

Comparison of diagnostic outcomes, safety, and cost of Franseen-tip 19G versus 22G needles for endoscopic ultrasound-guided liver biopsies

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ABSTRACT

Background and study aims Favorable outcomes were noted with refinement in newer endoscopic ultrasound-guided liver biopsy (EUS-LB) needle tips. Still, the overall usefulness and benefit are yet to be well explored.

Patients and methods This was a retrospective analysis of patients with EUS-LB (Franseen-tip 19G versus 22G FNB needle) over 2 years. EUS-LB was obtained in a one-pass, two-actuation, modified wet suction technique. Diagnostic yield, fragmentation rate, aggregate specimen length (AL), number of complete portal tracts (CPT), length of longest intact core (LIC), adverse events (AEs) (early), and cost of the procedure (1USD = 82 INR) were compared.

Results Fifty-four patients (33 [61.1%], female) successfully underwent EUS-LB with a median age of 46 years (interquartile range [IQR] 34–54); the majority 32 (59.2%) underwent 19G biopsies. There was a significantly increased median (IQR) AL in the 19G compared with 22G (20 mm [19–21] vs. 15 [14–15], $P < 0.001$), respectively. Similarly, significantly lengthier median LIC and CPT were seen, respectively. A nonsignificant diagnostic yield was noted (100% vs. 90.9%, $P = 0.082$), respectively. The fragmentation rate was higher in 22G FNB needles (36.4% [95% CI 16–56] vs. 12.5% [95% CI 1–24], respectively; $P = 0.038$). Seven patients (12.9%) had mild AEs with no difference between groups. The average procedure cost with 19G was INR 63000 (768\$), and with 22G needle was INR 54500 (664\$).

Conclusions The Franseen-tip 19G outperforms 22G with a significantly lower fragmentation rate, longer AL, LIC, and a higher number of CPT with a marginal increase in the procedure cost, without any difference in diagnostic yield and safety.

Introduction

Endoscopic ultrasound (EUS) has evolved from diagnostic imaging to a minimally invasive therapeutic modality [1]. The linear echoendoscope allows tracking a needle traversing toward the target lesion. EUS-guided fine needle aspiration (FNA) or biopsy (FNB) is an established technique. EUS-guided liver biopsy (EUS-LB) has recently been proposed as a safe alternative com-

pared with percutaneous and transjugular biopsy and has secured its role in various clinical settings [2]. EUS-LB is preferred because of its good histologic diagnosis rate, low adverse event (AE) profile, and less sampling variability [3, 4]. EUS has added advantages by evaluating the gallbladder, common bile duct, pancreas, mediastinum, and other structures simultaneously. With increased obesity, non-alcoholic steatohepatitis (NASH), and non-alcoholic fatty liver disease (NAFLD), [5] the future

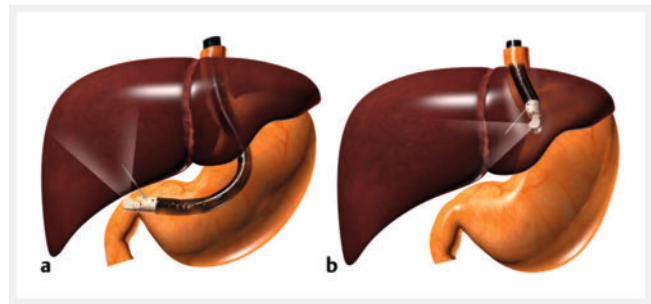
need for liver histology will likely increase. Despite the presence of other noninvasive tests, liver biopsy remains the gold standard for evaluating liver diseases. Of late, FNB or core biopsy needles have been designed to acquire larger “core” specimens that preserve tissue architecture, overcoming FNA’s limitations [6, 7]. More effective outcomes have been noted with improvement in newer EUS-LB needle tips (Franseen-tip 19G, 22G FNB needle) [7, 8]. But their overall utility, the impact of needle size, and effectiveness have yet to be well studied in the setting of EUS-LB. So, this study aims to compare the diagnostic outcomes, safety, and cost of therapy of Franseen-tip 19G versus 22G FNB needles.

