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Original Article

Body Composition Analysis as An Indicator of Steatosis Severity in Metabolic Dysfunction-Associated Steatotic Liver Disease (Previously Named as Non-Alcoholic Fatty Liver Disease)

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Abstract

Background and objectives: Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) is the most common chronic liver disease worldwide. The measurement of body composition may help in the prediction of hepatic steatosis. This work aimed to correlate the clinical and body composition parameters on one hand and the steatosis degree assessed by controlled attenuation parameter (CAP) and to detect the factors predicting advanced steatosis in MASLD patients.

Methodology: This cross-sectional hospital-based study included 80 adults with MASLD. Participants were clinically examined to detect buffalo hump, double chin, acanthosis nigricans, skin tags, and xanthelasma, laboratory investigations including a lipid profile, fibroscan and CAP measurement, and bio-electrical impedance analysis (BIA) to evaluate body composition. According to CAP, patients were categorized into S1, S2, and S3 groups.

Results: We included 41 males and 39 females, with a mean age of 41.62±8.57 years. Double chin, acanthosis nigricans , waist circumference (WC),mid-arm circumference (MAC), body fat mass, BMI, percent body fat (PBF), abdomen fat %, waist-hip ratio (WHR), visceral fat level, and obesity degree were significantly higher in S3 group. Higher MAC, and grade II and III fatty liver by ultrasound were independent predictors of severe steatosis.

Conclusions: Double chin, acanthosis nigricans, WC, MAC, body fat mass, BMI, PBF, abdomen fat %, WHR, visceral fat level, and obesity degree are significantly associated with severe steatosis. Thus, clinical phenotypes and body composition analysis by the BIA technique may provide non-invasive tools that possibly predict severe steatosis.

Keywords: MASLD, body composition, BIA, phenotypes, severe steatosis.

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Introduction:

Non-alcoholic fatty liver disease (NAFLD) is a globally widespread chronic hepatic problem, with an estimated increase in prevalence from 25.3% in 1990-2006 to 38.0% in 2016-2019. This demonstrates a rise of about 50% over 3 decades. [1]

The worldwide increase in obesity along with type II diabetes mellitus (T2DM) are responsible for this increase. [2,3]

In Egypt, the increasing obesity prevalence is responsible for the rise of the prevalence of NAFLD. About 58% of obese Egyptian adolescents have associated NAFLD. [4]

Recently, the global Delphi consensus and the Latin American Association for the Study of the Liver adopted a new more inclusive term, to replace the old terminology, NAFLD. Metabolic dysfunction-associated steatotic liver disease (MASLD) is diagnosed when steatotic liver disease comes in association with at least one cardiometabolic risk factor. [5]

The increasing obesity in young people raises the possibility of having NAFLD in early life, with longer disease duration. This increases the risk of fibrosis progression ending in cirrhosis. That is why early life obesity is an independent risk factor for liver cirrhosis and early hepatocellular carcinoma. [6,7]

NAFLD is strongly linked to high body fat, especially in the abdomen. [8]

Waist circumference (WC) has been documented to be more predictive for fatty liver than body mass index (BMI) in Taiwanese people. [9]

Moreover, people with obesity may have some characteristic signs such as buffalo hump.[10] and double chin. [11]

High abdominal fat is known as Central obesity or visceral fat (VF). This obesity form is linked to more severe patterns of liver disease. [12]

Hence, body composition is more predictive of fatty liver than BMI. [12,13] Bio-electrical impedance analysis (BIA) is a safe, non-invasive, simple, low-cost, accurate, and easy method compared to dual-energy x-ray to estimate body composition. [14] To the best of our knowledge, no Egyptian study has addressed the different phenotypic changes in Egyptian NAFLD patients. Moreover, data are scarce on the value of these phenotypes and body composition analysis in the assessment of steatosis in those patients. Thus, this work aimed to correlate the clinical and body composition parameters with the degree of steatosis evaluated by controlled attenuation parameter (CAP) in patients with MASLD, and to detect the factors predicting severe steatosis in those patients.

Patients and methods:

Study design, population, and settings

This hospital-based cross-sectional study included 80 asymptomatic adult subjects (≥ 18 years) with MASLD, which was diagnosed based on the presence of radiological evidence of hepatic steatosis in addition to at least one cardiometabolic risk factor. [5] Participants were randomly recruited from the patient's relatives from the Tropical Medicine and Gastroenterology Department outpatient clinic, Sohag University Hospital between August 2021, and August 2022. Fatty liver was diagnosed based on ultrasonographic evidence of hepatic steatosis.

Inclusion criteria: All adult subjects with an ultrasonographic diagnosis of fatty liver with at least cardiometabolic risk factor were included in the current study.

