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BRIEF ARTICLE

Hepatic steatosis in overweight/obese females: New screening method for those at risk

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Abstract

AIM: To identify which parameters could help to distinguish the "metabolically benign obesity", which is not accompanied by insulin resistance (IR) and early atherosclerosis.

METHODS: Eighty two of 124 overweight/obese females formed the study population, which was divided into two groups (52 and 30 subjects, respectively) with and without IR according to a HO meostatic Metabolic Assessment (HOMA) cut-off of 2, and were studied in a cross-sectional manner. The main outcome measures were waist circumference, serum uric acid, high-density lipoprotein-cholesterol and triglycerides, alanine amino-transferase, blood pressure and the two imaging parameters, hepatic steatosis and longitudinal diameter of the spleen, which were measured in relation to the presence/absence of IR.

RESULTS: A variable grade of visceral obesity was observed in all subjects with the exception of three. Obesity of a severe grade was represented more in the group of IR individuals (P = 0.01). Hepatic steatosis, revealed at ultrasound, was more pronounced in IR than in non-IR subjects (P = 0.005). The two groups also demonstrated a clear difference in longitudinal spleen diameter and blood pressure, with raised and significant values in the IR group. Metabolic syndrome was frequent in the IR group, and was not modified when adjusted for menopause (P = 0.001). At linear regression, the β values of waist circumference and body mass index predicting HOMA were 0.295, P = 0.007 and 0.41, P = 0.0001, respectively. Measures of spleen longitudinal diameter were well predicted by body mass index (BMI) values, β = 0.35, P = 0.01, and by HOMA, β = 0.41, P = 0.0001. Blood pressure was predicted by HOMA values, β = 0.39, P = 0.0001). HOMA and hepatic steatosis were highly associated (rho = 0.34, P = 0.002). Interestingly, IR patients were almost twice as likely to have hepatic steatosis as non-IR patients. Among the MS criteria, blood pressure was very accurate in identifying the presence of IR (AUROC for systolic blood pressure 0.66, cut-off 125 mm of Hg, sensibility 64%, specificity 75%; AUROC for diastolic blood pressure 0.70, cut-off 85 mm of Hg, sensibility 54.5%, specificity 75%).

CONCLUSION: As health care costs are skyrocketing, reliable and mainly inexpensive tools are advisable to better define subjects who really need to lose weight.

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Key words: Body mass index; Cardiovascular disease; Fatty liver; Insulin resistance; Metabolic fitness; Obesity

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INTRODUCTION

The incidence of both Overweight/Obesity (O/O) and Metabolic Syndrome (MS) is dramatically increasing. The generally accepted view is that being overweight causes similar health problems to that of obesity but to a lesser degree. The risk of death from all causes increases throughout the range of moderate and severe increases in body weight for both men and women in all age groups[1]. Further co-morbidities[2-4] are more frequent in O/O than in normal-weight females. Unless reversed, this trend predicts an epidemic of cardiovascular disease (CVD). Interventions are required to empower adults to increase physical activity and to modify eating habits. Nevertheless, it is mandatory to establish exactly which individuals should be treated and when. In fact, although the negative health consequences of O/O in the general population are well supported by the available published evidence, health outcomes in certain subgroups seem to be improved at an increased body mass index (BMI), a phenomenon known as the obesity survival paradox[5]. Furthermore, there is a high prevalence of clustering of cardiometabolic abnormalities among normal-weight individuals and a high prevalence of O/O individuals who are metabolically healthy[6]. Consequently, "metabolically benign obesity" which is not accompanied by insulin resistance (IR) and early atherosclerosis has recently been postulated to exist in humans[7].

