

Frequency of fibrosis in patients with incidentally detected hepatosteatosi

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SUMMARY

OBJECTIVE: In this study, we aimed to elucidate fibrosis in patients who visited our outpatient clinic with complaints such as abdominal pain and dyspepsia and who had fatty liver by ultrasound imaging.

METHODS: A total of 119 patients who were admitted to the gastroenterology outpatient clinic of our institution with incidentally detected hepatosteatosi on ultrasound imaging were included in the study. Patients with hepatosteatosi were examined for fibrosis with the FibroScan-502-touch (Echosens, Paris, France) elastic tissue ultrasonography device. The effects of these parameters on hepatosteatosi and possible fibrosis degree were investigated.

RESULTS: No fibrosis was detected in 75 (63.02%) patients with hepatosteatosi on ultrasound imaging, 20 (10.05%) F1, 22 (18.48%) F2, 1 (0.8%) F3, and 0.1 (0.8%) F4. Accordingly, as the degree of steatosi increases in patients with incidentally detected hepatosteatosi, the degree and frequency of fibrosis increase with statistical significance ($p < 0.05$). A statistically significant difference was found between the alanine transaminase increase and the hepatosteatosi degree ($p = 0.028$). The median value of gamma-glutamyltransferase was 15 U/L in S0, 18.5 U/L in S1, 22 U/L in S2, and 26 U/L in S3 ($p < 0.047$).

CONCLUSION: To date, no research exists on fibrosis in patients with incidental hepatosteatosi. The outcomes of this study elaborated that patients with hepatosteatosi in the community could be detected at least at an early stage by following up and diagnosing them with serum markers before they progress to end-stage fibrosis.

KEYWORDS: Non-alcoholic fatty liver disease. Liver cirrhosis. Fibrosis.

INTRODUCTION

Hepatosteatosi means that the liver has more than 5% of its weight as fat. Such patients are clinically observed as alcohol-related and non-alcoholic fatty liver disease (NAFLD). NAFLD is seen at an average rate of 25% across the world¹. Most cases of NAFLD are asymptomatic. It is usually discovered incidentally with mild ALT elevation in routine blood tests or abdominal USG. NAFLD may progress to non-alcoholic steatohepatitis (NASH) associated with lobular inflammation and apoptosis, which may lead to hepatic steatosi, fibrosis, and cirrhosis².

Although liver biopsy is the gold standard diagnostic method for NASH patients, its use today could be more practical due to certain limitations. Therefore, less invasive, easily reproducible methods were considered, and a transient elastography device was developed with the trade name Fibroscan. This device is used to perform elastic

tissue ultrasonography, which is a method that allows us to measure the elasticity of soft tissues with numerical data. This method simultaneously gives the patient's degree of fatty liver and the degree of possible fibrosis in the liver in light of numerical data³.

Within the scope of this research, we aimed to elucidate fibrosis, which may have developed in patients who visited our outpatient clinic with complaints such as abdominal pain and dyspepsia and who had fatty liver by USG. In addition, we compared the hepatosteatosi data of both methods and devices by considering those who underwent Fibroscan for fibrosis or any other reason.

METHODS

A total of 119 patients who were admitted to the gastroenterology outpatient clinic of our institution with incidentally

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Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.

Received on August 05, 2023. Accepted on August 26, 2023.

detected hepatosteatois on USG were included in the study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval was obtained from our institution, and informed consent was obtained from all participants.

Patients with hepatosteatois were examined for fibrosis with the FibroScan-502-touch (Echosens, Paris, France) elastic tissue ultrasonography device. The routine biochemical values of the patients such as fasting blood glucose, fasting insulin, AST, ALT, GGT, platelet count, triglyceride, TSH, HDL, and LDL were processed. The body mass index (BMI) and body fat percentage were examined via the TANITA device. The effects of these parameters on hepatosteatois and possible fibrosis degree were investigated.

Individuals under the age of 18 and above 65 years, pregnant women, patients with known liver diseases such as liver cirrhosis, drug use that may cause hepatosteatois, diabetic patients, those with a BMI > 40 kg/m², those with narrow intercostal range, those with active malignancy and congestive heart failure, and those with acid fluid in the abdomen were not included in the study.

Statistical analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 23.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and mean and standard deviation for continuous data were given as descriptive values. The “independent sample T-test” was used to compare two groups, and the “Pearson chi-square test” was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

A total of 119 patients were enrolled, of whom 52 (43.7%) were males and 67 (56.3%) were females. The average age of the patients is 39.15 years, and their average BMI is 29 kg/m² (Table 1).