Exclusion criteria: Participants aged <18 years, alcohol consumption, patients suspected to have other chronic liver diseases, decompensated liver disease, other end-organ failure, patients taking medications that may cause fatty liver (e.g., corticosteroids, amiodarone, and tamoxifen), pregnancy, patients with an implantable electrical device such as a pacemaker as recommended by Fibroscan manufacturer. [15]

Procedure

The following was done for all participants:

1) **History taking and clinical exmination:** including age, gender, and med-ical diseases (e.g. hypertension, diabetes mellitus, and cardiovascular disease). All participants were subjected to clinical examination with special emphasis on:

1. Blood pressure was measured while the patient was sitting after resting for at least 5 minutes with a standard mercury sphygmomanometer. [16]

2. Examination for the presence of buffalo hump, double chin, acanthosis nigricans, skin tags, and xanthelasma. [17]
3. Anthropometric measurements were obtained including WC, hip circum-ference, and mid-arm circumference (MAC).

- WC was measured as described by the World Health Organization [18] at a level midway between the lower rib margin and iliac crest with tape all around the body. WC of 102 cm (40 inches) in men and 88 cm (35 inches) in women is recommended by WHO as cut-off points to diagnose abdominal obesity. [18]

- Hip circumference was measured at the maximum circumference of the buttocks**.** The tape used was stretch-resistant and the subject stood with feet placed together and in its correct position i.e. parallel to the floor at the level at which the measurement was made. [18]
  Both WC and hip circumference were measured while subjects were wearing minimal clothes.
- MAC measurement: The right arm was positioned halfway between the acromion and the tip of the olecranon, hanging freely. [19]

2) **Radiological investigations**

I. **Pelvi-abdominal ultrasound** was done for all participants**.** A convex-type transducer of an ultrasound device with 3.5–5 MHz frequency (Mindray DP-2200) was used. All exams were performed with the patient in supine position and fasting for a night.
The following data were recorded:

1. **Liver**

A. Size: The right lobe span was measured in the mid-clavicular line on oblique view. The average normal span length is (11-15 cm).[20]

B. Echogencity and grades of fatty liver:

Compared to renal echogenicity, hepatic echogenicity was evaluated. The steatosis grade was determined according to the clarity of the vasculature of the liver and the diaphragmatic visualization and posterior attenuation. The degree of hepatic steatosis was graded using a four-point scale as documented by Saadeh et al. [21]

- ✓ Grade 0, normal;
- ✓ Grade 1, slight, diffuse increase in fine echoes in hepatic parenchyma with normally visualized diaphragm and intrahepatic vessel borders;
- ✓ Grade 2, moderate, diffuse increase in fine echoes with slight impairment of visualization of intrahepatic vessels and diaphragm;
- ✓ Grade 3, a marked increase in fine echoes with poorly or non-visualized intrahepatic vessel borders, diaphragm, and posterior right lobe of the liver.

2. Measurement of subcutaneous fat thickness:

As described by Uchibori et al. [22], the left hepatic lobe was visualized in a sagittal scan. In order to scan the linea alba, the liver's surface was kept as parallel to the skin as possible. The thickness of the subcutaneous and preperitoneal fat was evaluated from the center of the left lobe of the liver **(Fig. 1)**.

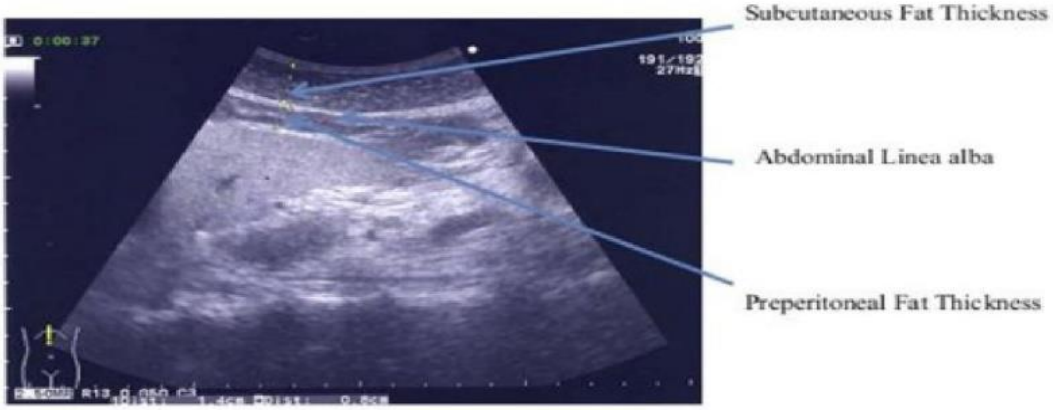

Fig.1. Thickness of subcutaneous fat and preperitoneal fat measurement by abdominal ultrasound in a fatty liver patient. [23]

II: Fibroscan examination: All participants were evaluated by transient elastography following a nighttime fasting. Fibroscan 430 **(Echosens, Paris, France)** was used to evaluate liver stiffness measurement (LSM) and CAP score. A single operator performed FibroScan examination with either the M or the XL probe, based on the software's recommendations. With the patient in dorsal decubitus and the right arm in maximal abduction, adequate pressure to the skin was applied by the probe across the right hepatic lobe through the intercostal spaces. The median of ten measures provided the LSM score, and it was only considered reliable if at least ten acquisitions were made successfully, the success rate was at least 60%, and the IQR-to-median ratio of the ten acquisitions was less than 0.3. LSM identified patients with fibrosis with Youden cutoff values for fibrosis F≥F1, F≥F2, F≥F3, and F=F4 were 5.5 kPa, 8.2 kPa, 9.7 kPa, and 13.6 kPa, respectively. [24]