A way of getting to the grass-roots of the problem could be to tackle the mechanisms underlying O/O. Evidence that this phenomenon can be regarded as a low-grade chronic inflammatory state comes from numerous studies[8]. Moreover, inflammation links obesity to early tumor promotion[9]. Inflammatory disease could represent a compensatory mechanism for increased adipose tissue turnover[10]. Apart from diabetes and atherosclerosis, another associated high-risk condition is non-alcoholic fatty liver disease (NAFLD), the etiologic factors of which include IR[11], high levels of serum interleukin-6 (Il-6[12]) and mitochondrial dysfunction[13]. The link between NAFLD and CVD has recently been established by the fact that the liver is involved in regulating/secreting numerous CVD risk factors[14], notably a cytokine [tumor necrosis factor-alpha (TNF-α)], an acute-phase protein [C-reactive protein (CRP)], glucose, lipoproteins, coagulation factors (plasminogen activator inhibitor-1[15]) and a substance which increases blood pressure (angiotensin Ⅱ[16]).

The NAFLD rate in the general adult population is increasing with large numbers, i.e. 20%[17], in obese non-diabetic adults being much higher[18]. Obviously, a clear differentiation between "simple" fatty liver (FL) and non-alcoholic steatohepatitis (NASH) in the spectrum of NAFLD is quite impossible without liver biopsy which is not always performed for ethical and technical issues. For this reason, we generally speak of hepatic steatosis (HS). Ultrasound (US) is widely used to detect HS, without exposing subjects to ionizing radiations. Indeed, more specific imaging techniques[19] are costly and not always useful in close follow-up. Tsushima *et al*[20] first identified the so-called liver-spleen axis in NAFLD patients. It has recently been proposed that increased spleen volume and serum levels of high sensibility (hs)-CRP contextually with HS, which "*per se*" unravels an inflammatory status[14], characterize young adult obese subjects[21]. Up-to-date findings from a nationally representative sample of adults indicate that the prevalence of MS increases substantially with increasing levels of serum uric acid (UA[22]). Actually, the menopause is associated with the aggravation of total cholesterol, LDL cholesterol and apolipoprotein B[23], representing a physiologic event which should be taken into consideration when evaluating multiple cardiovascular risk factors in O/O females, even though this status is highly correlated with age. Finally, researchers have demonstrated that elevated alanine aminotransferase (ALT) levels are independently associated with increased CVD- or diabetes-related mortality[24].

With numerous studies showing that O/O is a disease requiring long-term commitment to achieve the desired results, and that these results should be achieved as soon as possible[25], we aimed to identify which parameters could help distinguish between healthy and non healthy O/O individuals, by individualizing the boundaries within which is possible to "watch and wait". As health care costs are skyrocketing, the key point is to utilize tools which are reliable and mainly inexpensive. To achieve this aim we analyzed an anthropometric index, i.e. waist circumference (WC), in addition to the metabolic parameters, serum UA, high-density lipoprotein-cholesterol (HDL) and triglycerides, liver enzyme activity i.e. ALT, a CVD index, i.e. blood pressure, and two imaging parameters which were HS and spleen size, in relation to the presence/absence of IR.

MATERIALS AND METHODS

This research was performed by screening 124 consecutive female subjects with established (at least 4 years) O/O from February 2008 to April 2009. The study was carried out according to the principles of the Declaration of Helsinki and an informed written consent was obtained from each patient.

Exclusion criteria

Of the 124 initial subjects, 11 patients, who had undergone steroid therapy (four with bronchial asthma, five with rheumatoid arthritis and two with neuritis), as well as 15, who had received one or more of the following drugs, i.e. aspirin, metformin, statins and fibrates, were excluded from the study because these prior treatments may have caused a change in laboratory data. Three persons were excluded due to the detection of marked intestinal meteorism which made it difficult to perform US. Eight others were excluded due to the presence of co-morbidity (chronic viral hepatitis, alcohol abuse), and five subjects were considered drop-outs, because they avoided undergoing full laboratory-instrumental examinations.

