

Liver biopsy: Analysis of results of two specialist teams

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Abstract

AIM: To analyze the safety and the adequacy of a sample of liver biopsies (LB) obtained by gastroenterologist (G) and interventional radiologist (IR) teams.

METHODS: Medical records of consecutive patients evaluated at our GI unit from 01/01/2004 to 31/12/2010 for whom LB was considered necessary to diagnose and/or stage liver disease, both in the setting

of day hospital and regular admission (RA) care, were retrieved and the data entered in a database. Patients were divided into two groups: one undergoing an ultrasonography (US)-assisted procedure by the G team and one undergoing US-guided biopsy by the IR team. For the first group, an intercostal approach (US-assisted) and a Menghini modified type needle 16 G (length 90 mm) were used. The IR team used a subcostal approach (US-guided) and a semiautomatic modified Menghini type needle 18 G (length 150 mm). All the biopsies were evaluated for appropriateness according to the current guidelines. The number of portal tracts present in each biopsy was assessed by a revision performed by a single pathologist unaware of the previous pathology report. Clinical, laboratory and demographic patient characteristics, the adverse events rate and the diagnostic adequacy of LB were analyzed.

RESULTS: During the study period, 226 patients, 126 males (56%) and 100 females (44%), underwent LB: 167 (74%) were carried out by the G team, whereas 59 (26%) by the IR team. LB was mostly performed in a day hospital setting by the G team, while IR completed more procedures on inpatients ($P < 0.0001$). The groups did not differ in median age, body mass index (BMI), presence of comorbidities and coagulation parameters. Complications occurred in 26 patients (16 G team vs 10 IR team, $P = 0.15$). Most gross samples obtained were considered suitable for basal histological evaluation, with no difference among the two teams (96.4% G team vs 91.5% IR, $P = 0.16$). However, the samples obtained by the G team had a higher mean number of portal tracts (G team 9.5 ± 4.8 ; range 1-29 vs IR team 7.8 ± 4.1 ; range 1-20) ($P = 0.0192$) and a longer mean length (G team $22 \text{ mm} \pm 8.8$ vs IR team $15 \pm 6.5 \text{ mm}$) ($P = 0.0001$).

CONCLUSION: LB can be performed with similar outcomes both by G and IR. Use of larger dimension needles allows obtaining better samples, with a similar

rate of adverse events.

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Key words: Liver biopsy; Ultrasound-guided biopsy; Ultrasound-assisted biopsy; Menghini needle; Sample adequacy; Portal tracts.

Core tip: Gastroenterologists and interventional radiologists are equally proficient in performing liver biopsy, both in a day hospital and regular admission setting, even with different techniques used (ultrasound-guided and ultrasound-assisted). However, a biopsy performed with larger needles provides better samples for histopathological evaluation, with no increase of morbidity or mortality rates compared to those obtained using needles of smaller size.

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INTRODUCTION

Liver biopsy is an invasive procedure aimed at obtaining a sample of liver tissue for the evaluation of acute and chronic liver disease^[1]. Sampling can be performed either during surgery or by percutaneous needle biopsy using different techniques^[2]. Currently, this procedure is supported by imaging techniques, such as ultrasonography (US) or computed tomography, with a significant reduction of complications^[3-5].

Our study aimed to analyze the results of the same medical-surgical procedure, percutaneous liver biopsies (LB), performed by two different medical teams: gastroenterologists (G) and interventional radiologists (IR). The G team performs the procedure with the US-assisted method (the area in which to insert the needle is identified with US before LB) *via* an intercostal approach, while the IR team performs the procedure with a US-guided technique (LB is performed by the operator during US, sometimes with a needle supported and directed by a dedicated US probe) with a subcostal approach^[6,7].

There are presently no comparative data available on these two different modalities of LB performance. The two approaches were compared, analyzing the characteristics of patients undergoing LB, safety of the procedure, and capability of providing suitable material for histopathological evaluation.

MATERIALS AND METHODS

Medical records of consecutive patients evaluated at our GI unit, from 01/01/2004 to 31/12/2010, and for whom

Table 1 Details of the techniques adopted for liver biopsy by the two teams

	Gastroenterology team	Interventional radiology team
Needle characteristics	Menghini modified type needle 16 G (9 cm)	Menghini type needle semiautomatic, modified 18 G (15 cm)
Method	US-assisted	US-guided
Approach	Intercostal	Subcostal

US: Ultrasonography.