CAP score is a measurement of hepatic steatosis. It is measured in decibels per meter (dB/m). It ranges from 100 to 400 dB/ m. The median optimal cut-off value of CAP for steatosis is 215 dB/m for steatosis (S) ≥S1, 252 dB/m for S≥S2, and 296 dB/m for S≥ S3. [25] According to the degree of steatosis, our cohort was divided into three groups; S1, S2, and S3.

3) Laboratory investigations:

Morning blood samples were collected by venipuncture after fasting for 8 hours in a completely aseptic setting. All samples were analyzed for: Viral hepatitis markers: Hepatitis B surface antigen (HBsAg) & Hepatitis C virus (HCV) antibody, fasting blood glucose level (FBG), fasting lipid profile (Total cholesterol (TC), low-density lipoprotein (LDL-C), high-density lipoprotein cholesterol (HDL-C), very low-density lipoprotein (VLDL-C), and triglycerides (TG)), alanine transaminase (ALT), aspartate transaminase (AST), fasting serum insulin levels using ELISA kits by electochemileumence immunoassay by Cobas analyzer. The value of homeostasis model assessment -insulin resistance (HOMA-IR) was calculated as = fasting insulin (μU/ml) × fasting glucose (mmol/l)/ 22.5. [26]

4) Body composition analysis:

- Body composition analysis for all participants was performed using the BIA technique with InBody 270 by a trained nurse according to the manufacturer's protocol at ORO Health Club in Sohag**.** All the following parameters were automatically calculated [27] (https://inbodyusa.com/general/270-result-sheet-interpretation)

- **Body fat mass (kg)**: Represents all body fat, both subcutaneous and visceral.
- **Skeletal muscle mass (SMM) (Kg)**: It indicates the total weight of skeletal muscle.
- **Body mass index (BMI) (Kg/m^2)**
- **Percent body fat (PBF) (%)**: Shows the proportion of body fat to total weight.
- **Abdomen fat %** by segmental fat analysis. It detects the amount of fat mass in the abdomen.
- **Inbody score** was represented in points, reflecting the evaluation of body composition.
- **Waist-hip ratio (WHR)**
- **Visceral fat level:** It estimates the quantity of fat that surrounds the abdominal organs.
- **Fat-free mass (Kg):** It comprises all the tissues in the body, except for fat-based ones. It includes skeletal muscles, parenchymal tissues, and bones.
- **Obesity degree (%):** It is the proportion of optimal weight that is either over or below it. 90% - 110% is the normal range, which permits 10% above or below.
- **Skeletal muscle index (SMI) (Kg/m^2):** It is calculated by dividing the total skeletal muscle mass of the arms and legs by the square of the height in meters. [28]

Ethical consideration: This work was carried out following the Declaration of Helsinki and written informed consent was obtained from all participants. Confidentiality of data was assured, and data collection forms were anonymous. The Scientific Research Ethical Committee of the Faculty of Medicine, Sohag University approved the study protocol under IRB Registration number Soh-Med-21-06-13.

Statistical analysis

STATA version 17.0 (Stata Statistical Software: Release 17.0 College Station, TX: StataCorp LP)

was used to analyze data. The distribution of the various variables was determined using the *Shapiro-Wil*k normality test. The mean, standard deviation (SD), median, and range were used to display the quantitative data. *ANOVA* was used to compare the means of three or more groups, and the student *t-test* was used to compare the means of two groups. When data were not normally distributed, three or more groups were compared using the *Kruskal-Wallis* test, and two groups were compared using the *Mann-Whitney* test. Both the *Fisher exact* test and the *Chi-square* test were used to compare the qualitative data, which were displayed as numbers and percentages. Logistic regression analysis was used to determine odds ratios. Excel, STATA, and MedCalc programs were used to produce graphs. If the *P* value was below 0.05, it was regarded as significant.

Results:

Our study included 80 adult subjects (41 males and 39 females) having a bright liver by abdominal US: Their mean age was 41.62±8.57 years. In our study, 22 of the studied subjects were diabetic (27.5%), and 20 subjects were hypertensive (25%). Based on CAP, 20 cases were S1 (mild steatosis), 28 were S2 (moderate steatosis), and 32 were S3 (severe steatosis).