Inclusion criteria

The remaining 82 subjects whose median age was 46.5 (14-64) years, were divided into two groups on the basis of the presence or absence of IR, and formed the study

population. The degree of overweight or obesity was established on the basis of BMI cut-off points of 25-29.9, 30-34.9, 35-39.9 and > 40 kg/m^2, respectively. Visceral obesity was identified by measuring WC at the midpoint between the lower border of the rib cage and the iliac crest. MS was defined according to the revised Adults Treatment Panel Ⅲ (2001), and three or more criteria were considered: plasma glucose concentration of at least 100 mg/dL, WC > 88 cm, serum HDL concentration < 50 mg/dL, blood pressure of at least 130/85 mmHg, and serum triglyceride concentration of at least 150 mg/dL. HS was associated with recent US features of "bright liver", with or without aminotransferase increase of unknown origin, in the absence of other chronic liver disease. Women were classified as being menopausal if they had not menstruated in the 12 months before examination. IR status was determined by the HOmeostatic Metabolic Assessment (HOMA), which was assessed using the formula: fasting insulin (μU/mL) × fasting glucose (mg/dL)/405[26]. As a stringent measure of IR, a value of HOMA > 2 was introduced.

Ultrasound evaluation

Sonographic measurements were performed using an ESAOTE *Technos* (Genoa, Italy). Briefly, spleen longitudinal diameter (SLD) was measured by postero-lateral scanning. The maximum length and the cranio-caudal were measured and then averaged. All the indices were measured thrice directly from the frozen images using an electronic caliper. The classification of "bright liver" or HS was based on the following scale of hyperechogenicity: 0 = absent, 1 = light, 2 = moderate, 3 = severe, pointing out the difference between the densities of the liver and the right kidney[27].

Blood pressure measurements

The systolic/diastolic blood pressure (SBP, DBP) was the average of three consecutive readings taken by the physician during the day, during usual practice hours, and after subjects had rested for five minutes in the sitting position.

Laboratory data

Serum triglycerides, HDL, basal insulin, ALT, and UA were measured using standard in-house procedures. Hs-CRP was determined using an ELISA Kit, human CRP by BioSupply, UK with a sensibility of 0.03 mg/L and a range of normal values of 0.25-1.5 mg/L.

Statistical analysis

HDL data, derived from a normally distributed population [Shapiro-Wilk test (S-W), $P = 0.481$], are expressed as mean plus SD. Variables not normally distributed, such as age (S-W, $P = 0.000$), BMI (S-W, $P = 0.005$), SLD (S-W, $P = 0.002$), WC (S-W, $P = 0.002$), HOMA (S-W, $P = 0.001$), DBP (S-W, $P = 0.001$), SBP (S-W, $P = 0.001$), triglycerides (S-W, $P = 0.003$), UA (S-W, $P = 0.001$), hs-CRP (S-W, $P = 0.001$), and ALT (S-W, $P = 0.001$), are expressed as median (range). HS grades were considered ordinals and managed in the same way. The difference in medians was assessed by the Mann-Whitney test for independent samples. The difference in means of HDL was evaluated by the Two-Sample *t* test. The Two-Way Tables cross-tabulated one categorical row variable with one categorical column variable and the significance was set by the Pearson χ^2 test. Frequencies with a small number of the expected values were evaluated by Fisher's exact test. When cross-tabulation was stratified for another dichotomous variable, the Mantel-Haenszel χ^2 test was carried out. Tracking the degree of association between single parameters, i.e. HS scores and triglycerides levels, Spearman's rho for non uniform intervals was used. The Pearson's coefficient (*r*) was employed to analyze the correlation between HOMA and HDL. When confronted with the question of how accurate a parameter was in identifying the presence of IR, the discrimination with relative cut-off was evaluated using receiver operating characteristic curve (ROC) analysis, graphically expressed as area under the ROC (AUROC). Sensitivity (true positive rate) and specificity (true negative rate) were also weighted for the same purpose. Optimal cut-off was considered the threshold value with the best specificity/sensitivity. To predict the presence of IR, the logistic regression (Enter Method), with relative odds ratios and 95% confidence intervals (CI), was employed utilizing as independent variables, US values for SLD and HS, BMI and WC measurements, blood pressure determinations and UA, HDL, and triglycerides data. To assess the independent effect of a quantitative variable, i.e. HOMA, on the prediction of spleen size (SLD) values and SBP/DBP determinations, linear regression analysis (least squares) was used, evaluating the standardized coefficient beta (β). The same tool was used to verify the connection between IR severity and anthropometric measures. Factor analysis was applied to detect the structure in the relationships among variables selecting a subset of variables, which have the highest correlations with the principal component factors. The Cattell's Scree plot, with relative eigenvalues, was performed to screen the real factors. Extraction of the main components amounted to a variance maximizing (varimax) rotation of the original variable space. The critical value was calculated by the formula: doubling the Pearson's correlation coefficient for 1% level of significance (5.152)/square root of subjects minus 2, i.e. 0.576. The concordance correlation coefficient (ρ_c), which measures precision and accuracy, was adopted to evaluate the degree of pair observations at US. Statistical analysis was performed operating on Systat 12 (Richmond, CA, USA) and MedCalc Version 10.4.8® (Frank Schoonjans) software packages.

