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Predicting of hepatic steatosis in living liver donor via CT liver attenuation index (LAI) and fibroscan controlled attenuation parameter (CAP) correlation with biopsy result

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Abstract

Background The most prevalent persistent parenchymatous liver alterations in healthy individuals are thought to be hepatic steatosis. The liver biopsy is the most crucial procedure for the identification and measurement of hepatic steatosis. By identifying the liver attenuation index (LAI) at CT image with fibroscan controlled attenuation parameter (CAP), hepatic steatosis can be evaluated without the risk of liver resection.

Objective Using liver biopsy histological analysis as a reference standard, to examine the precision of the CT liver attenuation index (LAI) and fibroscan controlled attenuation parameter (CAP) for quantitative evaluation of macrovesicular steatosis in living related liver donors.

Methods In this cross-sectional study, comparing the CT liver attenuation index & fibroscan controlled attenuation parameter with liver biopsy result for the detection of the steatosis in subject's candidate for liver living donors, 50 subjects were conducted at Ain Shams Specialized Hospital and other private hospitals over about 2 years.

Results Our study reported that liver attenuation index of 9 is the cutoff value in post-contrast CT images with sensitivity 100% and specificity 80% that make it a very good method to exclude donor to have steatosis $\geq 15\%$, which mean that if donor had LAI index < 9 , we can safely do proceed do liver biopsy. Our study reported that CAP measurement had an AUROC OF 0.780, for detecting steatosis $\geq 15\%$, with sensitivity is only 60% with specificity as CT LAI of 80%, our results consider low compared to other studies, that could be due to small number of donors in our study with steatosis $\geq 15\%$ (five cases from 50 donors) unlike the other studies.

Conclusion When used to estimate the amount of liver fat in liver donors, the examined CAP and CT indices worked equally. But according to multivariate analysis, the only factor strongly linked with hepatic steatosis in a living donors was the CT LAI index. We contend that the combination of CT LS attenuation index and CAP allows for the detection of the degree of hepatic steatosis and can be used as an option to liver biopsy, reserving liver biopsy for those with positive steatosis donors.

Keywords Fibroscan controlled attenuation parameter, Hepatic steatosis, Living liver donor, CT liver attenuation index

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Background

Hepatic steatosis is one of the most frequent chronic parenchymatous liver changes in healthy people, and it can prevent a healthy donor from transplantation, because fatty changes that affect the graft's longevity can also affect the donor's own liver function [1].

The pattern of fatty infiltration varies, spanning from a more heterogeneous spread to a readily measurable uniform steatosis. The latter is caused by differences in the hepatic blood supply, with the right lobe, which gets more input from the portal venous circulation, exhibiting more marked fatty change [2].

The liver biopsy is the most crucial procedure for the identification and measurement of hepatic steatosis. Nevertheless, this approach is still invasive and exposes users to the danger of bleeding and infection [3].

In order to learn more about the spread of fat in hepatic lobules, liver biopsy is used as a reference standard for evaluation, but individuals with more diverse patterns of fatty infiltration may experience sampling mistakes [4].

The noninvasive radiological techniques of ultrasound (US), computed tomography (CT), and magnetic resonance (MR) imaging are considered useful methods for the identification and measurement of steatosis [5].

By identifying liver attenuation index (LAI) at unenhanced CT scan, which may reduce the need for liver biopsy among donors with unacceptably high levels of hepatic macrovesicular steatosis, CT scan is thought to be a safer alternative to liver biopsy for evaluating hepatic steatosis [6].

On unenhanced CT scans, the precise identification of fatty infiltration of the liver has been well documented. However, a lot of CT scans are done after administering IV contrast material, which frequently prevents correct identification. The controlled attenuation parameter (CAP) using fibroscan M or XL probe has been created for hepatic steatosis evaluation. In individuals with non-alcoholic fatty liver disease (NAFLD), moderate steatosis has been shown to respond favourably to CAP [7].

With liver biopsy histological analysis serving as a reference standard, the objective of this study was to evaluate the precision of the CT liver attenuation index (LAI) and fibroscan controlled attenuation parameter (CAP) for quantitative assessment of macrovesicular steatosis in living related liver donors.

Patients and methods

This study, which was carried out at Ain Shams Specialized Hospital and other private hospitals over the course of about 2 years, compared the CT liver attenuation index and fibroscan controlled attenuation parameter with liver pathology of steatosis in subject's candidate for

liver living donors. Convenience selection was used in the research.