Patients and methods

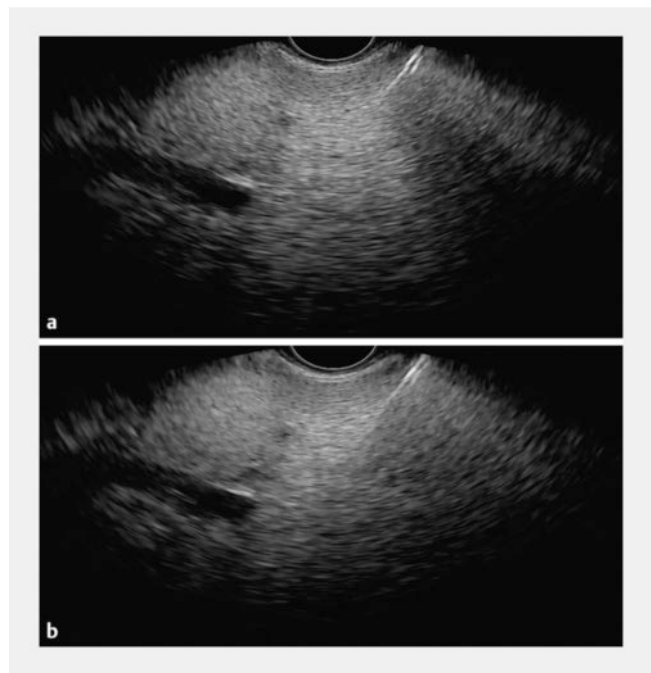
This was a single-center study wherein consecutive patients who underwent EUS-LB were retrospectively analyzed from a prospectively maintained database wherein the first and last patients were studied in January 2021 and February 2023, respectively. Patient demographics, needle characteristics, needle passes, specimen adequacy, histopathology characteristics, and AEs were reviewed. The study conforms to the ethical guidelines of the 1975 Declaration of Helsinki and its later amendments (7th revision, 2013). The study was approved by the Institutional Ethics Committee (approval number: IEC/OA-18/23). A waiver of informed consent was obtained since the study was retrospective. All included patients had been evaluated by a hepatologist at the site or referred from a tertiary care center wherein a liver biopsy was required for further evaluation of abnormal liver tests or abnormal imaging to rule out various liver diseases.

An endosonographer (AD) with adequate expertise in therapeutic EUS performed all the procedures in an endoscopy suite with the patient in the left lateral position with a curvilinear echoendoscope (GF-UCT180, Olympus, Japan) under total intravenous anesthesia (TIVA). TIVA was administered in the form of lidocaine, dexmedetomidine/midazolam, nalbuphine, and glycopyrrolate; sedation was maintained with propofol. Supplemental oxygen was provided. Patient vital signs were checked by multipara monitors.

EUS-LB was performed as an outpatient procedure with real-time ultrasound guidance using a 19G (1.14 mm) or 22G (0.72 mm) FNB needle (Acquire, Boston Scientific, United States). The stylet was removed, and the needle was flushed with 5 mL of saline. A 10-cc syringe prefilled with 3 mL of normal saline is left attached to the proximal port and later used for aspiration after puncturing the liver. The left hepatic lobe (Segment II or III) was located from the proximal stomach or the right hepatic lobe (Segment VI or VII) through the duodenal bulb (► Fig. 1a, ► Fig. 1b). A suitable trajectory was found avoiding larger vessels where the needle would travel during the biopsy, typically 3 to 5 cm. Tissue was obtained from the right/left or both lobes at the performers’ discretion in a one-pass, two-actuation, a modified wet suction technique [9] (► Fig. 2a, ► Fig. 2b). Before removing the needle from the liver, the suction was turned off. Color Doppler imaging was used to look at the liver parenchyma for bleeding within the tract, and



► Fig. 1 a Illustration of right lobe biopsy. b Illustration of left lobe biopsy. Source: Milind Jadhav, Institute of Gastrosiences, Mumbai



► Fig. 2 a, b EUS-guided biopsy showing needle passing through the right lobe of the liver.

the needle was removed. The biopsy sample was expressed onto the glass slide and washed with saline; macroscopic on-site inspection of the collected specimen was done to assess specimen length and fragmentation. The specimen was then sent for histopathology assessment in formalin. Adverse events, if any, were noted. Successful completion of the EUS-LB procedure was considered a technical success. Patients were shifted to recovery for observation.

