ORIGINAL ARTICLE

Comparison of tru-cut biopsy and fine-needle aspiration cytology in an experimental alcoholic liver disease model

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SUMMARY

INTRODUCTION: *Liver biopsies such as tru-cut (sharp needle) and fine-needle aspiration cytology (FNAC) are the most commonly preferred techniques to detect the grade and stage of certain liver diseases. In this study, we aimed to compare the efficiency of USG-guided tru-cut biopsy and fine-needle aspiration cytology in an experimental alcoholic liver disease model.*

METHODS: *Thirty-six female Wistar albino rats, 4-6 months old, and weighing from 190 to 250 g, were used in this study. The animals were randomly divided into six equal groups: G1 (control), G2 (tru-cut control), G3 (FNAC control), G4 (Alcoholic liver disease model), G5 (Alcoholic liver disease model + FNAC), and G6 (Alcoholic liver disease model + tru-cut biopsy). After a histopathological evaluation by light microscopy, the sensitivity, specificity, positive and negative predictive values of FNAC and tru-cut biopsy for the diagnosis of liver lesions were calculated.*

RESULTS: *No pathology was detected in G1 except for mild congestion. On the other hand, hepatocyte damage, periportal inflammation, congestion, and fatty changes were detected in all liver tissues of the alcoholic liver disease groups. The sensitivity of hepatocyte damage, inflammation, congestion, and fatty change parameters for FNAC were 33.3%, 80%, 0%, and 0%, respectively, while the sensitivity of the same variables for tru-cut were 66.7%, 40%, 100%, and 20%, respectively.*

DISCUSSION: *Both techniques were superior in some aspects. FNAC can be an attractive alternative to tru-cut biopsy and applied in routine practice in the diagnosis of non-tumoral liver diseases.*

KEYWORDS: *Liver diseases, alcoholic. Biopsy, fine-needle. Biopsy. Aspiration Biopsy.*

INTRODUCTION

Alcoholic liver disease (ALD) is known as a progressive disease that worsens with the prolonged use of alcohol[1]. The main risk factors of ALD are genetic and metabolic traits, sex, obesity, and volume and duration

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of alcohol use[2]. ALD represents a wide-range spectrum of liver pathologies such as steatosis, steatohepatitis, steatofibrosis-cirrhosis, cholestasis, alcoholic foamy degeneration, megamitochondria, perivenular fibrosis-central hyaline sclerosis, and siderosis[3]. Steatosis (fatty changes), which is generally seen in 90% of heavy drinkers, is the first liver response to alcohol[4]. Alcohol shows its pathogenesis in different pathways by increasing NADH/NAD+ in the hepatocytes, disrupting fatty acid oxidation, increasing triglyceride synthesis, upregulating lipogenic enzymes, leading to lymphocyte recruitment, increasing gut permeability, translocation of bacterial products such as LPS into the portal circulation, triggering neutrophilic infiltration, secretion of cytokines and chemokines, and inhibiting the anti-fibrotic action of natural killer cells[4-6].

Ultrasonographic imaging (USG), computed tomography (CT), or magnetic resonance imaging (MRI) are frequently and effectively used techniques to evaluate benign and malignant diseases of the liver, including in the diagnosis and grading of alcoholic liver disease[7,8]. However, histopathological examinations are more reliable in cases where a radiological examination is insufficient to guide diagnosis and treatment[9]. On the other hand, liver biopsies such as tru-cut (sharp needle) biopsy and fine-needle aspiration cytology (FNAC) are the most commonly preferred and performed techniques to detect the grade and stage of certain liver diseases. Therefore, these methods are candidates for the "gold standard method"[10,11]. The role of liver biopsy in alcoholic liver disease is to provide accurate clinical data, facilitate diagnosis, and predict the severity, grade, and stage of the disease by using semi-quantitative tools[3].

FNAC is a simple, rapid, less expensive, and relatively safe investigation, while tru-cut biopsy is more expensive and takes more time[12]. Additionally, FNAC causes less tissue damage and has fewer complications than tru-cut biopsy. Compared to FNAC, the risk of complications such as hemorrhage, tumor seeding, infection, fistula formation, bleeding, perforation, and pain can be encountered more in tru-cut biopsy[11]. Despite its advantages, such as the high sensitivity and specificity rates and reducing the need for other biopsy techniques such as tru-cut, in some types of lesions, FNAC may not provide enough cellular details[13].