The research included patients from both sexes who were presenting to an outpatient liver donation centre for a living liver donor and were between the ages of 18 and 40. Patients with other chronic parenchymatous liver illnesses, pregnancy, those under the age of 18, and individuals over the age of 40 were all disqualified from the research.

After telling the patient of the nature and goal of the research and explaining the risks and complications to them, including radiation exposure, written consent was acquired from the department of radio diagnosis at the Ain Shams Specialized Hospital.

The patients were required to fast for the recommended minimum of 4 h, prepare a volunteer for hepatic fibroscan evaluation on the same day as the CT scan, and schedule a liver biopsy that would be performed in conjunction with the CT scan either that day or in the following few days.

The CT scanning process went as follows. A CT machine will be used to conduct the CT scan (SIEMENS, SOMATOM Definition flash, 256 dual-source, Germany). Usually, the sufferer is supine on his back. He was requested to hold his breath before a reconnaissance picture was taken to identify the proper beginning position for the scans. Straps and cushions may be used to help him keep the correct posture and stay still throughout the test. Then, as the real CT scanning was being done, the table was gently manoeuvred through the apparatus. The full CT included arterial, Porto venous, and delayed scan. After injecting between 120 and 180 ml of a non-ionic contrast substance (Omnipaque 350, GE Healthcare, USA), we were able to acquire the pictures. We used real-time bolus monitoring and scanning that was immediately initiated to identify 180 HU at the lower thoracic aorta, followed by the capture of the portal phase at 22 s, the hepatic venous phase at 28 s, and the delayed phase at 300 s after the arterial phase. Oral contrast is not provided.

The acquired data were moved to a computer for image analysis and post-processing. Using the average of 25 readings from five different areas of interest (ROIs), each donor liver's mean hepatic attenuation was calculated (five ROIs per section). On the delayed period, the average ROI area was estimated to be between 250 and 350 mm². Nine different ROIs recorded on three parts are averaged to determine the mean splenic attenuation (three ROIs per sections). The formula for calculating the liver attenuation index (LAI), which is the difference between the average attenuation of the liver and the average attenuation of the spleen on a non-enhanced CT phase, was adapted from Limanond et al. [6]. Mean

hepatic attenuation + Mean splenic attenuation = CT liver attenuation index.

For a fibroscan evaluation, elastography measures the velocity of ultrasonic waves travelling through the liver to quantify liver fibrosis; as the fibrosis advances, the liver tissue becomes more stiff, causing the waves to spread more quickly. Therefore, the degree of rigidity and, by extension, the level of liver fibrosis, can be determined. There are various kinds of ultrasonic elastography; however, TE, 2D-SWE, and pSWE are the most frequently used varieties for studying the liver [8]. The TE device's controlled attenuation parameter (CAP), an operator-independent instrument, is used to measure the degree of liver steatosis. The CAP readings (in dB/m) have the same acquisition structure as the FibroScan measurements. Although it is less dependable for identifying the level of involvement, CAP has been shown to spot steatosis with reasonable accuracy [8]. The (LOGIC S8 XDclear 2.0) with XL instrument was used to conduct our fibroscan evaluation. Each subject was inspected while lying on their back with their arm raised above their heads. Through the intercostal cavity, the right lobe of the liver was examined. In order to prevent touching the bottom margin of the lung during respiration, the point of the transducer probe is placed on the skin in the area between the ribcage at the level of the anterior or middle axillary line. Ten measurements were collected, and the CAP was determined automatically.

For liver biopsy: After the CT and fibroscan scans were completed the same day or within 3 days for histopathological evaluation and steatosis degree, the liver biopsy was performed on all volunteers. Within 10 days of the biopsy date, the histopathological findings were received.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 26.0, Microsoft Excel 2016, and MedCalc programme software version 19.1 were used to tabulate and quantitatively evaluate the gathered data. The proper statistical analysis was then conducted, with a level of significance set at *P* 0.05 being significant and non-significant otherwise.

Results

This study included 50 donors, 40 donors (80.0%) were men and 10 donors (20.0%) were women. The median age of the donors was 28 years old (range: 18–40) years. Forty-five donors had no steatosis (<15% fat) with only five had ≥15% fat. The mean value of liver attenuation index (LAI) was 10.96 and for fibroscan CAP was 237.34 db/m with 29 donors were S0, nine donors were S1, 10

donors were S2, and two donors were S3 (steatosis grading by fibroscan) (Table 1).