All cases of grade 3 steatosis had double chin which was significantly higher than in patients with grade 1 and 2 steatosis (P =0.006, 0.02 respectively). Fifty percent of cases of grade 3 steatosis had acanthosis nigricans which was significantly higher than in patients with grade 1 steatosis (P2 =0.01). As regards the anthropometric measurements, we found that WC was significantly higher in the grade 3 steatosis than the others (P2 =0.002, P3 =0.02 respectively). Also, we found that MAC was significantly higher in grade 3 steatosis than the others (P2 =0.003, P3=0.03 respectively) **(Table 1).**

Table (1): Demographic, clinical, and anthropometric measurements of the studied groups

Variable	S1 N=20	S2 N=28	S3 N=32	P value
Age (year)				
Mean ± SD	41.35±10.41	40.89±8.73	42.41±7.28	0.79
Median (range)	40.5 (25:57)	40 (29:60)	42 (29:56)	
Gender				
Females	9 (45.00%)	14 (50.00%)	16 (50.00%)	0.93
Males	11 (55.00%)	14 (50.00%)	16 (50.00%)	
DM (n=22)	5 (25.00%)	5 (17.86%)	12 (37.50%)	0.23
Hypertension (n=20)	4 (20.00%)	5 (17.86%)	11 (34.38%)	0.28
P1=0.96, **P2=0.01, P3=0.005**				
Buffalo hump (n=25)	7 (35.00%)	5 (17.86%)	13 (40.63%)	0.15
Double chin (n=70)	15 (75.00%)	23 (82.14%)	32 (100%)	**0.01**
P1=0.72, **P2=0.006, P3=0.02**				
Acanthosis nigricans (n=28)	3 (15.00%)	9 (32.14%)	16 (50.00%)	**0.03**
P1=0.18, **P2=0.01**, P3=0.16				
Skin tags (n=50)	11 (55.00%)	20 (71.43%)	19 (59.38%)	0.46
Xanthelasma (n=2)	1 (5.00%)	0	1 (3.13%)	0.53
WC (cm)				
Mean ± SD	103.7±6.55	106.21±10.12	112.72±9.23	**0.001**
Median (range)	100.5 (97:121)	109.5 (82:128)	110 (100:132)	
P1=1.00, **P2=0.002, P3=0.02**				
Hip circumference (cm)				
Mean ± SD	107.55±5.63	107.32±6.06	111.06±8.65	0.20
Median (range)	106.5 (98:119)	108.5 (97:119)	110 (98:130)	
MAC (cm)				
Mean ± SD	33.9±2.73	34.82±3.45	37.38±4.42	**0.007**
Median (range)	33 (30:41)	34 (27:42)	36.5 (29:47)	
P1=0.31, **P2=0.003, P3=0.03**				

Pairwise comparison was done if P value <0.05, P1 compare grade 1&2, P2 compare grade 1&3, P3 compare grade 2&3.
Quantitative data were represented as mean, SD, median and range. Qualitative data were presented as numbers and percentage
SD: standard deviation; DM: diabetes mellitus; WC: waist circumference; MAC: mid-arm circumference

The ultrasonographic and Fibroscan findings of the study groups are described in **Table 2**.

Table (2): Ultrasonographic and Fibroscan findings of the studied groups.

Variable	S1 N=20	S2 N=28	S3 N=32	P value
Ultrasonographic findings				
Right lobe span (cm)				
Mean ± SD	17.3±2.05	17.49±1.49	18.63±1.54	**0.007**
Median (range)	17.35 (13.6:21)	17.3 (14.8:21)	19 (16:21)	
P1=1.00, **P2=0.02, P3=0.03**				
Subcutaneous fat (mm)				
Mean ± SD	13.45±3.47	14.64±3.89	17.04±5.61	0.08
Median (range)	13.05 (6.16:19.3)	14.95 (8:22.2)	16.7 (9:30.8)	
Fibroscan findings				
CAP measurement (dB/m)				
Mean ± SD	235.95±8.59	268.04±10.40	336.97±18.91	**0.0001**
Median (range)	236 (222:250)	264 (256:293)	340 (300:368)	
P1=0.0001, P2=0.0001, P3=0.0001				
Fibrosis stage				
F0	11 (55%)	19 (67.86%)	14 (43.75%)	
F1	8 (40%)	6 (21.43%)	14 (43.75%)	0.19
F2	0	0	3 (9.38%)	
F3	1 (5%)	2 (7.14%)	0	
F4	0	1 (3.57%)	1 (3.13%)	
LSM (kPa)				
Median (range)	5.15 (3.6:12.9)	4.45 (3.2:15.5)	5.8 (3.7:41.1)	**0.02**
P1=0.05, P2=0.50, **P3=0.008**				

Pairwise comparison was done if P value <0.05, P1 compare grade 1&2, P2 compare grade 1&3, P3 compare grade 2&3.SD: standard deviation.
Quantitative data were represented as mean, SD, median and range.
SD: standard deviation
CAP: controlled attenuation parameter; dB/m: decibels per meter; SD: standard deviation; LSM: liver stiffness measurement; kPa: kilo Pascal

The right lobe span was significantly higher in the grade 3 steatosis group than in the grade 1 & 2 steatosis groups (P=0.02, 0.03 respectively). The subcutaneous and fat thickness was higher in the grade 3 steatosis group compared to the other two groups but without a statistically significant differenc**.** By Fibroscan, LSM was statistically significantly higher in the grade 3 steatosis group than the grade 2 steatosis group (P3=0.008).