Considering the current literature, FNAC is generally used for lesions suspected of malignancy in the liver, not in benign lesions[14,15]. Therefore, in this study, we aimed to compare the efficiency of USG-guided tru-cut biopsy and fine-needle aspiration cytology concerning some histological parameters such as inflammation, hepatocyte damage, congestion, and fatty change and intended to detect the sensitivity, specificity, positive/negative predictive values, and diagnostic accuracy of the two methods in an experimental alcoholic liver disease model.

METHODS

After the study was approved by the Local Ethics Committee of Animal Experiments of the Kafkas University (Ethical Approval Date 17.02.2016 and Number: 2016/053), thirty-six female Wistar albino rats, 4-6 months old and weighing 190 to 250g, were purchased from the Ataturk University Medical Experimental Research and Application Center and used in this study. Female rats are chosen for the study because they are more prone to alcoholic damage[16].

The rats were housed in an animal room maintained at a temperature of 22-25 °C, in 12-hours light periods, and were fed ad-libitum. Then, the rats were randomly divided into the following six experimental groups (n=6 per group):

Group 1: (1st control group) Nothing was done. The animals were only fed ad-libitum for 28 days (n=6).

Group 2: (2nd control group) Nothing was applied. The animals were only fed ad-libitum for 28 days, followed by tru-cut biopsy (n=6).

Group 3: (3rd control group) Nothing was applied. The animals were only fed ad-libitum for 28 days, followed by FNAC (n=6).

Group 4: Alcoholic liver disease was inducted by applying Ethanol (7 g/kg/day) + Water (50%) for 28 days (n=6).

Group 5: Alcoholic liver disease was inducted by applying Ethanol (7 g/kg/day) + Water (50%) for 28 days, followed by FNAC (n=6).

Group 6: Alcoholic liver disease was inducted by applying Ethanol (7 g/kg/day) + Water (50%) for 28 days, followed by tru-cut biopsy (n=6).

Ethanol was administered considering the time to create subchronic damage using the dosage modified per Bharrhan et al.'s study[17]. At the end of the 28-days, the rats were not fed overnight. After applying the anesthesia protocol, the samples were taken by USG-guided tru-cut biopsy or FNAC. After the interventions, the rats were subjected to cervical vertebra dislocation according to ethical rules.

Imaging during FNAC

The samples were obtained by the FNAC technique following local anesthesia using a 20 cc injection syringe with 21G needle from the non-vascular area of the liver with the guide of an ultrasonography (USG) device (Toshiba Aplio XG).

Imaging during tru-cut biopsy

The samples were obtained by the tru-cut biopsy technique following local anesthesia using a 18G tru-cut needle from the liver tissue with the guidance of USG (Toshiba Aplio XG).

The harvested tru-cut biopsy and hepatectomy samples were fixed in 10% buffered formaldehyde solution for 24 hours for pathological examinations. They were dehydrated in graded alcohol series and embedded in paraffin wax. Then, four-µm thick sections of paraffin blocks were obtained and stained with hematoxylin & eosin (H&E). The sections were evaluated by light microscopy (Clinical Microscope BX46, Olympus, Japan). The cytological materials were also analyzed by light microscopy both as direct smear and thin-prep method, which is a cell replication method. Since direct smears revealed more diagnostic features than the thin-prep method during the microscopic evaluation, direct smear was used for cytology findings that constitute the main framework of the study. The hepatectomy materials, tru-cut biopsies, and FNAC preparations of all experimental groups were evaluated for histopathological assessments of the following parameters: congestion, inflammation, hepatocyte damage, and steatosis (fatty change).

Statistical Analysis

The sensitivity, specificity, positive and negative predictive values of FNAC and tru-cut biopsy in the diagnosis of liver lesions were determined using histopathological diagnoses of the liver tissues as the gold standard.