Table 2 shows the relationships between the biopsy fat result and others as showed a significant relation with age with high significant relation with liver attenuation index and fibroscan cap result.

Figure 1 shows that: The sensitivity of liver attenuation index is 100.0% and specificity 80.0% according to cutoff point ≤9 with AUC 0.922, however the sensitivity of fibroscan 60.0% and specificity 80.0% with AUC 0.780 correlation to biopsy result.

Table 3 shows that there is high significant relationship between fat detected by fibroscan and age. Also it shows that no relationships between fat detected by fibroscan and sex.

Table 4 shows the relationships between fat by liver attenuation index and demographic data, fat by biopsy, and fibroscan results as showed a highly significant relation with fat by biopsy.

Sample of study cases (Figs. 2 and 3).

Discussion

The most prevalent diffuse condition that prevents a fit patient from donating is hepatic steatosis. Organ donation is made more risky by the rising frequency of NAFLD in the general community. A nonalcoholic obese liver donor was the first surviving liver transplant recipient to pass away, according to reports from Japan [9].

Hepatic steatosis raises the chance of postoperative problems for the donor because it inhibits the regeneration of residual lobes after resection, which can impact

Table 1 Demographic data, characteristics, fat by biopsy, liver attenuation index, and fibroscan data of the studied cases

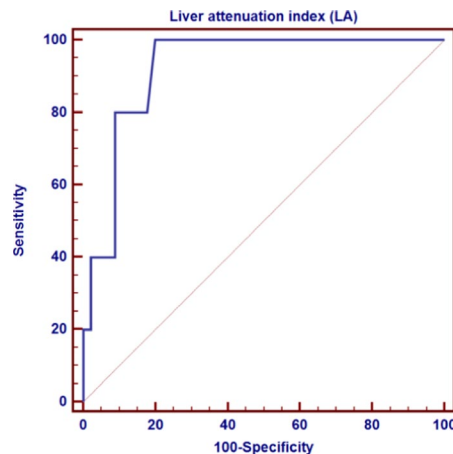
No. = 50		
Age	Mean ± SD	28.68 ± 5.48
	Range	18–40
Sex	Females	10 (20.0%)
	Males	40 (80.0%)
Fat by biopsy	No fat	45 (90.0%)
	Fat > 15	5 (10.0%)
Liver attenuation index (LA)	Mean ± SD	10.96 ± 3.72
	Range	2–18.6
Fibroscan cap (db/m)	Mean ± SD	237.34 ± 33.04
	Range	118–290
Fibroscan grade	S0	29 (58.0%)
	S1	9 (18.0%)
	S2	10 (20.0%)
	S3	2 (4.0%)
Fat by fibroscan	No fat	39 (78.0%)
	Fat > 15	11 (22.0%)

Table 2 Relation of biopsy results with demographic data, liver attenuation index, and fibroscan results among the studied cases

		No fat by biopsy No. = 45	Fat > 15 by biopsy No. = 5	Test value	P value	Sig.
Age	Mean ± SD	28.13 ± 5.33	33.60 ± 4.72	-2.196•	0.033	S
	Range	18–39	29–40			
Sex	Females	9 (20.0%)	1 (20.0%)	0.000*	1.000	NS
	Males	36 (80.0%)	4 (80.0%)			
Liver attenuation index (LA)	Mean ± SD range	11.52 ± 3.39 3–18.6	5.90 ± 2.84 2–9	3.564•	0.001	HS
Fibroscan cap (db/m)	Mean ± SD range	233.36 ± 32.24 118–280	273.20 ± 12.46 262–290	-2.720•	0.009	HS
Fibroscan grade	S0	29 (64.4%)	0 (0.0%)	22.716*	0.000	HS
	S1	7 (15.6%)	2 (40.0%)			
	S2	9 (20.0%)	1 (20.0%)			
	S3	0 (0.0%)	2 (40.0%)			
Fat by fibroscan	No fat Fat > 15	36 (80.0%) 9 (20.0%)	2 (40.0%) 3 (60.0%)	3.947*	0.047	S