Table (3): Laboratory findings of the studied groups.

Variable	S1 N=20	S2 N=28	S3 N=32	P value
FBG (mg/dL)				
Mean ± SD	91.3±42.95	87.75±31.76	107.84±50.48	**0.02**
Median (range)	82 (55:260)	75.5 (60:192)	88.5 (60:284)	
P1=0.40, P2=0.12, **P3=0.005**				
Fasting serum Insulin level (mIU/ml)				
Median (range)	7.4 (2.5:16.9)	6.1 (2.5:49.1)	11.7 (3:22.8)	**0.008**
P1=0.44, **P2=0.03, P3=0.004**				
HOMA-IR				
Median (range)	1.6 (0.5:4.3)	1.38 (0.4:19.5)	2.1 (0.63:14.25)	**0.02**
P1=0.35, **P2=0.07, P3=0.007**				
TC (mg/dL)				
Mean ± SD	187.85±36.72	177.14±35.75	190.63±58.19	0.46
Median (range)	186 (110:252)	175 (117:278)	187.5 (121:446)	
LDL-C (mg/ dL)				
Mean ± SD	119.89±36.94	110.08±30.10	115.93±56.30	0.47
Median (range)	117.2 (25:176)	120 (54:178)	107.3 (33:358.8)	
HDL-C (mg/ dL)				
Mean ± SD	38.0±7.68	40.82±12.37	38.71±10.21	0.77
Median (range)	40 (25:60)	36.5 (25:78)	35 (26:67)	
VLDL-C (mg/ dL)				
Median (range)	25 (14:122)	27.2 (9:55)	32.8 (14:112.5)	0.11
TG (mg/ /dL)				
Mean ± SD	139.65±57.78	139.96±55.90	190.09±97.30	**0.01**
Median (range)	119.5 (70:285)	146 (48:275)	175 (70:550)	
P1=0.99, **P2=0.02, P3=0.01**				
ALT (IU/L)				
Median (range)	40 (15:108)	34 (16:284)	36.5 (13:128)	0.89
AST (IU/L)				
Mean ± SD	36.5±17.27	35.79±40.68	34.59±21.77	0.47
Median (range)	32 (15:66)	30 (11:235)	29 (14:94)	

Pairwise comparison was done if P value <0.05, P1 compare grade 1&2, P2 compare grade 1&3, P3 compare grade 2&3.

Quantitative data were represented as mean, SD, median and range.

FBG: fasting blood glucose; SD: standard deviation; HOMA-IR: homeostasis model assessment of insulin resistance; TC: total Cholesterol; LDL-C: low density lipoprotein-cholesterol; HDL-C: high density lipoprotein-cholesterol; VLDL-C: very low-density lipoprotein-cholesterol; TG: triglycerides; ALT: alanine transaminase; AST: aspartate transaminase

showsthe results of laboratory findings of the studied groups. FBG was significantly higher in group 3 steatosis compared to group 2 (P3=0.005). The same was found with fasting serum Insulin (P3= 0.004) & HOMA-IR (P3=0.007). Serum TG was significantly higher in group 3 steatosis compared to both groups 1 & 2 steatosis (P2=0.02, P3=0.01 respectively). Other laboratory parameters were not significantly different between the three groups.

By body composition analysis, we found that body fat mass, BMI, PBF, abdomen fat %, WHR, visceral fat level, and obesity degree were significantly higher in group 3 steatosis than in group 1 and 2 steatosis. While inbody score was significantly lower in grade 3 steatosis than in group 1 & 2 steatosis **(Table 4).**

Table (4): Body composition analysis of the studied groups.

Variable	S1 N=20	S2 N=28	S3 N=32	P value
Body fat mass (Kg)				
Mean ± SD	26.87±8.85	34.01±9.58	39.97±13.28	**0.001**
Median (range)	28.4 (13.7:46.2)	32.35 (19.2:57.1)	40.6 (15.1:66.8)	