RESULTS

In order to allow readers to gauge the internal validity of this study, we determined the minimum required sample size, with a type I error of 0.01 and type 2 error of 0.01 when dividing the population in two groups using HOMA (difference of means = 1.8, SD of non-IR females = 0.4 and SD of IR females = 1.8), which was calculated in 26 subjects. In addition, to assess how well

Table 1 Anthropometric, clinical, laboratory and ultrasound data of the study population

Variables [females (82)]	Median (Range) mean ± SD		*P*-value
	IR present (52)	IR absent (30)	
BMI (kg/m^2)	33 (25-53.7)	32 (25.6-39.7)	0.78
Overweight (*n*)	7	6	0.6
Obesity 1° grade (*n*)	23	15	0.8
Obesity 2° (*n*)	12	9	0.7
Obesity 3° (*n*)	10	0	0.01[a]
HS score at US	1 (0-3)	2 (0-3)	0.005
DBP (mmHg)	90 (65-110)	80 (60-110)	0.03
SBP (mmHg)	120 (100-170)	135 (110-180)	0.0008
Triglycerides (mg/dL)	141 (25-386)	113 (41-249)	0.11
HDL (mg/dL)	48.2 ± 8.6	50.1 ± 10.1	0.36
Uric acid (mg/dL)	4.3 (2.7-8.2)	4.4 (2.7-7.6)	0.6
ALT (U/L)	22 (11-117)	22 (12-53)	0.9
hs-CRP (mg/L)	2.4 (0.2-11.7)	1.6 (0.3-6.2)	0.71
SLD at US (mm)	115 (92-150)	102 (90-127)	0.0001
MS (*n*)	18	6	0.0001
Menopause (*n*)	20	11	0.9

[a]Fisher's exact test. IR: Insulin resistance; BMI: Body mass index; HS: Hepatic steatosis at US; US: Ultrasonography; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; HDL: High-density lipoprotein-cholesterol; ALT: Alanine aminotransferase; hs-CRP: High sensibility C-reactive protein; SLD: Spleen longitudinal diameter at US; MS: Metabolic syndrome; *n*: No. of subjects.

the study findings applied to the patients (external validity) the eighty two subjects divided into two cohorts of 52 and 30, were well balanced for BMI ($P = 0.78$), WC ($P = 0.45$) and age ($P = 0.79$), but different for HOMA ($P < 0.001$), and were studied in a cross-sectional manner.

Prevalence

A variable grade of visceral obesity was determined in all subjects with the exception of three (two without IR). Only obesity of the severest grade was represented more in the patients with IR than in the non-IR patients ($P = 0.01$). HS, revealed at US, was more pronounced in subjects with IR than in those without IR ($P = 0.005$). MS was more frequent in IR patients than in non-IR patients. These figures were not modified when adjusted for menopause (Mantel-Haenszel χ^2 test, $P = 0.001$). The same physiological status was unable to distinguish females with IR from those without IR. No difference in ALT activity was detected between the two cohorts on the basis of IR. The two groups demonstrated no resemblance when analyzing SLD, HS and blood pressure, with raised and significant values in the IR group (Table 1).