P > 0.05: non-significant (NS); P < 0.05: significant (S); and P < 0.01: highly significant (HS)

*Chi-square test; •: independent t-test



	Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
Liver attenuation index (LA)	≤9	0.922	100.0%	80.0%	35.7%	100.0%
Fibroscan	--	0.780	60.0%	80.0%	25.0%	94.7%

Fig. 1 Receiver operating characteristic curve (ROC) for the diagnostic accuracy of liver attenuation index and fibroscan to differentiate between patients without fat and those with fat > 15% according to biopsy results (as a gold standard)

the recipient’s ability to use the transplant. Therefore, to reduce possible problems in donors and to improve the outcome of the procedure, preoperative hepatic steatosis determination is crucial [10].

For living donors, 30% steatosis has been deemed to be an acceptable upper limit; however, this number is not set or universal, and some organizations prefer more cautious cutoffs [9].

The majority of liver transplant centres in Egypt set a 15% threshold for steatosis when accepting liver donor

contributions. Therefore, it is crucial to assess the relative diagnostic accuracy of various imaging techniques in the light of various liver steatosis limit levels [9].

Liver biopsy is currently the most reliable way to find hepatic steatosis. However, due to its invasiveness, potential complications, and mistake during pathological analysis, liver biopsy is frequently only performed on carefully chosen donors and is not appropriate for screening or tracking [11].

Table 3 Relation between fat by fibroscan and demographic data, liver attenuation index, and fat by biopsy

		No fat by fibroscan No. = 38	Fat > 15 by fibroscan No. = 12	Test value	P value	Sig.
Age	Mean ± SD	27.45 ± 5.46	32.58 ± 3.42	3.061•	0.004	HS
	Range	18–39	28–40			
Sex	Females	8 (21.1%)	2 (18.2%)	0.110*	0.741	NS
	Males	30 (78.9%)	9 (81.8%)			
Liver attenuation index (LA)	Mean ± SD	11.19 ± 3.89	10.21 ± 3.17	0.795•	0.431	NS
	Range	2–18.6	4–15			
Fat by biopsy	No fat	36 (94.7%)	9 (75.0%)	3.947*	0.047	S
	Fat > 15	2 (5.3%)	3 (25.0%)			

$P > 0.05$: non-significant (NS); $P < 0.05$: significant (S); and $P < 0.01$: highly significant (HS)

*Chi-square test; •: independent t-test

Table 4 Relation between fat by liver attenuation index and demographic data, fat by biopsy, and fibroscan results

		LAI > 9 (No fat) No. = 36	LAI ≤ 9 (Fat ≥ 15) No. = 14	Test value	P value	Sig.
Age	Mean ± SD range	27.45 ± 5.46 18–39	32.58 ± 3.42 28–40	1.604•	0.115	NS
Sex	Females	7 (19.4%)	3 (21.4%)	0.025*	0.875	NS
	Males	29 (80.6%)	11 (78.6%)			
Fat by biopsy	No fat Fat > 15	36 (100.0%) 0 (0.0%)	9 (64.3%) 5 (35.7%)	14.286*	0.000	HS
Fibroscan grade	S0	23 (63.9%)	6 (42.9%)	6.058*	0.109	NS
	S1	6 (16.7%)	3 (21.4%)			
	S2	7 (19.4%)	3 (21.4%)			
	S3	0 (0.0%)	2 (14.3%)			
Fibroscan cap (db/m)	Mean ± SD range	226.29 ± 30.10 118–262	272.33 ± 7.60 265–290	1.529•	0.133	NS
Fat by fibroscan	No fat	29 (80.6%)	9 (64.3%)	1.463*	0.226	
	Fat > 15	7 (19.4%)	5 (35.7%)			

$P > 0.05$: non-significant (NS); $P < 0.05$: significant (S); and $P < 0.01$: highly significant (HS)

*: Chi-square test; •: independent t-test

The majority of medical facilities in Egypt perform liver biopsies on all volunteers as the final stage of the preoperative examination, even if their biochemical and radiological assessments of hepatic steatosis are within normal limits.

Due to the limitations of biopsy, many noninvasive methods, particularly radiological methods for the assessment of steatosis, have emerged. These methods include CAP, US assessment, CT, magnetic resonance imaging (MRI), and liver stiffness measurements (LSMs) based on US signal [9].