Tissue blocks were made for histopathology assessment and stained with hematoxylin and eosin, Masson’s trichrome, reticulin, and other special stains (Orcein staining, Prussian blue) whenever needed for iron and copper-associated protein. Objective specimen characteristics such as aggregate specimen length (AL), complete portal tracts (CPT), and length of longest intact core (LIC) were assessed. The histologic interpretation was performed. For cost analysis, fee-for-professional service (endoscopist, anesthesia, nursing), endoscopy charges, and

► **Table 1** Baseline characteristics of EUS-guided liver biopsy patients.

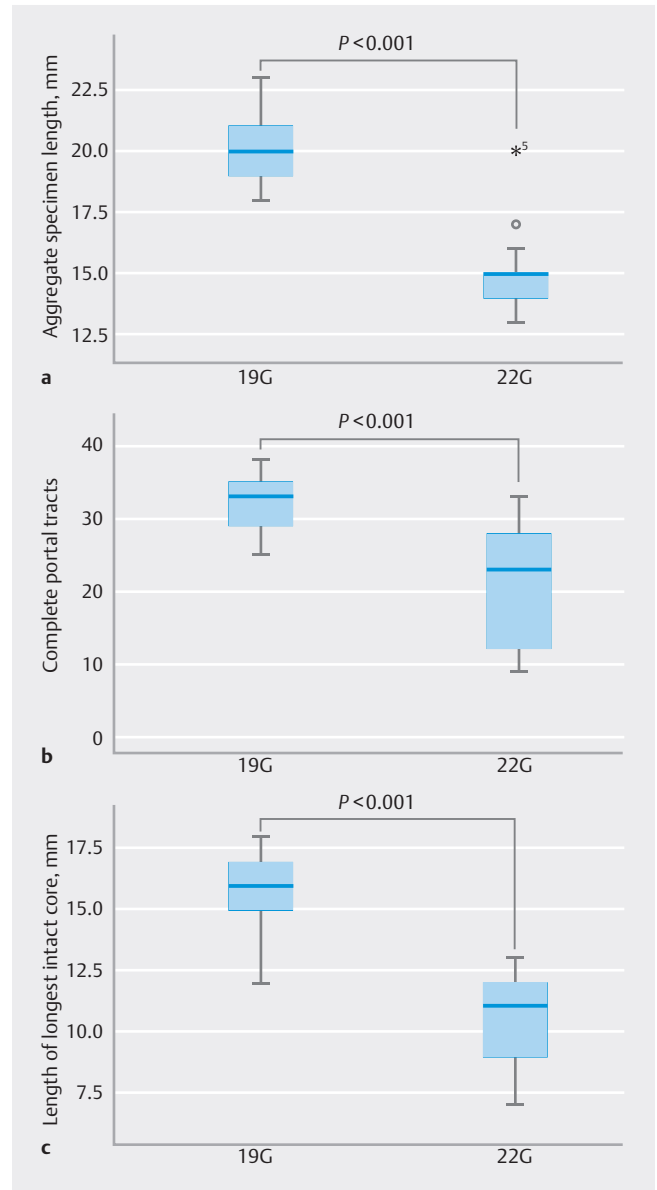
Variable	n = 54
Age, median (IQR), y	46 (34–54)
Range	18–62
Gender, female, n (%)	33 (61.1)
Female: male	1.57:1
Hemoglobin (g/dL), median (IQR)	12.7 (12.1–13.6)
Total bilirubin (mg/dL), median (IQR)	1.2 (0.9–1.4)
Aspartate aminotransferase (U/dL), median (IQR)	36 (23.7–64)
Alanine aminotransferase (U/dL), median (IQR)	63.5 (46–148.2)
Platelet Count (/μL), median (IQR)	188000 (147000–277300)
International normalized ratio, median (IQR)	1.06 (0.97–1.2)
Indication of EUS-LB, n (%)	
Suspected AIH	18 (33.3)
Suspected NASH/NAFLD	16 (29.6)
Drug induced liver injury	8 (14.8)
Unexplained transaminitis	6 (11.1)
Chronic hepatitis	3 (5.6)
Non-cirrhotic portal fibrosis	2 (3.7)
Wilson's disease	1 (1.8)
Biopsy from hepatic lobe, n (%)	
Both lobes	3 (5.6)
Left lobe	54 (100)
FNB needle, n (%)	
19G	32 (59.3)
22G	22 (40.7)

IQR, interquartile range; EUS-LB, endoscopic ultrasound-guided liver biopsy; AIH, autoimmune hepatitis; NASH, non-alcoholic steatohepatitis; NAFLD, non-alcoholic fatty liver disease; FNB, fine-needle biopsy.

the cost of an FNB needle were included. Only direct costs were considered for outpatient procedures performed in the hospital; pathology fees were not evaluated. The cost in Indian rupees (INRs) was converted to US dollars according to the average exchange rate in March 2023 (82 INR = 1USD).

