October 2001 and July 2008. There were 429 males and 355 females. The average age was 45 years (between 15-73 years). The indications for liver biopsies were listed in Table 1. Before the biopsies, all patients were informed about the procedure and its risks. All subjects gave written informed consents. The hemograms, prothrombin times, international normalized ratios and activated partial thromboplastin times of all patients were checked before the procedure. The liver biopsies were performed in an outpatient setting with a standard method: following one-night fasting, the puncture site was marked in the intercostal region at the best seen part of the best-thickest liver distant

TABLE 1: Indications of the liver biopsies.

Indications of the liver biopsies	No. of patients
Ch. Hepatitis C	347
Ch. Hepatitis B	253
Ch. Hepatitis D	7
Autoimmune Liver Disease	9
Ch. Hepatitis B+C	7
Hepatitis B+NAFLD	1
Hepatitis B+AFLD	1
Fatty Liver Disease	99
Primary Biliary Cirrhosis	9
Metabolic Liver Disease	4
Cholestasis	5
Hepatoportal Sclerosis	4
Toxic Hepatitis	3
Abnormal Liver Function Tests	14
Cryptogenic Cirrhosis	2
Storage Disease	1
Portal Hypertension	1
Celiac Disease	1
Miscellaneous	13

Ch: chronic, NAFLD: non-alcoholic fatty liver disease, AFLD: alcoholic fatty liver disease.

from the adjacent organs ultrasound and the biopsy was performed by experienced gastroenterologists. No more than 1 min was necessary for such a determination. Hitachi EUB-525 ultrasonography with convex probe 3.5-MHz transducer was used. After cleansing with povidon-iodine, 5-10 ml prilokain 2% for local anaesthesia was injected to the marked region and to the passage site of biopsy needle, while the patient was lying on the bed and his/her right arm raised. The biopsy was performed in inspiratory apnea. The shapes, sizes and, number of the biopsy specimens were recorded, and then they were sent to the pathology department for histopathological examination. After the procedure, the vital signs of all patients were monitored for the probable complications for 6-8 hours, and the signs were recorded. Later, the patients without any problems were discharged and advised to rest at home for 24 hours, and to contact to us or nearest hospital in the case of any problem. The next day, control ultrasounds of all biopsy performed patients were evaluated for any complications.

RESULTS

In 780 cases (99.5%), adequate tissue was obtained macroscopically, furthermore 768 (98.5%) of these were reported as sufficient material by the pathology department. The overall rate of histopathologically adequate tissue was 97.5% in all patients. In four patients (0.5%), no specimens could be obtained and all of these were female chronic hepatitis C patients. In 755 patients (96.7%), adequate tissue was obtained after one pass, in 13 (1.6%) patient after two passes, in 11 patients (1.4%) after three passes and one patients (0.1%) after four passes; however, any complications did not develop in latter two groups (Table 2). Obtained tissue sample was one piece in 266 cases, two pieces in 239 cases, three pieces in 128 cases, four pieces in 48 cases, five pieces in 22 cases, six pieces in 12 case, seven pieces in 4 cases, and eight pieces in one case. Specimens were granular in 60 cases. The average length of the specimens were 15.5 mm and the average number of pieces were 2.2.

No biopsy related deaths occurred and no complications developed in 587 patients (74.8%). In 197 patients (25.2%), one of the complications developed (Table 3). The most common complication was various degrees of localized pain (n:171, 89.5% of all complications). The most common type was mild pain around the biopsy area that was seen in 148 patients; in 5 of than an intraparanchimal hematoma was determined on the ultrasound performed next day. Other early complications were one epigastric pain, five diffuse abdominal pain, three right shoulder-arm pain, 10 right shoulder pain, five severe pain around the biopsy area, and

TABLE 2: Results of ultrasound-assisted percutaneous liver biopsies.

Macroscopically adequate tissue	780/784 (99.5%)
Histopathologically adequate tissue	768/784 (97.5%)
No. of passage for adequate tisue	
1 passage	755/780 (96.7%)
2 passage	13 (1.6%)
3 passage	11 (1.4%)
4 passage	1 (0.1%)

TABLE 3: Complications of ultrasound-assisted liver biopsies.

