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Feasibility of Liver Fibro Scan in Assessing Early Hepatic Affection In Patients With OSA

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Abstract

Background

OSA has an overall prevalence of 2-4 %t with an approximate incidence of 14 percent in males and 5 percent in females aged (30-70) years [1].

Non-alcoholic fatty liver disease (NAFLD) is associated with OSA, which leads to increased morbidity and mortality in patients with OSA. [2].

Objective: The aim of this study was to assess the reality of elastogram in evaluating early hepatic changes in patients with OSA and also its relationship with the severity of OSA.

Results This study included seventy (70) participants, 25 healthy volunteers as a control group, 45 OSA patients (6 mild, 14 moderate, and 25 severe). In our study, there was no substantial difference between OSA patients and healthy control subjects regarding serum levels of ALT and AST. In OSA patients with different severity, AST and ALT levels were also not substantially different.

Our study revealed that evaluating liver stiffness measurement (LSM) by fibro scan showed statistically significant increase among patients with OSA compared with control (obese) healthy subjects.We found that LSM increased with increase severity of OSA. At cutoff point >1.46cm.sec, LSM has 68% sensitivity & 80% specificity in detecting severe OSA. In the present study; we found positive correlation between LSM and AHI in the studied OSA patients.

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According to Metavir score in staging of liver fibrosis; in our study liver fibrosis is more among OSA patients than control obese. We found that 62.2% of the OSA patients had mild – moderate fibrosis, while; 31.1% of them had normal – mild fibrosis, and 6.7% had normal liver.

Conclusion:

Even in the presence of normal liver enzymes, liver affection is common in OSA patients and can be evaluated by liver stiffness measurement using fibro-scan.

Keywords

Liver stiffness measurement, obstructive sleep apnea, liver fibrosis.

Abbreviations

LSM :Liver stiffness measurement **TE** :transient elastography**NAFLD**: nonalcoholic fatty liver disease

OSA : obstructive sleep apnea**ODI** : oxygen desaturation index

Introduction

OSA is a common disease that is associated with subsequent systemic comorbidities.Its hypoxia-related consequences may lead to the development and exacerbation of NAFLD[3].Compared to the general population, patients with OSA have a high prevalence of NAFLD, suggesting that patients with OSA should be screened for NAFLD presence and severity. [4].

NAFLD entails numerous histologic hepatic lesions, ranging from simple steatosis, steatohepatitis, and fibrosis, leading eventually to liver cirrhosis in the end stage. Several studies have shown that in patients with NAFLDD, the extent of liver fibrosis is the primary determinant of liver prognosis.[5].

Liver biopsy is the primary method for determining liver fibrosis,however, it is an invasive process and is associated with a significant complication rate of about 1% and a significant expense. [6].Noninvasive screening methods have been developed and validated for liver fibrosis, including serum liver enzymes and transient elastography (TE) devices.[7, 8]. TE is a rapid technique with strong reproducibility and immediate outcomes at the bedside or in the outpatient clinic. It can be done by liver stiffness measurement (LSM) using TE (Fibro-Scan). [9].

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Subjects and methods:

For the purpose of the current study 70 subjects were recruited. Forty five subjects were patients with confirmed OSAS according to the results of sleep studies, and 25 subjects were healthy control. The patient's group and the control group were matched for age, sex and BMI.From all participantswritten informed consent was obtained.

Inclusion criteria:

Adult patients with OSAas confirmed by polysomnography

Exclusion criteria

Patients younger than 18 years old, any concurrent diseases that may interfere with the sleep study ,Any illness that may accentuate the degree of hypoxemia and hence the cofounding effect of OSA on the reported polysomnographic parameters, any other disease condition that could have effect on liver functions (e.g heart failure , pregnant female, drinking alcohol), also patient with history of chronic liver disease due to any cause were excluded.

