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ORIGINAL ARTICLE

# Endoscopic ultrasound-guided fine needle aspiration for benign liver diseases: Single-center experience

## Benign karaciğer hastalıklarında endoskopik ultrason eşliğinde ince iğne aspirasyonu: Tek merkez deneyimi

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**Background and Aims:** To report the efficacy and safety results of our initial experience with the endoscopic ultrasound-guided liver biopsy. **Materials and Method:** Retrospective analysis of a prospectively maintained database in a tertiary care referral center. Consecutive patients who had endoscopic ultrasound-guided liver biopsy for benign parenchymal diseases, using a 19 gauge fine needle with single-pass, three actuations and wet suction technique between June 2022 and December 2022 were included. Patient demographics, procedure-related parameters and the quality of specimens were investigated. **Results:** The technical success was 100%. Of the 16 patients, four had a second procedure due to inadequate sampling. The median total sample length, the median number of pieces and the median length of the longest piece in fragmented samples, and the median number of complete portal tracts were 11 mm (range, 0.2-2.5), 9.6 (range 0-20), 0.2 mm (range 0.2-1.5) and 3.5 (range 0-19) respectively. None of the patients had any adverse events following the procedure. **Conclusion:** Endoscopic ultrasound-guided liver biopsy may be an alternative to other liver biopsy procedures but further studies are needed to determine the ideal needle type and technique.

**Key words:** Endoscopic ultrasonography, fine needle aspiration biopsy, liver diseases

**Giriş ve Amaç:** Endoskopik ultrason kılavuzluğunda karaciğer biyopsisi ile ilgili ilk deneyimimizin etkinlik ve güvenlik sonuçlarını bildirmek. **Gereç ve Yöntem:** Üçüncü basamak merkezimizde, ileriye dönük olarak tutulan bir veri tabanının geriye dönük analizi yapıldı. Haziran 2022 ile Aralık 2022 tarihleri arasında, benign parankimal hastalıklar nedeniyle, tek geçişli, üç hamleli ve ıslak aspirasyon tekniği ve 19 gauge ince iğne kullanılarak endoskopik ultrason kılavuzluğunda karaciğer biyopsisi uygulanan ardışık hastalar çalışmaya dahil edildi. Hastaların demografik bilgileri, işlem ile ilgili parametreler ve örneklerin kalitesi değerlendirildi. **Bulgular:** Teknik başarı %100 idi. Toplam 16 hastadan dördüne yetersiz örnekleme nedeniyle ikinci kez işlem uygulandı. Medyan toplam numune uzunluğu, medyan parça sayısı ve parçalanmış numunelerdeki en uzun parçanın medyan uzunluğu ve tam portal yolların medyan sayısı sırayla 11 mm (aralık, 0.2-2.5), 9.6 (aralık, 0-20), 0.2 mm (aralık 0.2-1.5) ve 3.5 (aralık 0-19) olarak bulundu. İşlem sonrası hiçbir hastada yan etki görülmedi. **Sonuç:** Endoskopik ultrason kılavuzluğunda karaciğer biyopsisi, diğer karaciğer biyopsi prosedürlerine bir alternatif olabilir, ancak ideal iğne tipini ve tekniğini belirlemek için daha fazla çalışmaya ihtiyaç vardır.

**Anahtar kelimeler:** Endoskopik ultrasonografi, ince iğne aspirasyon biyopsisi, karaciğer hastalıkları

## INTRODUCTION

Despite the increasing knowledge about hepatic parenchymal diseases and the routine use of non-invasive markers, liver biopsy (LB) is still the gold-standard diagnostic tool in some patients. Historically liver tissue sampling was performed by either percutaneous (PLB) or transjugular (TJLB) routes. The sampling success of these methods has been demonstrated by numerous studies in the literature, but they have some significant risks. PLB can cause adverse events such as bleeding, pneumothorax, infection, bile leakage, and most commonly pain. Even death may ocur (1). Pain is less of an issue in TJLB but it can cause adverse events such as bleeding, hematoma, arrhythmias, and vascular

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damage and the sample quality can be somewhat lower compared to PLB (2,3).

Recently, endoscopic ultrasound (EUS)-guided liver biopsy (EUS-LB) has emerged as an intriguing alternative to these methods because it has advantages such as preventing injury to surrounding organs by providing real-time high-resolution images, increasing needle passage safety thanks to its Doppler feature, increasing patient comfort by applying anesthesia and shortening recovery time (4). There are many studies in the literature using techniques such as aspiration, slow-pull, dry or wet suction, and needles of different sizes such as 19 gauge, 22 gauge, and 25 gauge or types such as aspiration needles (FNA) or biopsy needles (FNB) to obtain the best possible core samples (5). Although the superiority of these techniques is still controversial, they are still obtaining better specimens than PLB and TJLB (6).

We herein report our initial experience of EUS-LB in a cohort of 15 patients, the sampling quality, and the safety of the procedure.