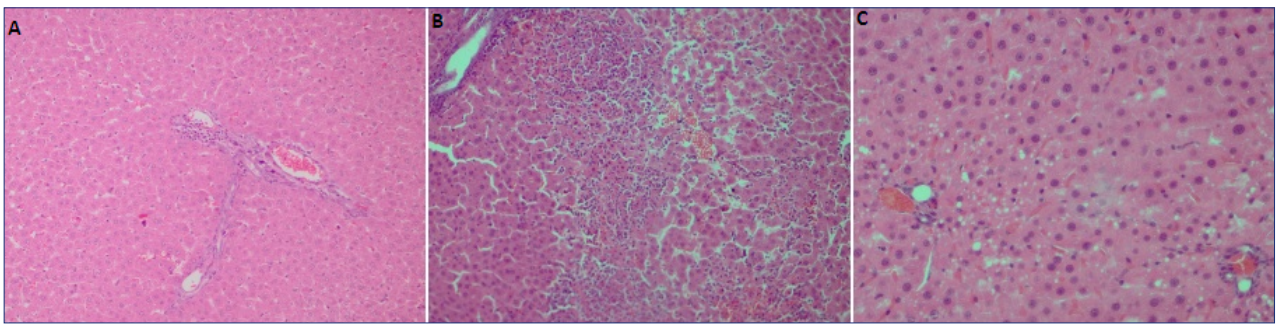
RESULTS

Per the histopathological evaluation, no histopathological changes were detected in Group 1 (1st control group) except for mild congestion (Figure 1A). Group 2 and Group 3 had similar histopathological properties to Group 1 in terms of hepatocyte damage, periportal inflammation, congestion, and changes in fatty parameters (no histopathological changes were detected except mild congestion). On the other hand, hepatocyte damage, periportal inflammation, congestion, and fatty changes were detected in the liver tissues of the ethanol-administrated group (Group 4) (Figure 1B-C).

The sensitivity, specificity, diagnostic accuracy, positive and negative predictive values of the histopathological parameters (hepatocyte damage, inflammation, congestion, and fatty change) of Group 5 and Group 6 (Figure 2A-B) are shown in Table 1 and Table 2.

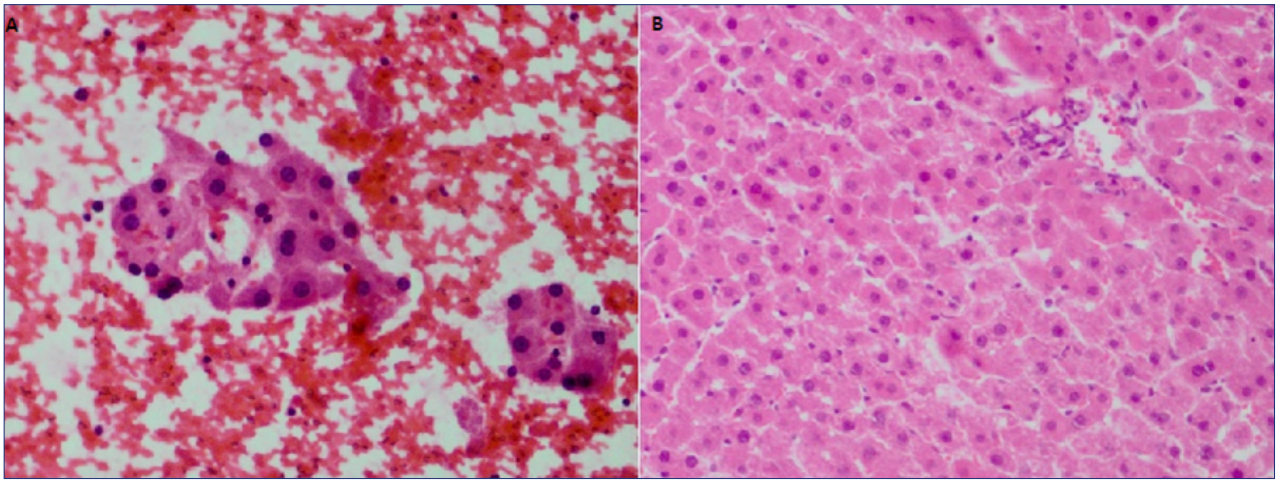
The sensitivities of hepatocyte damage, inflammation, congestion, and changes in fatty parameters for FNAC were 33.3%, 80%, 0%, and 0%, respectively, while, the sensitivities of the same variables for the tru-cut biopsy were 66.7%, 40%, 100%, and 20%, respectively. On the other hand, the diagnostic accuracy of congestion was the same both for tru-cut and FNAC (100%). The diagnostic accuracies of tru-cut biopsy regarding fatty changes (33.3% vs. 16.7%) and hepatocyte damage (66.7% vs. 33.3%) were higher than those of FNAC, while the diagnostic accuracy of FNAC concerning inflammation (83.3% vs. 50%) was higher than the tru-cut biopsy method.

FIGURE 1. THE HISTOPATHOLOGICAL MICROGRAPHS OF GROUP 1 AND 4.



A: Group 1, mild congestion (H&E, 200x); B: Group 4, periportal inflammation (H&E, 200x); C: Group 4, microvesicular steatosis and hepatocyte damage (H&E, 400x).