Unenhanced CT has typically been used to diagnose hepatic steatosis because studies have demonstrated its dependability and demonstrated its use in assessing steatosis in candidates for living donor liver transplantation. However, the use of contrast enhancement CT is still not well understood.

According to a research by Kim et al. [9], the CT study is the best radiological noninvasive technique for determining the presence of hepatic steatosis has a high sensitivity range of 88%–95% and a high specificity range of 90%–99%.

In many studies, non-contrast CT was favoured over contrast phases in order to reduce the possibility of measurement errors due to liver attenuation in connection to contrast injection technique and scanning duration.

The various factors for hepatic steatosis diagnosis on contrast-enhanced CT have generally been documented in many published papers.

The optimum liver–spleen threshold (sensitivity range, 54%–71%) was found to be highly affected by the contrast injection rate and timing of the scan, according to Johnston et al. research [12].

We used contrast segmented CT in our research (especially the delayed one). Since the non-contrast

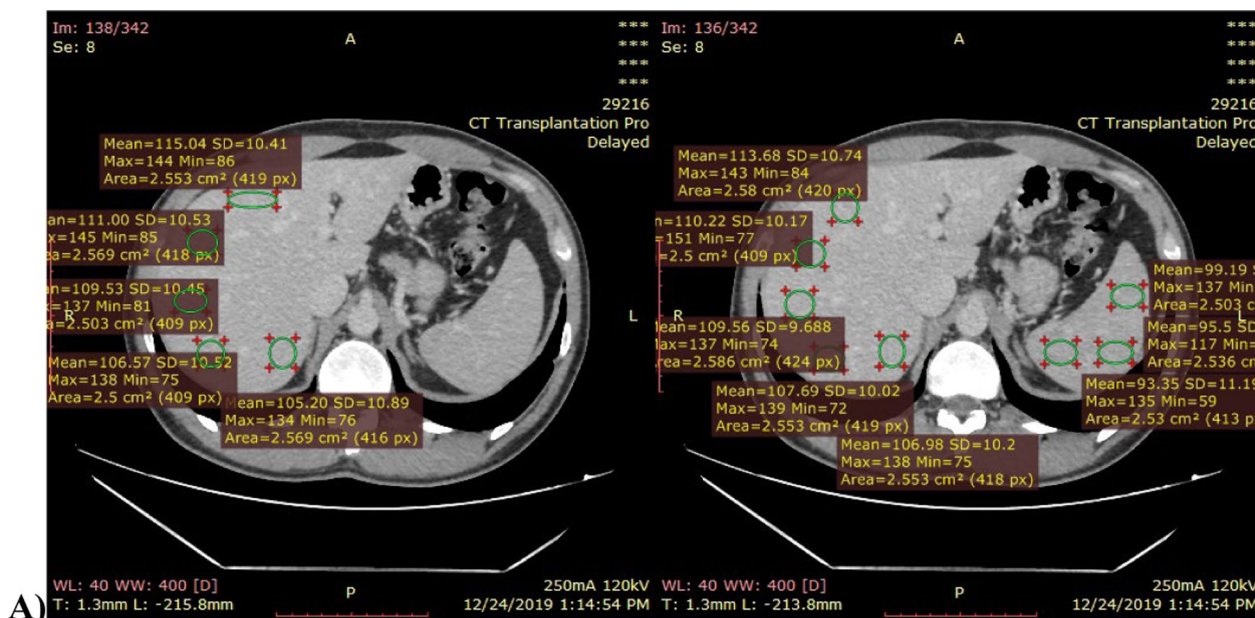


Fig. 2 A 35-year-old man patient seeking orthotopic living donor liver surgery. Traditional abdominal imaging and laboratory findings from his original assessment indicate that there is no discernible steatosis. CT transplantation protocol was done with assessment of LAI which was done in delayed phase showed (LAD= 12.2), which according to our cutoff value result of 9, suspected steatosis is 0–10%. Fibroscan study was done, and assessment of CAP showed CAP = 162 db/m, which keep with SO grade that equals to 0–10% steatosis. Liver biopsy was done and showed 0% steatosis. Both LAI and CAP results are true positive to biopsy result. **A** CT scan. **B** Fibroscan

CT phase is typically not included in the protocol at our facility, we wanted to use every tool at our disposal to determine which donors had the highest likelihood of having steatosis above the cutoff value of 15% and which ones did not, allowing us to avoid requiring all donors to undergo liver biopsy.