Statistical methods

The anonymized patient details were available in Microsoft Excel (Office 2016 Professional for Windows; Microsoft). Statistical analysis was done by Statistical Package for the Social Sciences (SPSS, version 26.0, Professional, IBM Corporation, New York, United States) for Windows. Missing data, if any, were an-

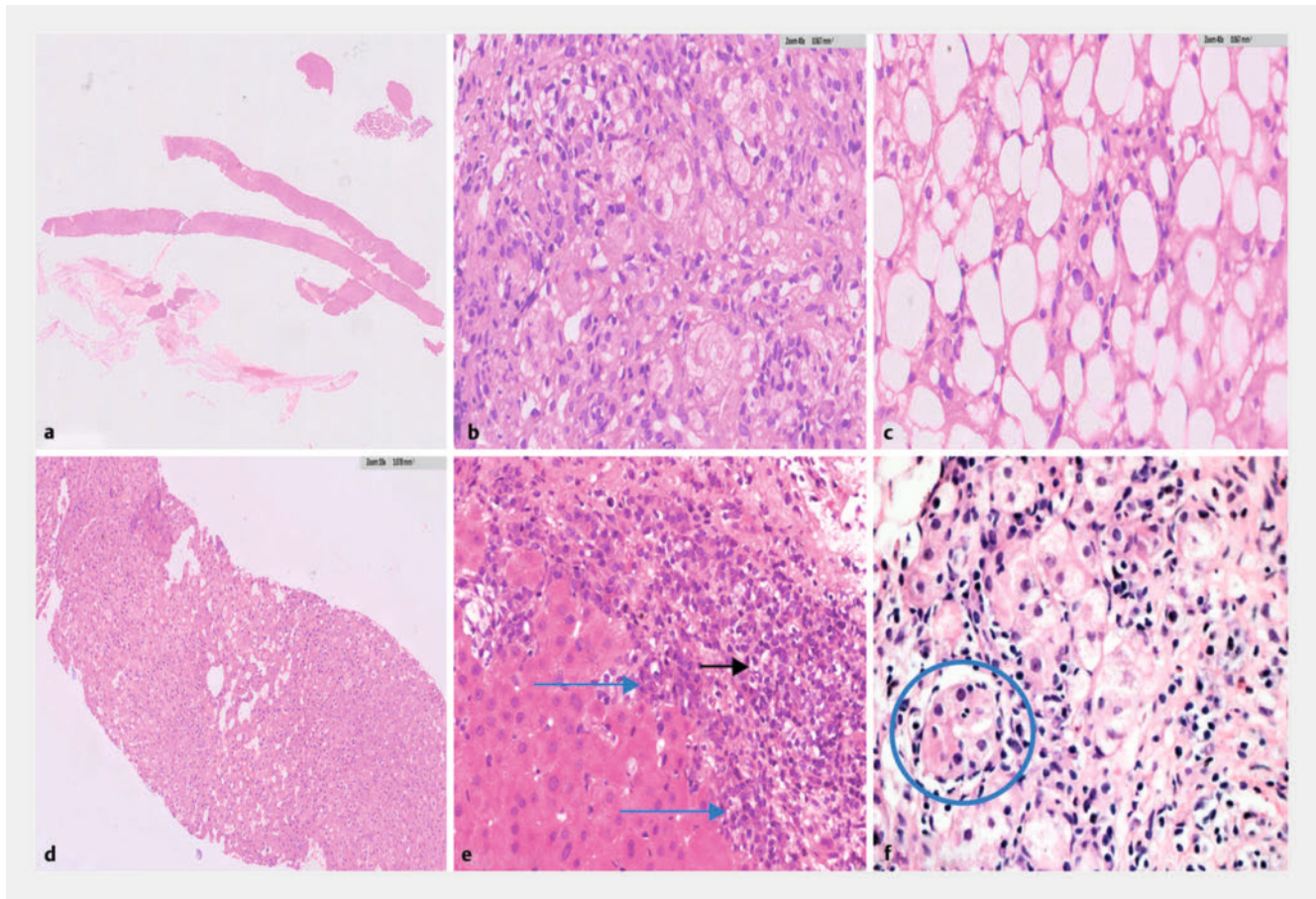


► **Fig. 3** **a** Box plot of aggregate specimen length between 19G and 22G. **b** Box plot of complete portal tracts between 19G and 22G. **c** Box plot of length of longest intact core between 19G and 22G.

alyzed using available case analysis. Categorical variables are expressed as frequency and percentage, while continuous variables are presented with descriptive statistics as appropriate. Student t test was used to compare continuous variables. 95% CI for proportion is presented. $P < 0.05$ was considered significant.