## MATERIALS and METHOD

We performed a retrospective analysis of our prospectively maintained database. Consecutive patients who underwent EUS-LB procedures at our tertiary care referral center between June 2022 and December 2022 were included. Demographic information of the patients, procedure parameters, and tissue examination results were recorded. This study was performed per the principles of the Declaration of Helsinki, and the study protocol was approved by the local ethics committee (Date: 21.12.2022, number: 2022/220).

### Patient Selection

Patients aged between 18 to 65 years old were included after obtaining written informed consent. The exclusion criteria were patients who underwent EUS-LB for targeted mass lesions, patients who had malignancy, patients that had decompensated cirrhosis, coagulopathy (platelets < 50.000 µ/mL and INR > 1.5), use of anticoagulant agents, patients who had altered anatomy and pregnancy.

### Endoscopy Procedure

All procedures were performed under endoscopist-directed anesthesia, using a combination of midazolam, propofol, and ketamine with monitored anesthesia care. Patients were placed in a semi-prone position. Jaw-thrust maneuver and oxygen at a rate of 3 L/min were administered routinely.

All procedures were performed by the same endoscopist, who performed > 500 diagnostic and interventional EUS procedures annually. A standard linear echoendoscope (EG34-J10U, Pentax Medical, Hoya Corp, Japan) was used. The patients were followed up until the Modified Aldrete Score > 9 after the procedure, and then they were discharged (7).

### EUS-LB Technique

All biopsies were performed with a standard 19 gauge FNA needle (Acquire, Boston Scientific, Marlborough, USA). Biopsy needles were used without stylets and primed with diluted heparin (1:1 ratio) to obtain samples by wet-suction technique to prevent clot formation. All the biopsies were performed from the left lobe of the liver as one pass and three actuations only, using 20 cc suction.

*https://drive.google.com/file/d/1DMcRlsS62xsl98KqNOsXHhyH_4U_wp6m/view*

### Sample Preparation and Examination

The specimens were transferred to cassettes and flushed with saline to remove residual clots and then placed into formic acid. After obtaining tissue blocks, a pathologist examined the specimens

and determined the number of complete portal tracts, total sample length, number of pieces, and the length of the longest piece if the sample is fragmented.

### Study Outcomes

Designed as a feasibility and safety study, the primary outcome of the study was technical success, and the quality of the samples was defined as total sample length > 15 mm and the number of complete portal tracts > 6. The secondary outcome was the rate of adverse events.

### Statistical Analysis

SPSS for Windows version 22.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Descriptive data were expressed as means ± standard deviation, medians (min – max), and numbers with frequencies, as appropriate. Only descriptive analysis was performed due to the small sample size and the study design.

## RESULTS

Between June 2022 and December 2022, a total of 16 EUS-LB procedures were performed on 15 patients of which seven were female. The mean age was 56.8 ± 7.3 years and the mean body-mass index was 29.9 ± 3.4 kg/m$^2$. The most common indication for EUS-LB procedure was chronic hepatitis-B infection because our national health care policy mandates the assessment of liver parenchyma for therapy considerations. The technical success was 100%. Of the 16 procedures, four had a second procedure due to inadequate sampling. The median total sample length, the median number of pieces and the median length of the longest piece in fragmented samples, and the median number of complete portal tracts were 11 mm (range, 0.2 - 2.5), 9.6 (range 0 - 20), 0.2 mm (range 0.2 - 1.5) and 3.5 (range 0 - 19) respectively (Figure 1). None of the patients had any adverse events following the procedure and were discharged after a mean time of 82 ± 16 minutes (Table 1).

## DISCUSSION

In this study, we reported our initial experience with EUS-LB, its diagnostic efficacy, and safety for benign parenchymal liver diseases in a tertiary care referral center.

Diagnostic percutaneous liver biopsy is a 100-year-old procedure, but despite improved technology and patient care, its technical aspects and adverse