Complications	No. of patients
Uncomplicated patients	587/784 (74.8%)
Total complication	197/784 (25.2%)
Pain	171 (21.8%)
Mild, self limited	148 (18.8%)
Severe, analgesic requiring	13 (1.6%)
Vasovagal syncope	4 (0.5%)
Intraperitoneal hemorrhage	2 (0.2%)(one of them was clinically significant)
Nausea	5 (0.6%)
Nausea, vomiting	2 (0.2%)
Intraparenchymal hematoma on ultrasound	9 (1.14%) (in 5, mild pain)
Skin ecchymosis	7 (0.8%)
Subcutaneous hematoma	3 (0.3%)
Fever	1 (0.1%)

two back pain that lasted for 8 hours. In one patient, severe pain was observed on the next day. Pain of most patients relieved spontaneously, on the other hand, analgesics required in 13 patients (1.6%). Vasovagal syncope occurred in four patients. In five patients nausea and, in two patients nausea-vomiting were observed. In one patient (0.12%) with chronic renal failure undergoing hemodialysis and chronic hepatitis C, the amount of ascites increased minimally on ultrasound performed on the next day of the procedure, and 2 gr/dl decrease in the hemoglobin level was determined; two units of erythrocyte suspensions were transfused, however, no problems occurred later on. Additionally, in one patient, minimal fluid at bursa omentalis and around the gallblader was detected on ultrasonography. No clinical symptoms were developed, and an intervention was not required in this patient. Furthermore, skin ecchymosis in seven patients, subcutaneous hematoma in three patients and fever in one patient were observed. Intrahepatic hematoma was determined in nine patients (1.14%) on the control ultrasonography on the next day after biopsies. The diameters of these lesions were less then 2.5 cm (1-2.2 cm). Two hematomas occurred in the patients whose biopsy particles were granular, however the specimens were taken after one pass in these cases. In these patients, we did not observe any problems related to biopsy. The control ultrasonography of 771 patients (98.3%) were normal. Furthermore, no hospitalisation was required after the procedures.

DISCUSSION

Under ultrasound assistance, the puncture of other organs other than the liver, the possibility of obtaining inadequate liver specimen and other complications can be prevented and a longer biopsy specimen can be obtained, which would increase the diagnostic yield.[1-3,11] Anyway, in 96.7% of our patients, adequate tissue was obtained in one pass. Obtained tissue length was 15.5 mm.

In addition, ultrasound assisted liver biopsy increases the probability of definitive pathological diagnosis. In the 99.5% of the cases, macroscopically adequate tissue was obtained, and in the 97.5%, obtained tissue sample was adequate for histological examination.

In our series, the overall rates of complications were 25.2% and most of them (86.5%) were minor-self limited and the pain releaved rapidly. Analgesia requiring pain was only developed in 1.6% of the patients. Literature determined that the ultrasound assisted percutaneous liver biopsy reduced post-biopsy pain significantly as well as the need of analgesics.[1,2,5,13,19] Post-biopsy pain rates are between 5% and 50% in the literature.[2,13]

In only nine patients (1.14%) intraparenchymal hematomas were detected on ultrasonography. Except mild pain at the puncture site in five of them, there was no clinical findings or symptoms. In a patient with chronic renal failure undergoing hemodialysis and having chronic hepatitis C, an increase in the preexisting minimal ascites was determined by control ultrasonography as well as 2 gr/dl decrease in the hemoglobin level. Although there was no clinical problems, we transfused two units of erythrocyte suspensions. In other 17 patients with chronic renal failure who had to the liver biopsy, there were no problems. The platelet count was >80.000/mm^3 and the prothrombin activity was >70% in all of our patients. In this respect, an evaluation of the bleeding time before the biopsy can be useful to avoid hemorrhagic com-

plications, especially in the presence of comorbidities such as hemodialysis patients.[6] Literature states that the complications. Such as bleeding and hematoma formation rates increase as to the number of passes incrases,[5] however in our series, in contrast to the literature, any complications did not develop in 12 cases in which more than two passes were made.

Death occurs infrequently after liver biopsies and its rate is reported as 0.5-0.33% in the literature.[2,14] No mortality was seen in our series.

With the development of newer generation, less-expensive equipments, the availability of ultrasound in clinical units has increased.[1,2] Thus, liver biopsies could be performed in an outpatient setting quickly, without any complications requiring hospitalisation by the use of ultrasound, therefore there is a significant decrease in the costs of the procedure.[1-3,5,6,9,10,12]

Major limitation of our study was the lack of comparative results with blind liver biopsy, because we have performed all percutaneous liver biopsies routinly under ultrasound guindance for ten years.

In conclusion, outpatient ultrasound assisted percutaneous liver biopsy is a very effective, sufficient, safe, and probably cost-effective procedure. The complication rate is very low. The percutaneous ultrasound guided liver biopsy modality should be applied to all cases.

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