LB was considered necessary to diagnose and/or stage liver disease, both in the setting of day hospital (DH) and regular admission (RA) care, were retrieved and the data entered in a database. Indications to undergo LB were those provided by the main international guidelines^[2]. Patients were divided into 2 groups: one undergoing a US-assisted procedure by the G team and one undergoing a US-guided biopsy by the IR team. For the first group, an intercostal approach (US-assisted) and a Menghini modified type needle 16 G (length 90 mm) were used. For the second group, the IR team used a subcostal approach (US-guided) and a semiautomatic modified Menghini type needle 18G (length 150 mm)^[6,7] (Table 1). The condition of the patients was monitored with subsequent blood pressure and complete blood count testing at two and four hours post-procedure^[8,9]. A telephone follow up call was made a week after the procedure in order to detect possible late adverse events/complications.

All the biopsies were evaluated for appropriateness according to the current guidelines by a team of pathologists experienced in the evaluation of liver parenchyma at our hospital. All specimens were fixed in formalin, embedded in paraffin and sectioned by microtome. Specimens were routinely stained with hematoxylin and eosin. The adequate specimen for diagnosis was considered to have a length between 1-4 cm^[2]. The number of portal tracts present in each biopsy was assessed by a revision performed by a single pathologist unaware of the previous pathology report. The portal tracts were identified by the presence of foci of connective tissue and at least two luminal structures embedded in the connective tissue and their number counted and entered in a database. The presence of at least 6 portal tracts was used to define an optimal sample.

Clinical, laboratory and demographic characteristics of the study patients, adverse events rate and diagnostic adequacy of LB were analyzed by the Student's t test for continuous variables and by Fisher's exact test in case of binary variables (Table 2). Data are expressed as percentage (number/total), median (range) for demographic and laboratory data, and as mean \pm SD for number of portal tract per bioptic sample and length of samples.

All patients gave informed consent for the use of clinical data at the time of admission.

RESULTS

During the study period, 365 patients underwent liver

Table 2 Patient characteristics in the two groups

Group	Team G	Team IR	P
Male sex, % (number/total)	60% (101/167)	42% (25/59)	0.021
AGE, years, median (range)	50.5 (16-70)	52 (19-73)	0.41
BMI, median (range)	24 (17-36)	24 (18-41)	0.94
PLATELETS/mm ³ , median (range)	199000 (77000-797000)	204000 (65000-394000)	0.65
INR, median (range)	1 (0.86-1.44)	1.02 (0.87-1.94)	0.24
Complications, % (number/total)	9.5% (16/167)	17% (10/59)	0.15

M: Male; BMI: Body mass index; INR: International normalized ratio; IR: Interventional radiology.

Table 3 Occurrence of adverse events following liver biopsy by setting and team performing the procedure

	Regular admission	Day hospital	Team G	Team IR
Total number of adverse events	13	13	16	10
Pain moderate to severe % (number/total)	77% (10/13)	70% (9/13)	68% (11/16)	80% (8/10)
Relevant biochemical abnormalities ¹ % (number/total)	15% (2/13)	31% (4/13)	25% (4/16)	20% (2/10)
Nausea/vomiting % (number/total)	7% (1/13)	(0/13)	6% (1/16)	(0/10)

¹Mild increase of white blood cells (4 cases); mild hemoglobin decrease < 2 mg/dL from baseline (1 case); thrombocytopenia (1 case). IR: Interventional radiology.

biopsy at our center. From this group, those who had a LB to investigate liver mass lesions were excluded ($n = 139$, 38%). The remaining 226 patients (62%) underwent LB to evaluate liver parenchyma. Of these 226 patients [126 males (56%), 100 females (44%)], 167 (74%) underwent LB performed by the G team (intercostal approach, US-assisted) and 59 (26%) by the IR team (subcostal approach, US-guided). The hospital setting in which LB was performed was significantly different between the two groups: RA = 29% (48/167) and DH = 71% (119/167) for the G team *vs* RA = 64% (38/59) and DH = 36% (21/59) for the IR team ($P < 0.0001$). The approach was intercostal in all 167 patients by the G team and subcostal in all 59 managed by the IR team. The G team performed LB in a slightly but significantly higher number of male patients with no differences in median age of patients in the two groups observed (Table 2). Median value of body mass index (BMI) was also similar in both groups (Table 2). Fifty-two patients (23%) were affected by significant comorbidities with no significant differences between the two groups. Similarly, median international normalized ratio and platelet concentration were not significantly different in the two groups (Table 2). The most frequent indication for LB was staging and grading liver disease caused by viral hepatitis B and C. In fact, out of a total of