Results

Fifty-four patients (33 [61.1%], female) successfully underwent EUS-LB with a median age of 46 years (interquartile range [IQR] 34–54). In total, 57 biopsy samples per needle were obtained. The commonest indications were suspicion of autoimmune hepatitis, non-alcoholic steatohepatitis/non-alcoholic fatty liver



► **Fig. 4** **a** Largest intact core specimen (magnification 0.5×). **b** Ectatic portal venules with centrilobular congestion suggestive of noncirrhotic portal hypertension (magnification 10×). **c** Hepatic steatosis 65–70%, lobular inflammation and ballooning degeneration (magnification 40×). **d** Acute hepatitis – Portal and lobular mixed inflammation with eosinophils (magnification 40×). **e** Portal inflammation with interface hepatitis (blue arrow) mMagnification 40×). Plasma cell rich dense portal inflammation (black arrow). **f** Rosette formation by hepatocytes and emperipolesis (magnification 40×).

disease. All procedures were completed in a median (IQR) time of 12 minutes (range, 10–14) (► **Table 1**) and the technical success was seen in 54 patients (100%). The majority 32 (59.2%) underwent EUS-LB with a 19G biopsy.

There was a significantly increased median (IQR) AL in the 19G group compared with the 22G group (20 [10, 11, 12] vs. 15 [13, 14] mm, $P < 0.001$), respectively (► **Fig. 3a**). A significantly better median CPT was seen (33 [29–34.7] vs. 23 [12–28.2], $P = 0.001$), respectively (► **Fig. 3b**). Similarly, lengthier median LIC was noted (16 [14, 15, 16] vs. 11 [8.7–12] mm, $P < 0.001$), respectively (► **Fig. 3c**). A nonsignificant diagnostic yield was noted [100% vs. 90.9%, $P = 0.082$], respectively. Histology assessment confirmed the diagnosis (► **Fig. 4a**, ► **Fig. 4b**, ► **Fig. 4c**, ► **Fig. 4d**, ► **Fig. 4e**, ► **Fig. 4f**). A significant proportion of patients had higher fragmentation rate in 22G compared with 19G FNB needles (36.4% [95% CI 16–56] vs. 12.5% [95% CI 1–24], respectively; $P = 0.038$). A nonsignificant difference ($P = 0.246$) in procedure time was noted.

Overall AEs (early) were noted in seven patients (12.9%) with no difference between the groups. Self-limited bleeding, pain abdomen, nausea and vomiting were the common adverse

events. Four patients had pain in the abdomen which was treated with analgesics (paracetamol). Pain had subsided, so abdominal ultrasound was not required. The average procedural cost of EUS-LB with 19G was INR 63000 (768\$), and the 22G needle was INR 54500 (664\$) with the only difference being the cost of 19G needle INR 40000 (487\$) vs. INR 31500 (384\$) for 22G FNB needle (► **Table 2**).

Discussion

By retrospectively analyzing patients treated with EUS-LB, we compared the characteristics of 19G and 22G FNB needles. 19G FNB needle performed better than 22G with a lower fragmentation rate, longer AL, LIC, and higher CPT. The key role of EUS in assessing various internal organs is well established, and the indications are increasing. This has changed the overall approach to diagnosing and managing pancreaticobiliary diseases. In a recent meta-analysis, the pooled diagnostic yield for EUS-LB was 93% [17]. Our overall diagnostic yield of 96.3% compares favorably with previously reported results [13, 18, 19, 20]. Sample fragmentation was frequent with a 22G needle.

► **Table 2** Comparison of outcome between 19G and 22G FNB needles for liver biopsy.