All subjects were subjected to

1- thoroughly history taking , General and local examination
2- Anthropometric measurements (BMI and neck circumference).
3- Routine laboratory investigations include :complete blood picture, renal function tests and liver function tests
4- Abdominal ultrasound
5- Spirometry was done for the patients group.
6- polysomnographic (PSG) data including apnea hypopnea index (AHI), oxygen desaturation index (ODI), Minimum O_2 value and Number of desaturations below90% were obtained from the sleep study of the patients group.
7- **Liver elastography:** Patients were examined while lying supine position with the right arm elevated above the head. Liver stiffness (LS) was measured by an operator who was blinded to the PSG results. The examinations were done using a Doppler ultrasound device ToshibaAplio 500 (**Toshiba Medical Systems Corp., Tokyo, Japan**) using 14 MHz linear-array transducer and 5 MHz curved array transducer. LSM was performed

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using shear wave elastography (SWE). LS was measured as the median value of 5-10 valid measurements that were performed in each patient [10].

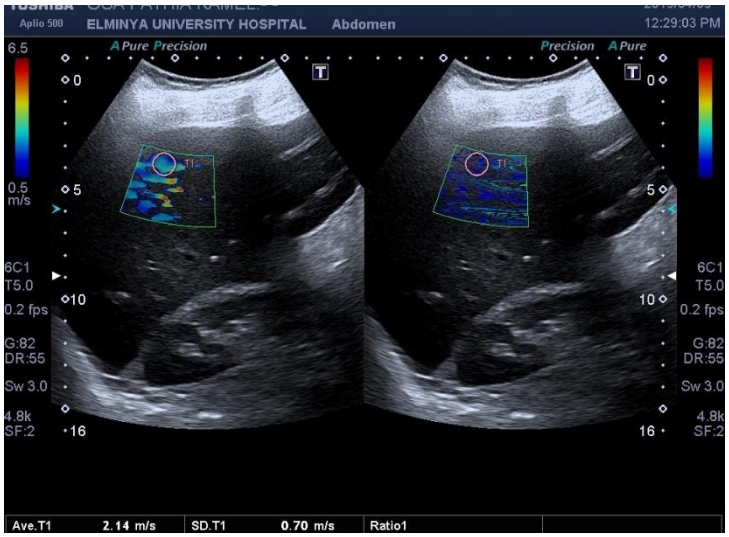

Fig. 1. Liver elastography**.**

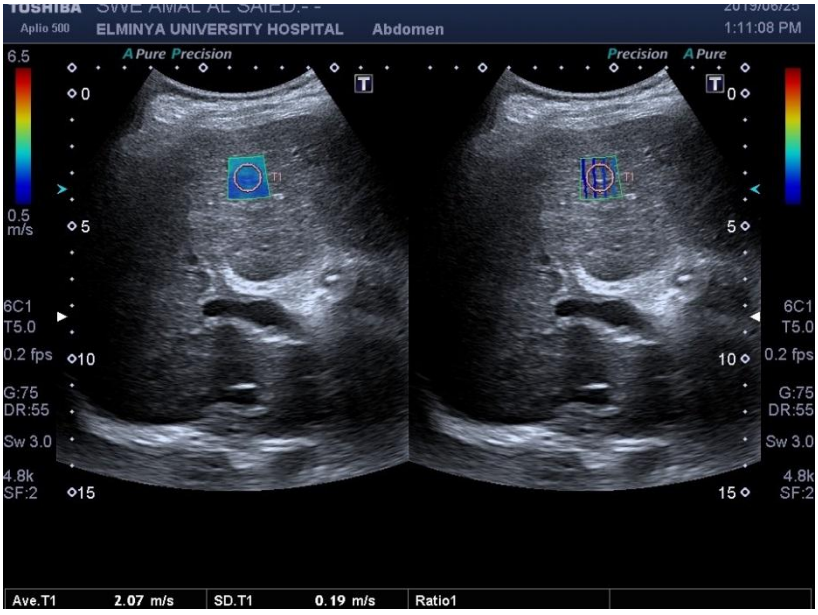

Fig. 2. Liver elastography.