Association & prediction

Anthropometric measurements in the study females showed a similar pattern of reliably predicting IR severity. In fact, the β values of WC and BMI in predicting HOMA were 0.295, $P = 0.007$ and 0.41, $P = 0.0001$, respectively. HDL levels were not associated with HOMA values ($r = 0.8$, $P = 0.5$). SLD measures were well predicted by BMI values, $\beta = 0.35$, $P = 0.01$, and by HOMA, $\beta = 0.41$, $P = 0.0001$ (Figure 1). SBP determinations were predicted by HOMA values, $\beta = 0.39$, $P = 0.0001$ (Figure 2). HOMA

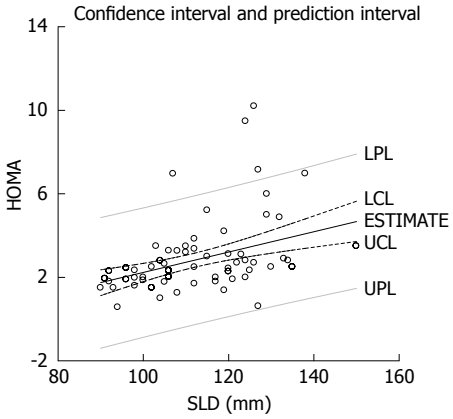


Figure 1 Prediction of spleen size by insulin resistance severity. SLD: Spleen longitudinal diameter at ultrasonography (US); HOMA: HOmeostatic metabolic assessment for insulin resistance; LPL: Lower prediction limit; LCL: Lower confidence limit; UCL: Upper confidence limit; UPL: Upper prediction limit.

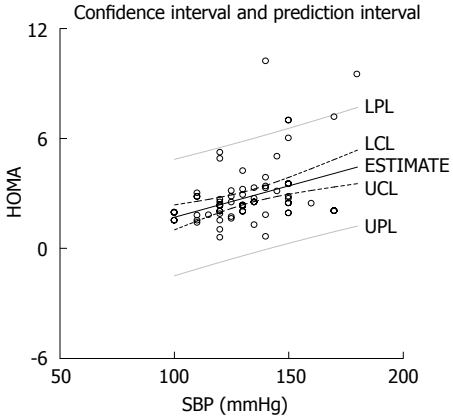


Figure 2 Prediction of systolic blood pressure by insulin resistance severity. SBP: Systolic blood pressure.

and HS scores at US were highly associated (rho = 0.34, $P = 0.002$). In IR patients, the grade of HS severity was not correlated with serum triglycerides levels (rho = 0.245, $P = 0.08$). IR patients were almost twice as likely to have HS as those who did not have IR. Further predictions are shown in Table 2.

The complex of WC, HOMA and SLD as well as age, HS and SBP had the highest correlations among the variables, contributing to the loading of the principal component factors (factor 1 and 2). Triglyceride concentrations (loading factor 3) seemed to play an isolated role (Figure 3).

Accuracy

Among the MS criteria, blood pressure was very accurate in identifying the presence of IR (AUROC for SBP 0.66, cut-off 125 mm of Hg, sensibility 64%, specificity 75%; AUROC for DBP 0.70, cut-off 85 mm of Hg, sensibility 54.5%, specificity 75%).

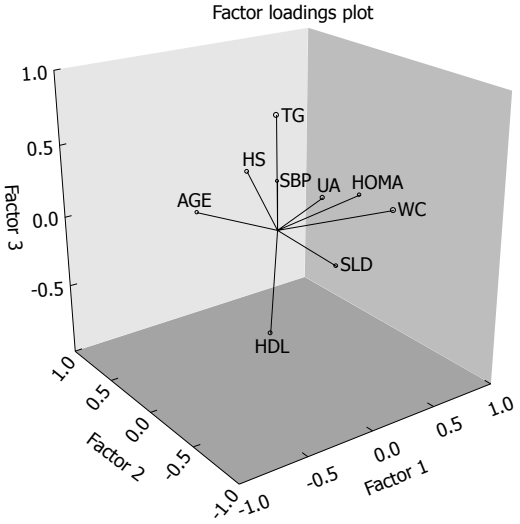
Precision

The concordance correlation coefficient to evaluate the degree of intra-operator pair observations at US was high, $\rho_c = 0.91$.