P1=0.01, P2=0.001, P3=0.8				
SMM (Kg) Mean ± SD Median (range)	29.66±9.58 31.45 (4.4:43.2)	27.43±5.75 27.1 (18.4:38.5)	30.41±6.56 29.1 (21.3:47.1)	0.26
BMI (Kg/m^2) Mean ± SD Median (range)	29.69±4.57 29.5 (21.1:39.5)	31.53±4.46 30.8 (24:43.2)	34.58±6.01 33.5 (25.3:49.4)	**0.01**
P1=0.17, **P2=0.006, P3=0.05**				
PBF Mean ± SD Median (range)	32.44±9.71 32.2 (18.5:49.7)	40.59±8.01 40.7 (25.5:53.8)	41.78±10.22 43.95 (17.6:54.4)	**0.005**
P1=0.007, P2=0.003, P3=0.35				
Abdomen fat % Mean ± SD Median (range)	316.05±106.98 308.15 (160.6:528.1)	389.84±85.28 364.05 (247.8:580.2)	447.62±149.38 416.6 (182.4:820)	**0.003**
P1=0.01, P2=0.002, P3=0.16				
Inbody score (points) Mean ± SD Median (range)	71.85±13.85 67.5 (53:112)	59.64±8.66 61.5 (42:75)	57.94±12.46 57 (38:88)	**0.003**
P1=0.002, P2=0.002, P3=0.69				
WHR Mean ± SD Median (range)	0.96±0.07 0.965 (0.82:1.08)	0.99±0.08 0.995 (0.8:1.17)	1.03±0.07 1.02 (0.85:1.18)	**0.01**
P1=0.27, **P2=0.0.01, P3=0.03**				
Visceral Fat Level Mean ± SD Median (range)	12.45±4.50 12.5 (6:20)	15.54±3.49 16 (8:20)	16.75±4.28 20 (6:20)	**0.002**
P1=0.02, P2=0.001, P3=0.09				
Fat Free Mass (Kg) Mean ± SD Median (range)	56.21±12.39 58.95 (38.5:75.6)	49.48±9.33 49.55 (34.8:67.7)	54.46±10.90 52.75 (38.9:52.7)	0.15
Obesity Degree (%) Mean ± SD Median (range)	136.6±20.99 135.5 (103:184)	144.71±21.03 141.5 (109:201)	158.84±27.86 155.5 (115:230)	**0.01**
P1=0.17, **P2=0.006, P3=0.05**				
SMI(Kg/m^2) Mean ± SD Median (range)	8.11±1.22 8.35 (6.1:10.3)	7.56±1.02 7.3 (5.7:9.7)	8.10±0.995 8 (6.6:10.8)	0.1

Pairwise comparison was done if P value <0.05, P1 compare grade 1&2, P2 compare grade 1&3, P3 compare grade 2&3.
Quantitative data were represented as mean, SD, median and range.
SD: standard deviation; SMM: skeletal muscle mass; BMI: body mass index; BPF: percent body fat; WHR: waist hip ratio; SMI: skeletal muscle index

Studying the relation between CAP score and both anthropometric measurements and body composition analysis showed that WC and MAC were significantly correlated with CAP score (P=0.0003). Among body composition parameters, there was a significant positive correlation between CAP score and body fat mass, BMI, PBF, abdomen fat%, WHR, and obesity degree (P=0.0008, 0.006, 0.007, 0.004, 0.002, and 0.006 respectively). However, there was a significant negative correlation between inbody score and CAP score (P=0.01) (**Tabl e 5).**

Table (5): Correlation between CAP and both anthropometric measurements and body composition analysis

Variable	Spearman correlation co-efficient (r)	P value
WC (cm)	0.39	**0.0003**
Hip circumference (cm)	0.20	0.07

MAC (cm)	0.39	**0.0003**
Body fat mass (Kg)	0.37	**0.0008**
SMM (Kg)	0.08	0.5
BMI (Kg/m^2)	0.31	**0.006**
PBF	0.30	**0.007**
Abdomen fat %	0.32	**0.004**
Inbody score (points)	-0.27	**0.01**
WHR	0.34	**0.002**
Visceral Fat Level	0.04	0.75
Fat Free Mass (Kg)	0.04	0.75
Obesity Degree (%)	0.31	**0.006**
SMI (Kg/m^2)	0.08	0.5

CAP: controlled attenuation parameter; WC: waist circumference; MAC: mid-arm circumference; SMM: skeletal muscle mass; BMI: body mass index; PBF: percent body fat; WHR: waist hip ratio; SMI: skeletal muscle index.

Logistic regression analysis of predictors of severe steatosis (Grade 3 steatosis) is shown in **Table (6).**

Table (6): Logistic regression analysis of factors predicting severe steatosis (S3)

Variable	Univariate analysis		Multivariate		Final	
	Unadjusted odds ratio (95% Cl)	**P**	**Unadjusted odds ratio (95% Cl)**	**P**	**Unadjusted odds ratio (95% Cl)**	**P**
DM	2.28 (0.84:6.19)	0.11				
Hypertension	2.27 (0.81:6.35)	0.12				
Buffalo Hump	2.05 (0.78:5.37)	0.14				
Acanthosis Nigricans	3 (1.16:7.78)	**0.02**	0.1 (0.04:2.7)	0.09		
Skin tags	0.80 (0.32:2.01)	0.64				
Xanthelasma	1.51 (0.09:25.15)	0.77				
WC (cm)	1.10 (1.04:1.17)	**0.001**	0.84 (0.45:1.55)	0.58		
Hip circumference (cm)	1.07 (1.01:1.15)	**0.03**	0.57 (0.32:1.02)	0.06		
MAC (cm)	1.23 (1.08:1.41)	**0.003**	10.52 (1.12:98.62)	**0.04**	1.29 (1.11:1.51)	**0.001**
Right lobe span (cm)	1.57 (1.16:2.12)	**0.003**	2.17 (0.66:7.10)	0.2		
Grades of fatty liver by US I II III	 Reference 5.78 (1.49:22.39) 17.5 (3.27:93.49)	 **0.01** **0.001**	 Reference 18 (1.29:2.5) 119 (1.73:815)	 **0.04** **0.04**	 Reference 8.74 (1.55:49.34) 19.49 (2.59:146.97)	 **0.01** **0.004**
FBG (mg/dL)	1.01 (0.998:1.02)	0.08				
Fasting serum Insulin level (mIU/ml)	1.08 (0.99:1.18)	0.09				
HOMA-IR	1.14 (0.94:1.39)	0.19				
TC (mg/dL)	1.004 (0.994:1.01)	0.40				
LDL-C (mg/dL)	1.00 (0.99:1.01)	0.86				
HDL-C (mg/dL)	0.99 (0.95:1.03)	0.69				
VLDL-C (mg/dL)	1.02 (0.99:1.05)	0.15				
TG (mg/ /dL)	1.01 (1.00:1.02)	**0.01**	0.88 (0.73:1.07)	0.2		
ALT (IU/L)	0.996 (0.98:1.01)	0.61				
AST (IU/L)	0.998 (0.98:1.01)	0.82				
Body fat mass (Kg)	1.07 (1.02:1.12)	**0.002**	0.21 (0.03:1.62)	0.13		