According to the data obtained from the transient elastography examinations performed on the patients with hepatosteatois, S0 indicates no fatty liver, S1 indicates first-degree fatty liver, S2 indicates second-degree fatty liver, and S3 indicates third-degree fatty liver. The population had a statistically significant difference between hepatosteatois and advanced age, weight gain, increased BMI, and increased body fat ratio (p < 0.001) (Table 2).

Table 1. Comparison of fibroscan and hepatosteatois measurement with demographic characteristics.

		Fibroscan hepatosteatois measurements (E-CAP)											p-value	
		S0			S1			S2			S3			
		med	min	max	med	min	max	med	min	max	med	min		max
Age (years)		30	20	49	29	19	65	40	24	62	45	19	80	<0.001
Height (cm)		159	151	177	171	154	185	166	151	188	161	139	183	<0.037
Weight (kg)		68.6	44.9	95.4	79.3	48.8	119.2	80.6	51.6	106.6	83.1	43.6	114.2	<0.001
BMI (kg/m ²)		26.3	16.4	37.7	27.0	20.1	36.0	29.4	20.9	38.7	31.4	17.7	42.2	<0.001
Fat (%)		26.9	4.1	53.5	24.1	13.3	39.4	34.6	14.9	47.6	35.6	12.1	49.4	<0.001
		n			n			n			n			
Gender	M	9.00			9.00			10.00			24.00			
	F	18.00			7.00			17.00			25.00			

Table 2. Comparison of ultrasound imaging and fibroscan hepatosteatois measurements.

		Fibroscan hepatosteatois measurements (E-CAP)								X ² p-value	Kappa p-value
		S0		S1		S2		S3			
		n	%	n	%	n	%	n	%		
USG hepatosteatois measurements	Grade 1	20	74.1	9	56.3	12	44.4	12	24.5	0.001	0.046
	Grade 2	7	25.9	7	43.8	13	48.1	28	57.1		
	Grade 3	0	0.0	0	0.0	2	7.4	9	18.4		

During the evaluation of hepatosteatosi by transient elastography of patients with hepatosteatosi detected on USG, 20 of 53 patients with grade 1 hepatosteatosi detected by USG did not detect steatosi by transient elastography. Accordingly, when the hepatosteatosi detection rates of USG and transient elastography are compared, although both devices do not agree in detecting low-grade hepatosteatosi, they seem more compatible in detecting advanced hepatosteatosi. This difference in compatibility may be due to the relative operator-dependent results of USG and the choice of cutoff values of the transient elastography device.

No fibrosis was detected in 75 (63.02%) patients with hepatosteatosi on USG, 20 (10.05%) F1, 22 (18.48%) F2, 1 (0.8%) F3, and 1 (0.8%) F4. Accordingly, as the degree of steatosi increases in patients with incidentally detected hepatosteatosi, the degree and frequency of fibrosis increase with statistical significance ($p < 0.05$) (Table 3).

The average fasting insulin in the group called S0 by Fibrosan was 7.9 mU/L, the average fasting insulin was 9.65 mU/L in S1 patients, the average fasting insulin was 12.7 mU/L in S2 patients, and the average fasting insulin in S3 patients was 16 mU/L. A statistically significant increase was observed between increased fasting insulin and hepatosteatosi ($p < 0.001$).

The ALT average of the patients with S0 was 20 U/L, the average of those with S1 was 25 U/L, the average of those with S2 was 26 U/L, and the average of those with S3 was 34 U/L.

A statistically significant difference was found between the ALT increase and the hepatosteatosi degree ($p = 0.028$). The edian value of GGT was 15 U/L in S0, 18.5 U/L in S1, 22 U/L in S2, and 26 U/L in S3 ($p < 0.047$).

DISCUSSION

In this study, the frequency of liver fibrosis of various degrees and the parameters affecting fibrosis were investigated and discovered incidentally in patients not expected to have hepatosteatosi. Considering that obesity is a worldwide pandemic, early detection of fatty liver disease is important in terms of public health in order to prevent it from developing

into an advanced liver disease such as cirrhosis. The prevalence of hepatosteatosi can be obtained even from the demographic characteristics of patients who visit outpatient clinics for any reason. Hepatosteatosi is seen more frequently in patients with advanced age, increased BMI, and increased body fat percentage⁴.

Patients with chronic diseases such as diabetes mellitus and other conditions that may cause hepatosteatosi were not included in this study. Data such as age, gender, BMI, total fat mass and body fat percentage, lean body mass, and total body water were compared in a study of 253 patients with similar inclusion and exclusion criteria suggested by Lédinghen et al., who reported that the use of body composition parameters in NAFLD disease has a diagnostic value, which is similar to our research⁵.