As it is the phase that is closest to the non-contrast phase with association to our result the histopathological result, which consider the most benefit of our research, we used the delayed phase of contrast CT as the phase to evaluate the liver–spleen attenuation index.

According to our study, a liver–spleen attenuation index cutoff value of 9 has a 100% sensitivity rate and

an 80% specificity rate, making it a very effective way to rule out donors who have steatosis levels of 15% or higher. If a donor has an LS index below 9, we can proceed with a liver biopsy without risk.

Due to the lack of positive donors as the majority of them are typically disqualified from giving at the initial screening stage using abdominal ultrasound—our results revealed reduced specificity.

While both unenhanced and contrast-enhanced CT can predict hepatic fat content, Kodoma et al., in his study on 88 patients who underwent metastatic liver resection comparing liver attenuation and liver–spleen attenuation index in both unenhanced and enhanced CT, found that the unenhanced method is superior, but his

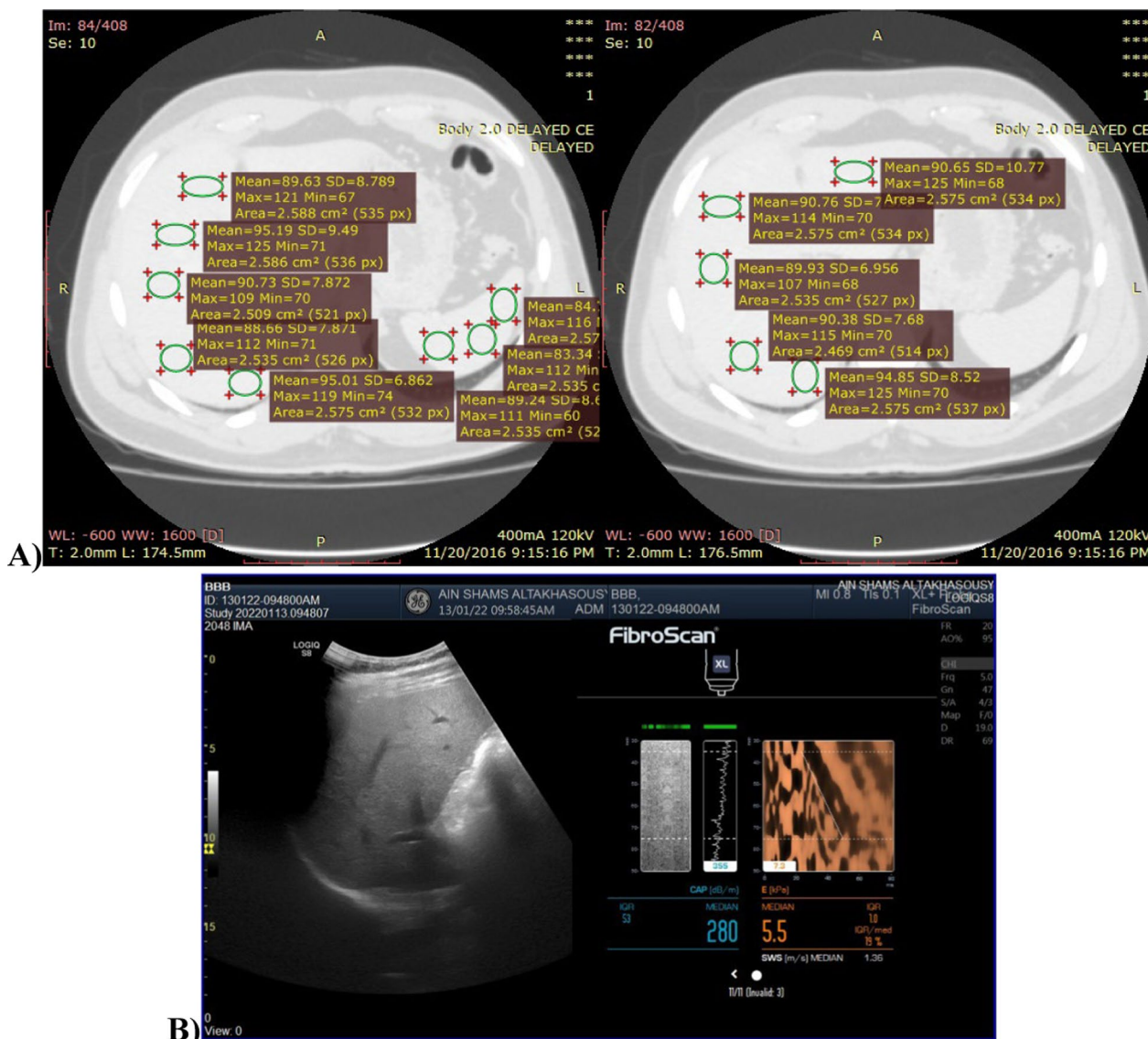


Fig. 3 A male patient 33 year's old, candidate for orthotopic living donor liver transplantation. His initial evaluation shows no visible steatosis according to traditional abdominal ultrasound and laboratory result. CT transplantation protocol was done with assessment of liver attenuation index (LAI) which was done in delayed phase showed (LAD=10), which according to our cutoff value result of 9, suspected steatosis is 0–10%. Fibroscan study was done, and assessment of controlled attenuation parameter (CAP) showed CAP = 280 db/m, which keep with S2 grade that equals to 0–10% steatosis. Liver biopsy was done and showed 10% steatosis, LAI result only is true positive to biopsy result. **A** CT scan. **B** Fibroscan

result for donor with fat cutoff value 30% was not (which high for living donor liver transplant in Egypt).

Numerous benefits of the CAP determined by TE, such as its noninvasive, nonionizing, quantitative, quick, and repeatable characteristics, indicate that this parameter may be an effective method for identifying prospective living liver transplants.

The CAP determined by TE has been used in numerous but small investigations to assess hepatic steatosis in

living liver donations. The effectiveness of CAP for identifying steatosis in 55 living liver donation prospects was assessed by Hong et al. [14]. They discovered that using US-guided liver biopsy as the reference standard, the AUROC of CAP for detecting complete steatosis (> 33%) was 0.88 with a cutoff value of 276 dB/m.

Fifty-four living donors were evaluated using the CAP in a different research by Yen et al. [15], and the outcomes were compared with those from intra-operative

biopsy. With a cutoff value of 257 dB/m in that research, the CAP had an AUROC of 0.96 for identifying complete steatosis (> 5%).