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Statistical analysis

The data collected was statistically analyzed using **software version 25 of the SPSS** (Statistical Kit for Social Sciences) program. Descriptive statistics were carried out by median and interquartile range (IQR) for non-parametric quantitative data, and by number and percentage for categorical data.

Distribution of the data was done using **Shapiro Wilk test.** Analysis were done for parametric quantitative data between the three groups using **One way ANOVA test** followed by **Post Hoc** Analysis between each two groups and for non-parametric quantitative data between the three groups using **Kruskal Wallis Test**and y **Mann Whitney test ..**

Analyses were carried out using the **Independent Samples T test** for parametric quantitative data between the two groups and the **Mann Whitney test** for non-parametric quantitative data between the two groups. Qualitative data analyses were conducted using **the Chi square test**.

Ethical considerations

The study was approved by Minia University Hospital's Research Ethics Board, Minia University, Egypt.

Results

This observational cross sectional, case control study was carried on 70 subjects((45 patient with OSA, (25) obese healthyvolunteers) selected from those who sought for medical advice in outpatient chest clinics or from inpatient wards at cardiothoracic Minia university hospital during the period between January 2019 to January 2020.

In this study table (1) shows Socio- demographic, and anthropometric measures among the studied groups which include control obeseand OSA patients.

Table (2) shows shows Socio-demographic, and anthropometric measures among the diseased groups (mild, moderate and sever) (A, B and C respectively).It was found that neck circumference were significantly higher among severe group than moderate and mild groups (P= 0.007*).

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Table (3) shows liver function tests among OSA patients (mild, moderate, and severe).It was found that there were no statistically significant difference in liver enzymes and seum albumin among OSA patients.

Table (4) shows liver elastography among OSA patients and control group.It was found that there were statistically significant increase in the liver elastography among OSA patients more than control subjects (P= <0.001*).

Table (5) shows liver elastography among the diseased groups (mild, moderate, and sever groups). It was found that there were statistically significant increase in liver elastography among sever OSA patients more than moderate and mild group (P= <0.001*).

Table (6) shows significant positive correlation between liver elastography, and AHI, and SPO2 time less than 90 (P= 0.008, P= 0.007, and P= 0,003, respectively).

Table (7) Displays the degree of liver fibrosis affection among OSA patients and control groups according to the Metavir score.It was found that there was significant increase in liver fibrosis among OSA patients than in control subjects (P= <0.001*).

It was found that 62.2% of OSA patients and 4.3% of control subjects had mild – moderate liver fibrosis, while; 31.1% of OSA patients, 30.4% of control subjects had normal – mild affection, and 6.7% of OSA patients, 68% of control subject had normal liver.

In the present study (Figure 3) shows ROC curve analysis for prediction of severity of OSA patients.At cutoff point >1.46m/s, liver elastography has 68% sensitivity & 80% specificity in detecting severe OSA.

Discussion

Hepatic affection is common with OSA and ranging from NAFLD, simple steatosis, steatohepatitis, fibrosis, and cirrhosis(14,15).Intermittent hypoxia (IH)induces triglyceride accumulation as well as hepatic inflammation and liver injury. IH accelerates hepatic steatosis progression by inducing lipolysis of adipose tissue, Induces liver oxidative stress and up-regulates factor 1 alpha inducible hypoxia [11].

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Fibro Scan is a novel ultrasound technology that is helping in assessment of hepatic steatosis and fibrosis. The Controlled Attenuation Parameter (CAP) measures the degree of ultrasound attenuation by hepatic fat together with liver stiffness measurements (LSM). CAP values significantly correlated with the degree of steatosis on liver biopsy [12]

The present study was conducted on 70subjects ,25 control healthy obese, and 45 OSA patients (6 mild, 14 moderate, and 25 severe),no significant difference exist between the patient group and the control group regarding; age sex, smoking status or BMI

Many studies have shown an association between OSA and NAFLD [13-15].NAFLD has a complex continuum of disease severity that vary from basic steatosis without inflammation to non- alcoholic steatohepatitis (NASH) that can lead to liver cirrhosis [16].