FIGURE 2. THE HISTOPATHOLOGICAL MICROGRAPHS OF GROUP 5 AND 6.



A: Group 5, hepatocyte damage (H&E, 400x); B: Group 6, hepatocyte damage (H&E, 400x).

The positive predictive values of FNAC in terms of hepatocyte damage, inflammation, and congestion were 100%, whereas it was 0% regarding fatty changes. However, the positive predictive values of the tru-cut biopsy method were 100% for all histopathological parameters. On the other hand, the negative predictive values of hepatocyte and congestion of both techniques were 0%, while negative predictive values of inflammation (50% vs. 25%) and fatty changes (33.3% vs. 20%) were higher in the FNAC compared to the tru-cut biopsy method.

DISCUSSION

Only a few studies compare FNAC and tru-cut biopsy in non-tumoral liver diseases. In this study, we performed tru-cut biopsy and FNAC to rats with experimental alcoholic liver disease and observed that tru-cut biopsy had higher sensitivity and diagnostic accuracy concerning hepatocyte damage when compared to FNAC. However, positive predictive values were similar for both methods. For inflammation, FNAC had higher sensitivity, diagnostic accuracy, and negative predictive value than tru-cut biopsy. For congestion and changes in fatty parameters, it was detected that tru-cut biopsy had higher sensitivity, diagnostic accuracy, and positive predictive value.

For any hepatic disease, the radiological, serological (such as alpha-fetoprotein), and clinical findings, among others, are not precisely and reliably able to differentiate benign and malign lesions;

TABLE 1. THE SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUES OF GROUP 5 (ALD WITH THE FNAC-APPLIED GROUP)

	Hepatocyte damage	Inflammation	Congestion	Fatty change
Sensitivity (%)	33.3	80	0	0
Specificity (%)	0	100	0	100
Diagnostic accuracy (%)	33.3	83.3	100	16.7
Positive predictivity (%)	100	100	100	0
Negative predictivity (%)	0	50	0	33.3

TABLE 2. THE SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUES OF GROUP 6 (ALD WITH THE TRU-CUT-APPLIED GROUP)

	Hepatocyte damage	Inflammation	Congestion	Fatty change
Sensitivity (%)	66.7	40	100	20
Specificity (%)	0	100	0	100
Diagnostic accuracy (%)	66.7	50	100	33.3
Positive predictivity (%)	100	100	100	100
Negative predictivity (%)	0	25	0	20

these methods can only increase the accuracy of the diagnosis[14]. At some point, liver biopsies become inevitable for the evaluation of patients and the management of the diseases[18]. Most liver biopsies are applied under radiological guidance, and the choice of the biopsy needle depends on the radiologist. Naturally, the experience of the radiologist may influence management. This decision also depends on many variants including the size and location of the tumor, and the risk of possible complications[19]. Currently, there are two commonly accepted and used techniques to obtain diagnostic material, namely, fine needle aspiration cytology (FNAC) and tru-cut biopsy. The FNAC technique usually provides a sample for cytological examination, whereas tru-cut biopsy primarily delivers a sample for histological assessment. Each method has different advantages and disadvantages, and both are considered safe[19]. Therefore, the sensitivity and specificity rates of these two techniques should be available for choosing the appropriate one.

There have been adequate scientific data about both tru-cut biopsy and FNAC techniques in the literature reporting the advantages and complications, as well as the rates of sensitivity and specificity. Ding et al.[20] performed a study with 46 hepatocellular carcinoma patients to distinguish primary and metastatic tumors and emphasized that FNAC is a useful technique. Li et al.[11] performed a tru-cut biopsy and FNAC techniques with 18G and 21G needles, respectively, on 94 patients with unresectable malignant tumors, and reported that the 21G FNAC and 18G tru-cut biopsy procedures were substantially similar. However, the safety of the 21G FNAC was found superior to that of 18G tru-cut biopsy. Tissues obtained by either of these two techniques are sufficient for any pathological and molecular diagnosis. Another study performed by Kaçar Özkara et al.[21] in 2013 pointed out that FNAC had a high sensitivity rate, especially in hepatic neoplasia. However, they also stressed that combined cyto-histopathology is superior to FNAC.