SMM (Kg)	1.04 (0.98:1.11)	0.21				
BMI (Kg/m^2)	1.15 (1.05:1.26)	**0.004**	0.21 (0.03:1.62)	0.13		
PBF	1.05 (1.00:1.10)	**0.048**	1.87 (0.05:63.82)	0.73		
Abdomen fat %	1.006 (1.00:1.01)	**0.005**	0.94 (0.37:2.44)	0.91		
Inbody score (points)	0.95 (0.92:0.99)	**0.02**	0.88 (0.75:1.03)	0.14		
WHR	12 (1.3: 107)	**0.01**	0.71 (0.29:1.69)	0.43		
Visceral Fat Level	1.16 (1.03:1.30)	**0.02**	3.75 (0.1: 73)	0.2		
Fat Free Mass (Kg)	1.02 (0.98:1.06)	0.39				
Obesity Degree (%)	1.03 (1.01:1.05)	**0.004**	1.23 (0.45:3.35)	0.68		
SMI (Kg/m^2)	1.32 (0.86:2.01)	0.20				

CI: confidence interval; DM: diabetes mellitus; FBG: fasting blood glucose; HOMA-IR: homeostasis model assessment of insulin resistance; TC: total Cholesterol; LDL-C: low density lipoprotein-cholesterol; HDL-C: high density lipoprotein-cholesterol; VLDL-C: very low density lipoprotein-cholesterol; TG: triglycerides; ALT: alanine transaminase; AST: aspartate transaminase; SMM: skeletal muscle mass; BMI: body mass index; PBF: percent body fat; WHR: waist hip ratio; SMI: skeletal muscle index

By the univariate logistic regression, we found that the presence of acanthosis nigricans, higher WC, higher hip circumference, higher MAC, enlarged right lobe span, grade II and III fatty liver by ultrasound, increased TG, and some of BIA parameters including higher BMI, body fat mass, PBF, abdomen fat%, inbody score, waist-hip ratio, visceral fat level, and obesity degree were possible predictors of the advanced steatosis. Multivariate logistic regression analysis of these possible factors revealed that higher MAC, and grade II and III fatty liver by ultrasound were independent predictors of severe hepatic steatosis, which was confirmed in the final model**.**

Discussion:

Previous studies investigated some phenotypic markers for early detection of IR and metabolic syndrome. These markers represent fat deposition at unusual sites. [29]

In this matter, our results showed that double chin was the most frequent phenotype in all studied patients (87.5%). When we investigated these phenotypic markers in different steatosis grades, we found that double chin and acanthosis nigricans had a significantly higher frequency in MASLD patients with severe steatosis compared to mild and moderate steatosis. The relevance of the above-mentioned observations is the easy detection of these phenotypic markers with simple clinical examination, denoting their important clinical role in screening of MASLD and even they may reflect severe hepatic steatosis.

Previous studies reported an association between fat distribution in different body parts with occurrence of MASLD. [30]

Therefore, anthropometric measurements may accurately predict hepatic steatosis. When we compared these anthropometric measurements in different steatosis grades, we found that WC and MAC were significantly higher in the grade 3 steatosis group than in the other two groups. However, hip circumference did not show a significant difference between the three groups. Yang et al., [31] Tomah et al. [32], and Razmpour et al. [33] found that WC correlated with increased severity of steatosis. Also, we found that WC and MAC had a significant positive correlation with CAP score. Previous studies investigated these anthropometric measurements where Lee et al. [34] found that WC was positively correlated with CAP score. Moreover, Rocha et al.[35] reported that WC was correlated with steatohepatitis and fibrosis in NAFLD patients.