When USG detected hepatosteatosi, it was re-evaluated by transient elastography. Thus, the hepatosteatosi seen in USG could not be detected with transient elastography. This situation may be attributed to the evaluation of the operator performing the USG and the fact that the values measured with the transient elastography device have different reference intervals for each degree of hepatosteatosi. However, as seen in our study, as the degree of hepatosteatosi increased, the relationship between the degree of hepatosteatosi detection of USG and transient elastography increased⁶. Xu et al., compared USG, Fibrosan, and hepatic adiposity index (HSI) in a biopsy-based study of patients with chronic hepatitis B. In this study, the accuracy of Fibrosan and HSI was higher than ultrasound in the evaluation of mild and moderate hepatosteatosi shown in biopsy⁷. Macabuag-Oliva et al., found that the Fibrosan device was more sensitive than USG in detecting hepatosteatosi in a study conducted by 102 diabetic and metabolic syndrome patients⁸.

Various degrees of fibrosis were detected in 44 (36.9%) of 119 patients with hepatosteatosi who were included in the study and had no condition to cause fibrosis. A multicenter study indicated that liver fibrosis was evaluated correctly with Fibrosan in patients with chronic viral hepatitis⁹. These data elaborated that individuals unaware that they have hepatosteatosi

Table 3. Fibrosis frequency according to ultrasound imaging grades.

		Fibrosan hepatosteatosi measurements (E-median)										p-value
		F0		F1		F2		F3		F4		
		n	%	n	%	n	%	n	%	n	%	
USG hepatosteatosi measurements	Grade 1	35	66.0%	10	18.9%	8	15.1%	0	0.0%	0	0.0%	0.032
	Grade 2	36	65.5%	6	10.9%	12	21.8%	1	1.8%	0	0.0%	
	Grade 3	4	36.4%	4	36.4%	2	18.2%	0	0.0%	1	9.1%	

in society develop fibrosis at a substantial rate. Our study diagnosed F4 fibrosis, and liver cirrhosis in one patient.

Fasting insulin, which is one of the biochemical parameters, is a part of the metabolic syndrome, which also includes obesity. In this study, when we compared fasting insulin with hepatosteatosi, it was observed that the degree of hepatosteatosi increased in patients with higher fasting insulin levels. Mikolasevic et al., conducted a prospective study of 648 patients on the effects of metabolic syndrome on fatty liver disease, and fibrosis and hepatosteatosi values were measured with Fibroscan. When the patients' insulin resistance was calculated by HOMA-IR and evaluated according to the degree of hepatosteatosi, a statistically significant positive correlation was found between insulin resistance and hepatosteatosi¹⁰.

When the patients' mean GGT and ALT values were compared, a statistically significant increase was observed between the increase in GGT and ALT levels and hepatosteatosi. Serum ALT values were statistically significantly higher in individuals with hepatosteatosi. At the same time, serum ALT values increased statistically significantly in correlation with the increase in the liver's adiposity severity. In the GGT arm of the same study, serum GGT values were statistically significantly higher in all the three groups with mild, moderate, and severe fatty infiltration in the liver¹¹. This allows us to speculate about hepatosteatosi by analyzing the serum parameters of patients who visited the outpatient clinic for any reason other than imaging.

CONCLUSION

To date, no research exists on fibrosis in patients with incidental hepatosteatosi. The outcomes of this study elaborated that patients with hepatosteatosi in the community could be detected at least at an early stage by following up and diagnosing

them with serum markers, Tanita measurements, and transient elastography before they progress to end-stage fibrosis.

INSTITUTIONAL REVIEW BOARD APPROVAL

Ethics committee approval was obtained from Kahramanmaraş Sütçü İmam University of Medical Faculty on 16 October 2019 with protocol number 488665165-302.14.01.

EDITORIAL SUPPORT

The editorial support of this article has been conducted by QA Executive Consultancy, Ozan Batigun MD, MBA in 2023. www.QAexecutiveconsultancy.com, Ozan.Batigun@outlook.com.

ETHICAL DECLARATION

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval was obtained from our institution. As this was a retrospective research, no informed consent has been obtained from participants.

AUTHORS' CONTRIBUTIONS

MÇ: Software, Supervision, Validation, Visualization, Writing – review & editing. **BK:** Software, Supervision, Validation, Visualization, Writing – review & editing. **MI:** Project administration, Software, Supervision, Validation, Visualization. **KG:** Formal Analysis, Investigation, Methodology, Writing – review & editing.

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