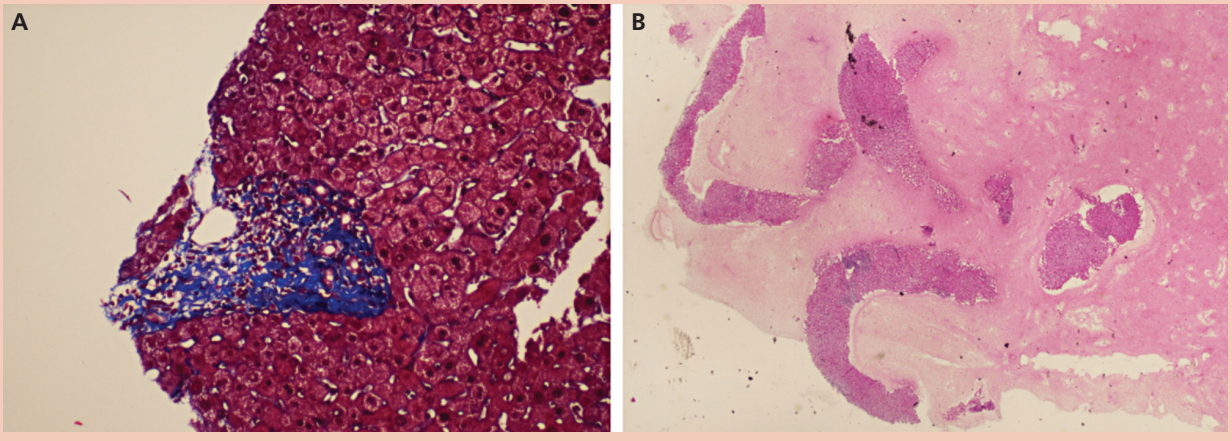


**Figure 1.** Biopsy specimens. **A.** Complete portal triads. **B.** Length of specimens.

**Table 1** Patient characteristics, procedure related parameters and quality of specimens

| | |
|---|---|
| Age (years, mean ± SD) | 56.8 ± 7.3 |
| Sex (n, M/F) | 8/7 |
| BMI (mean, kg/m$^2$) | 29.9 ± 3.4 |
| Indication (n, %) | CHB (14,93%)<br>Unexplained transaminitis (1,7%) |
| Procedure time (min, mean ± SD) | 6.3 ± 1.2 |
| Quality of specimens | |
| Total sample length (mm), median (min - max) | 11 (0.2 - 2.5) |
| Number of pieces (n), median (min-max) | 9.6 (0 - 20) |
| Longest piece in fragmented samples (mm), median (min-max) | 0.2 mm (0.2 - 1.5) |
| Complete portal tracts, median (min-max) | 3.5 (0 - 19) |
| Time to discharge (min, mean ± SD) | 82 ± 16 |

SD: Standard deviation; M: Male; F: Female; BMI: Body mass index; CHB: Chronic hepatitis B.

events have not changed significantly through this time (8). However, since its inception in 2007, different techniques and accessories have been produced to improve the EUS-LB procedure (9). These developments ignited a quest to find the ideal technique and the type of needle because the data in the literature is conflicting. Previous studies are highly heterogenous considering the number of passes, actuations, and the type of aspiration but the latest data support the single-pass, three actuations, wet suction technique (10). In our study, we also adopted this technique. The samples are obtained from the left lobe of the liver by single pass, three actuations, and wet suction technique. The type of needle also is up for debate. In the study by Mohan et al. (11) 19 G FNA needles had better outcomes compared to other needle types. But other studies found that FNB needles perform better compared to FNA needles (12,13). The rate of adverse events does not vary with technique, but rates are higher when FNB needles are used (14). Considering this data about safety, we used FNA needles. Indeed, we did not encounter any adverse events compared to the cumulative adverse event rate of 9.7%, irrespective of needle type and technique (13).

In our study, we found the median total sample length, the median number of pieces, and the median length of the longest piece in fragmented samples, and the median number of complete portal tracts was 11 mm (range, 0.2 - 2.5), 9.6 (range 0 - 20), 0.2 (range 0.2 - 1.5) and 3.5 (range 0 - 19) respectively. Our findings showed that, in 16 procedures, 12 of the samples did not meet the primary outcome criteria but of those 12, eight could get a diagnosis. These findings are also inferior compared to the literature. In the first study to perform EUS-LB with a 19 G FNA needle, the median number of complete portal tracts was nine and the median total sample length was 36.9 mm (15). Other studies which used 19 G FNA needles have also reported higher numbers of complete portal tracts and total sample lengths, up to 14 and 38 mm, respectively (4,6). It should be noted that in these studies, at least two passes and even three passes were performed but in our study, we only performed single-pass. The lower number of passes can explain these results because as the number of passes increases, the total sample length and the number of complete portal tracts also increase (10). We hypothesize that the increased number of frag-

mented samples can be explained by the indication of EUS-LB as in our cohort, all but one biopsy was performed in patients with chronic hepatitis-B infection. In these patients, the increased fibrosis can cause sample fragmentation (16).

This study has some limitations. First of all, this is a single-center, observational study without randomization and a control group. Another limitation is the low number of patients. Finally, the technique that we used may cause the lower rates of sample adequacy as these results may not be extrapolated to all clinical settings.

As a conclusion, our study showed that EUS-LB using 19 G FNA needles can be safe but comparing to the other techniques and needle types, the sample adequacy may be insufficient. Additional studies with a larger cohort using different techniques and needle types should be performed.

***Ethics Committee Approval:*** *The study protocol was approved by Düzce University Clinical Researches Ethics Committee (Date: 21.12.2022, number: 2022/220).*

***Informed Consent:*** *All patients signed the written informed consent*

***Conflict of Interest Statement:*** *None*

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***Author Contributions:*** *All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version*

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