Table 2 Estimates in predicting insulin resistance

Parameter	OR	Lower	Upper	*P*-value
SLD	1.073	1.027	1.121	0.002
SBP	1.045	1.015	1.075	0.003
DBP	1.046	1.003	1.090	0.036
HDL	1.022	0.974	1.072	0.378
TG	1.006	0.998	1.014	0.143
UA	1.047	0.676	1.623	0.837
BMI	1.083	0.989	1.187	0.086
WC	1.029	0.991	1.069	0.131
HS	1.971	1.234	3.147	0.004

TG: Triglycerides; UA: Uric acid; WC: Waist circumference.



Factor	1	2	3
WC	0.603	-0.424	0.132
AGE	-0.096	0.810	-0.120
HOMA	0.817	0.163	0.005
HDL	0.029	0.118	-0.804
TG	0.163	0.236	0.679
UA	0.440	0.096	0.091
SBP	0.488	0.669	0.026
HS	0.168	0.580	0.192
SLD	0.594	0.126	-0.461

Figure 3 Unravelling the hidden correlations. Total variance explained by factor: 1 = 20.9%; 2 = 19.36%; WC: Waist circumference; HOMA: HOmeostatic metabolic assessment for insulin resistance; HDL: High-density lipoprotein-cholesterol; TG: Triglycerides; UA: Uric acid; SBP: Systolic blood pressure; HS: Hepatic steatosis at US; SLD: Spleen longitudinal diameter at ultrasonography (US).

DISCUSSION

Authorities claim that (1) every subject with a body weight above the established criteria should be treated, stressing this point even to the extent of suggesting that just brief physician-nutritionist support by telephone could be useful in a busy primary care office[28], (2) substantial numbers of overweight/obese individuals remain insulin-sensitive[29]. Consequently, the question we pose is: beyond IR, might some other indicators play a role in identifying novel targets, i.e. typology of O/O patients and timing of interventions[30]? Accordingly, we propose parameters which may be worth investigating when dealing with the phenotypically O/O and when it is necessary to decide who the metabolically normal subjects are.

The body of pertinent knowledge based on data from the Third National Health and Nutrition Examination Survey testifies that each of the five components of MS, with the possible exception of obesity, independently predicts CVD[31]. In contrast, abdominal obesity, measured by WC, is a more accurate predictor of CVD risk than general obesity measured by BMI[32], even though, for a given BMI, women have more subcutaneous adipose tissue and insulin-sensitivity than men[33]. However, controversy exists over the type of blood pressure increase. Previous results showed that SBP represents the most prevalent type in obese women[34], being a stronger predictor of CVD than DBP[35]. Indeed, these data are challenged by more recent research based on longitudinal studies[36]. In addition, according to some other investigators, both blood pressure and plasma aldosterone correlate better with IR in men than in women[37], whereas, there is widespread agreement that NAFLD predicts CVD[38].

In the present study, it can be seen that our data in O/O females supports an association only between the more severe forms of adiposity and the highest grades of IR. Accordingly, MS was characterized by different values in the two groups with and without IR, and HOMA was correlated with severity of HS and to spleen size. The HS score was higher in IR patients, as was another index (hs-CRP), suggesting a possible link between inflammatory status and IR. These findings are consistent with the concept that a partially "benign" obesity, characterized by the absence of IR, lack of HS, or at most the presence of a "light" form of HS, low blood pressure, low expression of a marker of inflammation (SLD) exist in this particular population, at least during the course of this study.