Most of the related studies generally report that FNAC is a successful technique and can be used for the diagnosis of hepatic tumors. It was stated that FNAC is a suitable method to be used for open biopsy or when surgery is not possible[22]. Sattar et al.[23] performed a study on 450 patients with focal hepatic lesions and determined that USG-guided FNAC was a rapid, safe, easy, and uncomplicated method for diagnosis. A comprehensive study[24] performed in 2015 on 755 patients with malignant and benign hepatic lesions detected that the diagnostic accuracies of FNAC and tru-cut biopsy were in the range of 58.8%-98.9%. Additionally, no complication had been reported in this study. On the other hand, Nazir et al.[15] detected a diagnostic accuracy and specificity between 95.2% and 100%. According to these authors, FNAC was a cheap, easy, and safe method. However, they claimed that tru-cut biopsy should be the gold-standard method.

In light of these findings, we observed that these tests were each superior in some aspects and equivalent regarding different features. We consider that the selection of the diagnostic method in alcoholic liver disease according to the histopathological parameters is a central point for a patient-based individualized approach. For instance, if the "inflammation" parameter is to be evaluated, FNAC should be preferred, while tru-cut biopsy should be at the forefront for the assessment of "fatty changes." This way, it will be possible to make a more suitable selection of the biopsy methods in terms of patient comfort, complication risk, ease of application, and cost.

In conclusion, we think that FNAC can be an attractive alternative to the tru-cut biopsy method and applied in routine practice in the diagnosis of non-tumoral liver diseases. To get the best results, a combined approach of FNAC and tru-cut biopsy may also be used.

Study Limitation

This study has some limitations. First, the biopsy techniques could also be performed on other liver diseases such as hepatocellular carcinoma and/or cirrhosis, or any other hepatic illness in addition to alcoholic liver disease. Second, a prospective study on patients with hepatic diseases could yield better results. Third, clinical, radiological, and serological findings could be obtained and compared with the biopsy results. Lastly, we did not perform a detailed observation of the complications because we had cervical dislocation immediately after the procedures.

Conflict of Interest

The authors have no financial disclosure or conflict of interest in this study.

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Author's Contribution

Y.A. and M.G. conceived the presented idea. Y.A., H.A.E., M.M, S.S.K., G.F.G., and M.G. planned the experiments Y.A., H.A.E., M.M, S.S.K., and G.F.G. carried out the experiments. Y.A., H.A.E., M.M, S.S.K., and G.F.G. contributed to sample preparation and planned the experiments. Y.A., H.A.E., M.M, S.S.K., and G.F.G. contributed to the interpretation of the results. Y.A. took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

RESUMO

INTRODUÇÃO: *Biópsias hepáticas tais como por agulha tru-cut e por citologia aspirativa por agulha fina (CAAF) são as técnicas frequentemente preferidas para detectar o grau e o estágio de certas doenças hepáticas. Neste estudo, nosso objetivo foi comparar a eficiência da biopsia com agulha tru-cut guiada por ultrassom e a citologia aspirativa por agulha fina em um modelo experimental de doença hepática alcoólica.*

MÉTODOS: *Trinta e seis ratos Wistar albinos fêmeas, de 4 a 6 meses de idade e pesando entre 190 e 250g, foram utilizados neste estudo. Os animais foram divididos aleatoriamente em seis grupos: G1 (controle), G2 (controle tru-cut), G3 (CAAF), G4 (modelo de doença hepática alcoólica), G5 (modelo de doença hepática alcoólica + CAAF) e G6 (modelo de doença hepática alcoólica + biópsia tru-cut). Após uma avaliação histopatológica por microscopia de luz, foram calculados a sensibilidade, especificidade e os valores preditivos positivos e negativos da CAAF e biópsia por tru-cut para o diagnóstico de lesões hepáticas.*

RESULTADOS: *Nenhuma patologia foi detectada no G1, apenas leve congestão. Por outro lado, detectamos danos nos hepatócitos, inflamação periportal, congestão e alterações nos ácidos graxos nos tecidos hepáticos de todos os grupos de doença hepática alcoólica. As sensibilidades encontradas para os danos nos hepatócitos, inflamação, congestão e alterações nos parâmetros de ácidos graxos para a CAAF foram 33,3%, 80%, 0% e 0%, respectivamente, enquanto que as sensibilidades das mesmas variáveis para o método tru-cut foram 66,7%, 40%, 100% e 20%, respectivamente.*

DISCUSSÃO: *Ambas as técnicas foram superiores em alguns aspectos. A CAAF pode ser uma alternativa atraente à biópsia por tru-cut e aplicada como prática de rotina no diagnóstico de doenças hepáticas não tumorais.*

PALAVRAS-CHAVE: *Hepatopatias alcoólicas. Biópsia por agulha fina. Biópsia.*

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