Table 4 Characteristics of bioptic samples

Number of bioptic samples	G Team 167	IR Team 59	P = NA
Samples adequate for diagnosis % (number/total)	96.4% (161/167)	91.5% (54/59)	0.16
Sample length ¹ mean \pm SD	22 mm \pm 8.8	15 mm \pm 6.5	< 0.0001
Number of portal tract per sample ² mean \pm SD	9.5 \pm 4.8	7.8 \pm 4.1	0.0192

¹Evaluation performed on 215 (161 by G team, 54 by IR), considered to be adequate for diagnosis; ²Evaluation performed on 205 samples (151 by G team, 54 by IR). NA: not applicable; IR: Interventional radiology.

226 patients, 141 (62%) had chronic viral infection, 23% of whom were affected by hepatitis B (32/141) and 77% (109/141) by hepatitis C. There were 26 complications in as many patients (11.5%, 26/226). No difference in terms of incidence of complications was observed between the two teams (G team: 9.5%, 16/167; IR team: 17%, 10/59, $P = 0.15$) despite the different needles and approaches used. It was not necessary to convert to RA in any of the cases of adverse events occurring in patients undergoing LB in the DH setting. We also performed a subgroup analysis of the rate of adverse events observed in the RA setting and no difference in the G (6/48) *vs* IR (7/38) team was shown ($P = 0.548$). Subgroup analysis performed on the rate of adverse events observed in the DH setting also did not show any significant difference between the two groups, G (10/119) *vs* IR (3/21) ($P = 0.413$). The adverse events that occurred are summarized in Table 3. Telephonic surveillance at one week after the procedure was negative in all cases discharged without complications after LB.

The overall number of LB samples not suitable for histological evaluation was low (11/226, 4.9%) and there was no statistical difference in the number of suitable and unsuitable samples obtained by the two teams (Table 4). Data on the number of portal tracts per bioptic sample were evaluable for 205 biopsies, 151 performed by the G team and 54 by the IR team respectively. At the time of retrospective re-evaluation of bioptic samples for portal tract count, 10 samples, all from the G team, were no longer available. Interestingly, samples provided by the G team had a significantly higher number of portal tracts compared to those obtained by the IR team (Table 3; $P = 0.0192$). Overall, 30.7% (63/205) of bioptic samples had ≥ 11 complete portal tracts, 34% (52/151) and 20% (11/54) G *vs* IR respectively. Bioptic samples with ≥ 6 complete portal tracts were overall 76.6% (157/205), 78.1% (118/151) and 72.2% (39/54) G *vs* IR respectively. Moreover, the samples obtained by the G team were longer compared with those of the IR team (Table 4; $P = 0.0001$).

DISCUSSION

There are few studies comparing the outcomes of LB

on parenchyma adopting different approaches (subcostal versus intercostal) and different imaging modalities to aid its performance (US-guided *vs* US-assisted)^[7,10]. Thus, the results of our study add information to the available literature. From our data, it emerges that both LB performance modalities, supported and implemented by the use of US, allow achieving optimal results in terms of patient safety. These data are not present in the literature, which has been mainly focused on the comparison of US *vs* non-US-guided procedures^[2,11-13].

In addition, even with the limitations inherent to the retrospective nature of our analysis, since the patients had similar coagulative profiles, BMI and prevalence of comorbidities, there were no elements suggesting a preferential choice of one team over the other. The main reason that guided the choice of one team over the other was the availability of either team at the time the procedure was ordered.

Our results also show that the two groups are homogeneous regarding the occurrence of complications (9.5% *vs* 17%, $P = 0.15$) and that in all occurrences there was no increased morbidity, such as a requirement for surgery, blood transfusions and IR treatments, or death (mortality). Also, no complications that occurred in patients managed in DH led to the conversion to RA, further supporting the current data regarding the safety of LB^[2,14].

Unfortunately, the smaller number of procedures performed by IR might lead to underestimating the difference between the two groups, an intrinsic bias of the retrospective nature of this study, which in turn limits the power of data analysis. It has to be pointed out that in our study, localized pain at the site of needle insertion was also defined as a complication and that this contributed to more than 73% of all complications, a figure well within those reported in the literature (up to 84%)^[2,11,14-17]. This event is so common that some authors do not even include it among the complications. Thus, we performed a sub-analysis separating the adverse event pain from the other signs and symptoms that developed after the performance of LB. Again, no differences were observed between the results obtained by the G and the IR team ($P = 1$).