Our results showed that fasting blood glucose level, fasting serum insulin level, and HOMA-IR were significantly linked to severe steatosis, as determined by Fibroscan. There were also significant positive correlations between CAP score and both fasting serum Insulin level and HOMA-IR. These findings support the theory that there is a strong association between NAFLD and IR and

hepatic insulin's inability to stop glucose synthesis by liver. [36]

This causes hyperinsulinemia by stimulating insulin production and mildly raising blood sugar levels.

BIA is a simple rapid non-invasive tool to evaluate body composition with good reliability. [37]

As total body fat rises, the likelihood of developing hepatic steatosis increases. Thus, variables like total body fat, which can be quantified in BIA, could be used to predict fatty liver. [38]

Our study also found that BMI, body fat mass, PBF, abdomen fat %, WHR, visceral fat level, and obesity degree were significantly higher in the grade 3 steatosis group compared to the other two groups. Moreover, all these parameters except visceral fat level had positive correlations with CAP score. Tomah et al.[32] support our results where they reported that there was a positive association between rising steatosis stages and BMI. Also, in agreement with our results, excess weight, primarily the build-up of visceral fat, was closely associated with the NAFLD's severity. [35,39]

As Matsuzawa et al.[40] stated, compared to subcutaneous fat, visceral fat has a greater metabolism and mobilizes FFAs to the liver, which is a significant risk factor for NAFLD. In addition, Miyake et al.[41] found that patients with severe steatosis had considerably larger visceral fat area and fat mass than those with mild steatosis. The same was found as regards the WHR. Some investigations, however, presented conflicting findings. Choudhary et al. [42]

reported that the severity of NAFLD was linked to subcutaneous adipose tissue volume rather than visceral fat volume.

Choi et al. [38]investigated the link between parameters of BIA and both ultrasonography and CAP score. They found that BMI, body fat mass (Kg), body fat mass percent (%), and WHR were significantly higher in the severe grade of steatosis than the less grades (Grading was done by US). They also reported that the CAP score positively correlated with the absolute body fat mass, PBF, and fat mass index in BIA. Our study also found that inbody score was significantly higher in the MASLD patients with grade 1 steatosis compared to those with grade 2 and 3 steatosis.

Sarcopenia is linked to DM, metabolic syndrome, and cardiovascular disease and is a risk factor for hepatic steatosis and significant fibrosis (≥F2). [43,44]

The current study found that muscle indices including SMM & SMI were not significantly associated with severity of steatosis. Similarly, Miyake et al. [41] found that SMM was not linked to the histological severity of NAFLD.

Against our results, Choi et al. [38] found that there was a significant difference between the three steatosis grades as regards SMM and SMI. Moreover, Miyake et al.[41] found that SMI was significantly higher in patients with severe steatosis than in patients with mild steatosis. Petta et al.[45] also found that sarcopenia had significant correlation with fibrosis and steatosis severity after adjustment for metabolic risk factors. The difference between our results and previous studies could be explained by the nature of the studied subjects where all subjects in previous studies had obesity, while 37.5 % of subjects in the current study were either normal or overweight. Because adipose tissue-dependent metabolic disturbances including oxidative stress, inflammation, and insulin resistance have an adverse effect on muscle mass, obesity can result in independent loss of muscle mass and function. [46]

In our study, univariate logistic regression analysis of different studied variables for predicting severe steatosis (Grade 3 steatosis) revealed that the presence of acanthosis nigricans, higher WC, higher hip circumference, higher MAC, larger right lobe span, grade II and III fatty liver by ultrasound, increased TG, and some of BIA parameters including higher BMI, body fat mass, PBF, abdomen fat %, inbody score, waist-hip ratio, visceral fat level, and obesity degree were significant predictors of the severe steatosis. However, Multivariate logistic regression analysis of these factors showed that higher MAC, and grade II and III fatty liver by ultrasound were independent predictors of severe hepatic steatosis which was confirmed in the final model. In agreement with our results, Abdelrahman et al.[47] reported by univariate analysis of their studied variables for the prediction of moderate/severe steatosis that higher BMI, larger right lobe span, and higher fatty degree by US were significant predictors of severe steatosis. Also, the

multivariate analysis showed that moderate degree of fatty liver by ultrasound were independent risk factors for moderate/severe steatosis.

The strengths of our study are that we are the 1st Egyptian group to use BIA as a non-invasive tool for the assessment of body composition in MASLD patients through the use of Inbody 270. It is an easy approach, cheap, and safe. The diagnosis of fatty liver was done not only by ultrasound but also by Fibroscan which helped us in grading and staging of the disease. Our study has some limitations. First, it was a single-center study, secondly, just a few cases were lean MASLD.

Conclusion

In MASLD patients, the presence of double chin and acanthosis nigricans, high WC, MAC, body fat mass, BMI, PBF, abdomen fat %, WHR, visceral fat level, and obesity degree are significantly associated with severe steatosis. Thus, clinical phenotypes and body composition analysis by BIA technique may provide suitable non-invasive tools that possibly predict severe steatosis. In addition, Large MAC and high grade of fatty liver detected by the US are independent predictors of severe hepatic steatosis.

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