Measurement of alanine and aspartate aminotransferase serum levels (ALT and AST) is used to determine liver damage, but these are neither sensitive nor unique to diagnose NAFLD. [17].

in the current study there was no substantial difference in serum levels of ALT and AST between OSA patients and healthy control subjects. Also among OSA patients with different levels of severity, AST and ALT levels were also not significantly different. Our findings are in accordance with two previous studies [15, 18], in both studies the serum level of both ALT and AST values were within the normal range in all OSA patients regardless of its severity. Another cross-sectional studies by**Kheirandish et al**and**Kallwitz et al** have shown significantly higher serum ALT and AST in OSA patientscompared to healthy control subjects [13, 14, 19].

Tanne et al.[13]also found that The existence of severe OSA (defined as AHI>50) has been found to be an independent predictor of increased liver enzymes..

Studies found that elevated liver enzymes are neither sensitive nor specific markers of NAFLD and NASH [17, 20].One study reported a direct correlation between a serum marker of liver fibrosis, type III pro- collagen, triglyceride and fasting plasma glucose, but not ALT or AST in patients with OSA [21].

In the current study assessment of LSM using fibro scan showed significant increase among patients with OSA compared with control healthy subjects (P= <0.001).LSM alsowas increased

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with increase severity of OSA (P= <0.001).At cutoff point >1.46cm.sec, LSM has 68% sensitivity & 80% specificity in detecting severity of OSA.

This study findings are in agreement with histological data from previous studies [18, 22]that found that almost 50% of severe OSA patients present significant fibrosis (stage F2 or greater).

In accordance with our finding **Trzepizuret al.**[23] reportedsignificant liver disease (LSM ⩾7.3 kPa) in patients with severe OSA and metabolic comorbidities.they found also advanced liver fibrosis in severe OSA patients with (LSM ⩾9.6 kPa) after adjustment for the main factors contributing to the development and exacerbation of NAFLD.They also found that AHI and ODI were the factors with the strongest independent association with LSM.

Another studyby**Agrawal et al**.[24] found an independent correlation between the severity of intermittent hypoxia(IH) and increased fibrosis..

In the present study there was positive correlation between LSM and AHI in the studied OSA patients (P= 0.007*). This in agreement with **Bertha et al.**[25]whoshowed a positive association of liver stiffness with OSA patients and with severity of OSA (β 0.04 (95% IC 0.005; 0.07; p = 0.024)).

Conclusion

Early Liver affection is common in OSA patients and can be assessed by liver stiffness measurement using fibro-scan while liver enzymes are normal.

Table (1): Demographic characteristic of the studied subjects:

		Control group (I)	**Cases (II)**	**P value**
		N=25	**N=45**	
Age	Mean±SD	53.2±8.3	54.4±8.9	0.1

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Sex	Male Female	10(40%) 15(60%)	16(35.6%) 29(64.4%)	0.133
Smoking status	Current Ex-smoker No smoker	6(26.1%) 4(17.4%) 15(60%)	11(24.4%) 5(11%) 29(64.4%)	0.555
BMI	Mean±SD	40.6±3.5	43.3±6.4	0.07
Neck circumference	Mean±SD	37±2.7	45.9±4.9	<0.001*

BMI= body mass index.

Table (2): Demographic characteristic of the studied patients:

		Mild (A)	**Moderate (B)**	**Severe (C)**	**P value**		
		N=6	**N=14**	**N=25**			
Age	Mean±SD	52.7±10.1	55.3±9.8	56.5±7.6	0.454		
					A vs B	A vs C	B vs C
					0.72	0.47	0.74
Sex	Male	1(16.7%)	3(21.4%)	11(44%)	0.30		
					A vs B	A vs C	B vs C
	Female	5(83.3%)	11(78.6%)	14(56%)	1	0.36	0.19