In a different study by Sunyoung et al. [16], 204 living donors were evaluated using CAP measurement and compared to the histological results for biopsy with only Mas being taken into account and MiS being excluded from the study. It was found that CAP had an AUROC of 0.938 for MaS 10% with a sensitivity of 84.2% and a specificity of 92.4%.

Our study found that CAP measurement had an AUROC OF 0.780 for detecting steatosis 15%, with sensitivity only 60% and specificity as CT LAI of 80%, which is considered low compared to other studies. This could be because our study only included a small number of donors with steatosis 15% (five cases from 50 donors), in contrast with other studies.

Our research has some drawbacks. First, when compared to other studies, our sample group of 50 living liver donors was tiny. Second, a significant number of patients were initially excluded based on the screening US evaluation, and only five donors with histologically proven steatosis 15% were included and underwent later surgery. The study population included a large portion of donors with normal livers and hepatic steatosis less than 10%, as determined by histological assessment. Third, despite the fact that core liver biopsy results cannot accurately represent the entire liver due to the heterogeneous distribution, our study also assumed that the steatosis distribution was uniform. This assumption reduced the relevance of the correlation between histological quantification and imaging. Fourth, since it was a prospective, single-centre research, it is necessary to prove that extrapolating our findings to other centres is accurate.

Conclusion

The CAP and CT measures worked equally in determining the amount of liver fat in liver donors. But according to multivariate analysis, the only factor strongly linked with hepatic steatosis in living donors was the CT LAI index. We contend that the combination of CT LAI index and CAP allows for the detection of the degree of hepatic steatosis and can be used as an option to liver biopsy, reserving liver biopsy for those with positive steatosis donors.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43055-024-01335-7>.

Additional file 1.

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Author contributions

S M A and F S E selected the patients and reviewed their images and did the interventional procedure, collected, tabulated, and analysed the data. N A C and H I A supervised management of the cases, interpreted the patient data, and wrote the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data are available upon request of the editorial board.

Declarations

Ethics approval and consent to participate

This study was approved by the Faculty of Medicine Ain Shams University, Research Ethics Committee. Each patient was provided a written informed consent for analysis of anonymized data.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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