Variable	19G (n = 32)	22G (n = 22)
Aggregate length, median (IQR), mm	20 (19–21)	15 (14–15)
Largest intact core length, median (IQR), mm	16 (15–17)	11 (8.7–12)
Complete portal triads, median (IQR)	33 (29–34.7)	23 (12–28.2)
Fragmentation rate, n (%)	4 (12.5)	8 (36.4)
Diagnostic yield (%)	100	90.9
Technical success, n (%)	32 (100)	22 (100)
Biopsy from hepatic lobe*, n (%)		
Both lobes	2 (6.2)	1 (4.5)
Left lobe	32 (100)	22 (100)
Procedure time (mins)	12 (10–14)	12 (10–14)
Early adverse events, n (%)		
Self-limited bleeding	1 (3.1)	1 (4.5)
Nausea and vomiting	–	1 (4.5)
Pain abdomen	2(6.2)	2 (9.1)
Cost of FNB needle	INR 40000 (487\$)	INR 31500 (384\$)
Unit cost of EUS-LB Procedure including FNB needle	INR 63000 (768\$)	INR 54500 (664\$)

*Some patients may have had more than one lobe biopsied.
FNB, fine-needle biopsy; IQR, interquartile range; EUS-LB, endoscopic ultrasound-guided liver biopsy.

Multiple studies have used various needle types, including 19G and 22G [14, 15, 16]. Tissue adequacy has been higher with lower fragmentation for the 19G FNA than the 22G FNB needle [15]. 22G franseen-tip showed inferior specimen adequacy compared with the 19G non-Tru-Cut needle [16]. When 19G FNA and 19G FNB core biopsy needle was studied, the latter provided longer biopsy specimens [21]. The standard tissue acquisition techniques include wet suction, modified wet suction, wet heparin, fanning and slow pull technique. The wet heparin technique is comparable to the modified wet suction technique (used in the present study), which increases tissue sample length with the least fragmentation and maximum CPT [10]. None of the patients experienced severe AEs. The most common AE is abdominal pain, possibly due to diffuse peritoneal irritation from blood coming out of the puncture site [11].

AASLD recommends a specimen > 20 mm and at least 11 CPT, [12] a criterion that EUS-LB meets with good diagnostic yield. The other standards for adequacy include CPT > 6 and total specimen length >15 mm [22]. The tissue adequacy varies based on the operator's experience and needle size. EUS-LB has comparable efficacy for specimen adequacy to percutaneous and transjugular liver biopsy (TJLB) [23]. The core biopsy in EUS-LB is smaller, as the needle is 19G compared with 16G for the percutaneous method. EUS-LB is preferred for its usefulness in bi-lobar sampling, pediatric patients, patient comfort with reduced anxiety, safety, adequacy, decreased recovery time, reduced sampling variability, overall clinical outcomes, and cost [24]. Patients who need a second procedure might be appre-

hensive about the subsequent liver biopsy; in such cases, EUS-LB can be offered. EUS-LB is also beneficial in positions that are difficult to access by percutaneous approach. Real-time Doppler imaging helps to avoid intrahepatic blood vessels. Patients with coagulopathy/on antiplatelet medications and gross ascites are contraindications for EUS-LB.

EUS-LB is cheaper than TJLB at our center. But the indications are sometimes different. The cost of EUS-LB has been studied in only two studies. The total cost of EUS-LB was \$1705 EUS [25] and \$2610 [26]. The former used a 19G needle. The latter should have included relevant details for comparison. Our study involved less than half the cost of these studies, with the highest expenditure of \$768 per procedure. There will also be cost savings because this procedure does not require a separate admission. The costs apply to India; further research is required to assess generalizability.

The study does have its limitations. First, this was a retrospective study performed in India with inherent selection bias and a modest sample size, the results of which may not be generalizable. A prospective randomized study is required to compare outcomes between percutaneous with EUS-LB among the homogenous patient population. Secondly, there may be an element of referral bias. Third, indirect costs were not compared. The cost of treating patients varies across the globe and the cost of therapy mentioned in this study is applicable to India. Yet the decent results obtained act as a reference for future studies.

Conclusions

To summarize, the Franseen-tip 19G had superior outcomes compared with the 22G FNB needle with a significantly lower fragmentation rate, longer AL, LIC, and higher CPT. There was no difference in diagnostic yield, procedure time, AEs, and safety. EUS-LB is quicker and easier, with favorable diagnostic outcomes, and appears to be the most affordable strategy in liver biopsy and prognostication. It does appear to have a future role in post-liver transplant patients. Prospective studies comparing these outcomes in a larger patient cohort are warranted.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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