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Smoking status	Current	1(16.7%)	3(21.4%)	8(32%)	0.52		
	Ex-smoker	1(16.7%)	2(14.3%)	3(12%)	A vs B	A vs C	B vs C
	Non smoker	4(67.6%)	9(64.3%)	14(56%)	0.56	0.27	0.87
BMI	Mean±SD	40.2±3.9	42.8±4.6	45.4±7.2	0.145		
					A vs B	A vs C	B vs C
					0.7	0.17	0.40

Table (3): Liver function tests among the diseased groups:

		Mild (A)	**Moderate (B)**	**Severe (C)**	**P value**		
		N=6	**N=14**	**N=25**			
ALT	Median	27.5	30.5	27	0.515		
	IQR	(13.8-35)	(20.3-50.5)	(21.5-34.5)	A vs B	A vs C	B vs C
					0.322	0.725	0.340
AST	Median	23	26.5	22	0.359		
	IQR	(11.8-30.8)	(20-33.3)	(18.5-27.5)	A vs B	A vs C	B vs C
					0.341	0.861	0.172
Albumin	Mean±SD	4±0.1	3.9±0.4	4.1±0.4	0.494		
					A vs B	A vs C	B vs C
					0.955	0.847	0.476

Table (4): liver elastography among the studied groups:

		Control (I)	**Cases (II)**	**P value**
		N=23	**N=45**	

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liver elastography (m/s)	Mean±SD	1.1±0.2	1.5±0.2	<0.001*

Table (5) liver elastography among the diseased groups:

		Mild – Moderate	**Severe**	**P value**
		N=20	**N=25**	
Liver elastography (m/s)	Mean±SD	1.4±0.1	1.6±0.2	**<0.001***

Table (6): Correlation between liver elastography, with AHI, average SPO2, and SPO2 time less than 90:

Cases (n=45)	**Liver elastography**	
	r	**P value**
AH index	**0.396**	**0.007***
Average SPO2	-0.152	0.319
SPO2 time less than 90	0.184	0.226

Table (7: Degree of liver affection in the studied groups:

		Control (I)	**Cases (II)**	**P value**
		N=25	**N=45**	

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Liver elastography	Normal Normal-mild Mild-moderate	17(68%) 7(30.4%) 1(4.3%)	3(6.7%) 14(31.1%) 28(62.2%)	**<0.001***

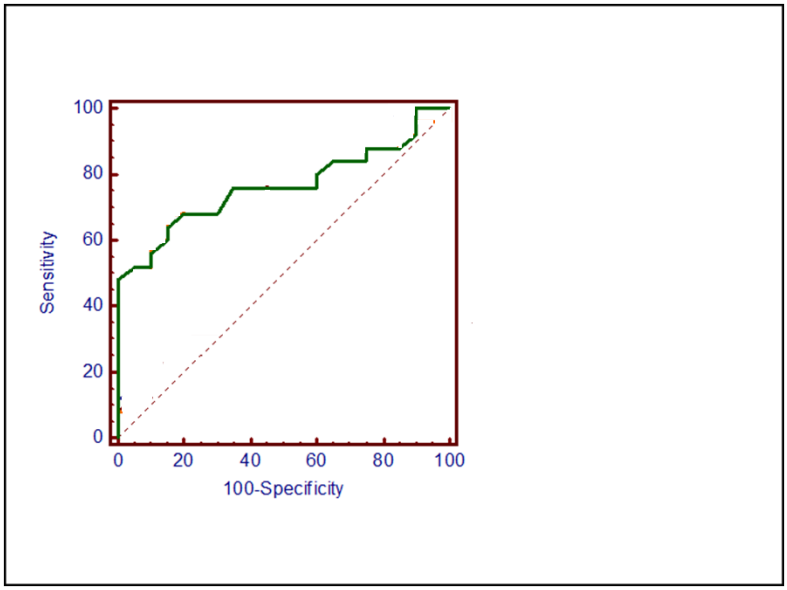

Figure (3): ROC curve analysis for prediction of severe cases (mild – moderate cases is reference group):

ROC curve analysis for prediction of severe cases (mild – moderate cases is reference group)

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