When discussing possible mechanisms for our findings, we pinpoint the following with regard to the liver-spleen axis: (1) peripheral IR determines increased hepatic synthesis of free fatty acids (FFAs) and decreased synthesis of apolipoprotein B, both leading to HS; (2) TNF-α, through JNK-dependent IRS-1 Ser307 phosphorylation, contributes to IR and is responsible for the induction of IL-6 in the liver, both of which aggravate triglyceride accumulation; (3) the overproduction of IL-6, which has "*per se*" a source in visceral and subcutaneous fat, could represent the cause of spleen enlargement in patients with HS *via* uncoupling protein 2[39]; (4) a further origin of the increased splenic volume may be found in the accumulation of activated macrophages inside this organ *via* monocyte chemoattractant protein-1 which is over-expressed in adipose tissue[40]; (5) once infiltrated, these macrophages produce a large amount of TNF-α which increases the release of FFAs, resulting in HS. With regard to blood pressure, O/O subjects not only exhibit impaired endothelial function in small arteries but also increased arterial stiffness[41]. However, IR is associated with greater cardiac reactivity in young women[42]. Finally, a recent study performed on a large population showed that patients with HS have increased intima media thickness (IMT[43]).

The limitations and strengths of our study deserve

comment. Concerning the limitations, to verify CVD risk, we should have studied a US parameter marker of early atherosclerosis, e.g. IMT in our population, however, this index, as previously emphasized[43], is correlated with HS grade. A further drawback may have been the lack of liver biopsies to assess the severity of NAFLD, even though the canonical difference between FL and NASH has been challenged recently[44]. Finally, we did not determine serum levels of folate which are related to elevated homocysteine or blood pressure. In relation to blood pressure, our data showed a new emerging trend, i.e. rather than focusing primarily on body weight, WC, or BMI as a health indicator, a number of scientists have suggested the use of a measure called Metabolic Fitness (MF). Authors define MF as "the absence of biochemical risk factors associated with obesity or elevated blood pressure". These measures are much better indicators of chronic disease risk, and reductions in these risks factors are not always dependent on weight loss[45].

Most people, who are unhappy with their weight, try to lose weight by changing unhealthy practices. This attitude could result in a dramatic increase in unrealistic goals. On the other hand, some lines of research support the notion that a lifestyle-modification program can reduce the risk of O/O-related comorbid conditions despite minimal or no weight loss. What is more, studies investigating weight loss have methodological limitations that restrict the applicability of findings to O/O patients assessed in clinical practice[46]. When we add all this evidence up, it does raise the question of what will our strategy in the near-to-medium term look like. This debate is still ongoing and is mainly related to health-related quality of life[47] and the not always favorable balance between costs and treatment outcomes.

COMMENTS

Background

The incidence of Overweight/Obesity in the last few years has dramatically increased in highly developed countries. There has also been a simultaneous rise in the frequency of metabolic syndrome. Being overweight causes similar health problems to that of obesity but to a lesser degree. The risk of death from all causes increases throughout the range of moderate and severe increases in body weight for both men and women in all age groups. Unless reversed, this trend predicts an epidemic of cardiovascular disease.

Research frontiers

It has recently been postulated that "metabolically benign obesity" exists, and is not accompanied by insulin resistance and early atherosclerosis. We sought to identify which parameters could distinguish between healthy and non healthy overweight/obese individuals.

Innovations and breakthroughs

We claim that "hepatocytes are the last cells to be involved in the progressive chain of fat accumulation and probably the first cells to tell us that something is wrong". If our proposed parameters are to be adopted more widely, they must be validated in a range of settings and different populations; until then, the most important message is that researchers should identify tools that suit clinicians in their clinical setting, allowing them to screen appropriate cases, in order to improve identification of patients who need to lose weight.

Applications

Interventions at home, in the office, and in the community are required to empower adults to increase physical activity and to modify eating habits. Nevertheless, before these intervention strategies are set up, it is mandatory to establish exactly which individuals should be treated and when.

Terminology

The main outcome measures in this study are extremely common, i.e. waist circumference, serum uric acid, high-density lipoprotein-cholesterol and triglycerides, alanine aminotransferase, blood pressure and the two imaging parameters, hepatic steatosis and spleen longitudinal diameter.

Peer review

This is quite an interesting article. The manuscript reports the studies on the use of simpler parameters in assessing the need for medical intervention with respect to healthy and non healthy overweight/obese individuals. It is suggested that adoption of simpler to perform measurements could not only reduce the cost of medical care but also provide more reliable identification of patients in need of weight loss.

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