Apart from pain, the most common adverse events were biochemical abnormalities such as a mild increased white blood cell count and a mild hemoglobin decrease (< 2 gm/dL) from baseline, observed in a marginal number of patients (Table 3). This absence of difference is interesting since higher percentages of complications have been reported when larger needles are used, as for the G team. Thus, performance of LB in a DH setting confirms its safety, with the post procedure monitoring protocol allowing safe discharge of patients after brief observation (4 h) and with the negative telephonic surveillance performed one week after the procedure integrating these safety data. This approach contributes to containing hospital costs by reducing the need for admission to perform this procedure. In addition, considering a health service system based on a disease related group

reimbursement such ours, ordering LB to a service or department not belonging to the one which has posed the indication for it has many potential positive aspects. Firstly, it is obviously less expensive since it uses resources already available to the unit ordering the procedure and secondly, it does reduce the burden of this relatively simple procedure to the already busy schedule of the IR team, without encumbering their high technology and expensive wards. Thus, being equally safe and possibly less expensive, LB should preferably be performed in-house in the gastroenterology department^[18,19].

Our results also show that even if the adequacy of samples obtained by the two teams are comparable in terms of overall dimension, the bigger needle used by the G team provided a larger number of evaluable portal tracts and sample length, a necessary requirement for better histopathological evaluation, as previously demonstrated^[20,22].

A further possible limitation of our data is represented by the percentage of samples with a number ≥ 11 of complete portal tracts (30.7%). As suggested by the 2009 AASLD guidelines, the presence of < 11 complete portal tracts should be noted in the pathology report, with recognition that diagnosis, grading and staging may be incorrect due to an insufficient sample size. Nevertheless, the presence of 6 portal tracts has previously been considered to be acceptable for diagnosis^[23] and overall, 76.6% (157/205) of samples obtained in our study were above this limit. Thus, since we have chosen the latter numeric parameter, we acknowledge that the reduced number of portal tracts obtained might have affected the accuracy of diagnosis. However, the significantly higher mean number of portal tracts obtained by the biopsy samples performed by the G team suggests a higher opportunity for better diagnostic findings.

Interestingly, even if intuitively a bigger needle should obtain a bigger sample and consequently a higher number of portal tracts, available evidence is at times contrasting. In fact, a systematic review by Cholongitas *et al*^[24] described that LB performed with bigger needles did obtain a slightly higher number of portal tracts and samples of longer length but that these differences did not reach statistical significance. On the other hand, data from other authors obtained in a single center study also suggested that the use of a bigger needle (16 G as in our case for the G team) can obtain samples with a significantly higher number of portal tracts^[25,26]. Considering that the use of a 16 G needle is also suggested by AASLD guidelines to obtain LB 3 cm long and to avoid sampling errors, especially for diffuse parenchymal diseases such as cirrhosis, we concluded that our data provide further support to the use of a biopsy needle of larger gauge to perform LB in terms of sample adequacy, with a comparable incidence of complications^[2].

Thus, our retrospective, single center study suggests that LB can be performed with equal safety with different techniques performed by specialists from different units. At the same time, the better performance in terms of sample adequacy obtained by needles of larger gauge

also suggests their use. Cost effectiveness analyses are needed to better define the economic burden inherent to the different approaches.

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COMMENTS

Background

Percutaneous liver biopsy is a pivotal diagnostic procedure in the management of liver diseases. In order to support the diagnosis process, an adequate sample of tissue is required. Several different technical approaches and devices have been developed and are available.

Research frontiers

Presently, percutaneous liver biopsies are carried out with the assistance of imaging techniques such as ultrasonography, with an ultrasonography (US)-assisted or US-guided technique. Furthermore, a wide range of needle sizes are used and the choice of one technique or needle over the other is mainly based on physician experience. To date, there are just a few comparative studies on this matter.

Innovations and breakthroughs

In previous studies, the use of bigger needles to perform liver biopsies was not univocally associated with more suitable samples, thus authors performed the analysis to confirm that the use of a bigger needle could provide more proficient biopsies with a similar safety profile.

Applications

The study results suggest that the use of bigger needles could supply more useful liver samples with a similar incidence of adverse events.

Peer review

Anania *et al* propose an interesting study comparing the parameters of two approaches of liver biopsy, US assisted and US guided, performed by two teams, one of gastroenterologists and one of interventional radiologists. The article has a very interesting idea behind it.

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