European Journal of Internal Medicine 63 (2019) 74–78

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

The fat-to-lean mass ratio, a novel anthropometric index, is associated to glucose metabolic disorders

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ARTICLE INFO

Keywords:
Fat
Muscle
Type 2 diabetes
Impaired fasting glucose
Impaired glucose tolerance

ABSTRACT

Objective: The aim was to evaluate whether the Fat-to-Lean Mass (FyM) ratio is associated to glucose metabolic disorders (GMD).
Design: Cross-sectional population based study.
Methods: Eligible subjects were healthy men and non-pregnant women with new diagnosis of GMD that were allocated into following groups: 1) Normal Glucose Tolerance (NGT), 2) Diabetes, 3) impaired fasting glucose (IFG) + impaired glucose tolerance (IGT), 4) IGT, and 5) IFG. The FyM index [Total body fat (Kg)/total lean mass (Kg)], and the odds ratio (OR) between FyM index and GMD were estimated.
Results: A total of 875 individuals with average age 41.62 ± 12.3 were enrolled; of them, 645 (73.1%) women and 230 (22.8%) men; 521 (59.5%), 71 (8.1%), 85 (9.7%), 53 (6.0%), and 145 (16.6%) individuals were allocated into groups with NGT, diabetes, IFG + IGT, IGT, and IFG, respectively. The FyM was significantly associated with prediabetes and diabetes in women (OR 4.2; $_{95\%}$CI 3.0–11.1 and OR = 7.2; $_{95\%}$CI 2.0–15.2) and men (OR = 2.6; $_{95\%}$CI 1.1–6.7 and OR = 4.6; $_{95\%}$CI 1.4–15.1). In the overall population, the OR between FyM index with IGT, IFG, and IFG + IGT was 8.4 ($_{95\%}$CI 2.6–17.4), 5.2 ($_{95\%}$CI 2.6–10.6), and 6.1 ($_{95\%}$CI 1.8–9.5).
Conclusion: The FyM index was strongly associated with all categories of GMD.

1. Introduction

A strong body of evidence shows that fat and muscle are interconnected in a way that, the imbalance between them may exert a synergistic effect on the risk of developing glucose metabolic disorders (GMD). It is well known that fat infiltration into muscle is associated with lower muscle strength [1,2] and progressive decline in total energy expenditure stemming from decreased physical activity and reduced basal metabolic rate [3]. In addition, it has been reported that fat infiltration into muscle, through activation of inflammatory pathways, is a triggering of insulin resistance [4,5].

Given the role of obesity and/or the fat/muscle imbalance in the pathogenesis of GMD, several anthropometric indexes, such as body mass index (BMI), total body fat, and the waist circumference (WC) have been used for both estimate the obesity status and early recognizing the risk of developing GMD [6–11].

Within this context, we evaluated whether the imbalance between total body fat and total lean mass, measured by the Fat-to-Lean Mass (FyM) ratio, is associated to GMD.

2. Materials/subjects and methods

With the approval of protocol by the Mexican Social Security Institute Research Committee, and after obtained the informed consent of participants, a cross-sectional study was conducted from February 2015 to January 2018.

Apparently healthy men and non-pregnant women, aged 30 to 65 years with new diagnosis of GMD were eligible to participate. Previous diagnoses of GMD, pregnancy, renal or hepatic diseases, malignancy, and corticoids therapies were exclusion criteria.

All participants underwent anthropometric measurements and 75 g oral glucose tolerance test.

2.1. Definitions

The FyM index was calculated as *total body fat* (Kg)/*total lean mass*

Abbreviations: FyM, Fat-to-Lean Mass; GMD, metabolic disorders; NGT, Normal Glucose Tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OR, odds ratio; FPG, fasting plasma glucose; BMI, body mass index; WC, waist circumference; $_{95\%}$ CI, Confidence Interval

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https://doi.org/10.1016/j.ejim.2019.03.017
Received 17 July 2018; Received in revised form 21 January 2019; Accepted 28 March 2019
Available online 02 April 2019

(Kg).

According to fasting and 2-h post-load serum glucose levels, GMD were classified as following: 1) Diabetes (glucose levels 2-h post-load $\geq$11.1 mmol/L), 2) Prediabetes, and 3) Normal Glucose Tolerance -NGT- (FPG < 5.6 mmol/L and 2-h postload glucose levels < 7.8 mmol/L).

Prediabetes included a) impaired fasting glucose -IFG- (fasting plasma glucose (FPG) $\geq$5.6 < 7.0 mmol/L), b) impaired glucose tolerance -IGT- (glucose levels 2-h postload $\geq$7.8 < 11.1 mmol/L), and c) IFG + IGT [12].

2.2. Measurements

In fasting conditions with the subjects in light clothing and without shoes, the BMI and the total body fat were estimated using a body composition monitoring equipment (Tanita TBF-215, Tokyo, Japan), based in bioelectrical impedance systems that employes fat-free mass prediction equations using traditional two-compartment reference methods, such as underwater weighing or total body water, for estimating the components that represent muscularity and total body fat [13].

WC was measured using a flexible steel tape measure, midway between the lowest portion of the rib cage and iliac crest, and anteriorly midway between the xiphoid process of sternum and the umbilicus.

Personnel in charge of anthropometric measurements were blinded regarding results of oral glucose tolerance test.

2.3. Assays

Serum glucose levels were measured using the glucose-oxidase method (Sigma Diagnostics, St. Louis, MO, USA), with intra- and inter-assay CVs of 2.4 and 3.8. Measurements were performed using an A15 Clinical Analyzer (Byosistems, USA).

2.4. Statistical analysis

The SPSS for Windows, v15.0 (Chicago, IL.) was used for data management and statistical analysis. The bivariate analysis was performed using Unpaired Student *t*-test for numerical data and χ^2 test for testing differences between nominal variables.

Differences between more than two groups were estimated using ANOVA one-way analysis, with Bonferroni *post-hoc* test.

Spearman correlation was used for estimating the relationship between the FyM index and categories of GMD.

A logistic regression analysis was used to computes the odds ratio (OR) between the FyM index (independent variable) and GMD (dependent variables).

A 95% Confidence Interval ($_{95\%}$ CI) and a two-sided *p* value < .05 defined the level of statistical significance.

3. Results

A total of 875 individuals with average age 41.6 ± 12.3 were enrolled; of them, 645 (73.1%) women and 230 (22.8%) men; 521 (59.5%), 283 (32.3%), and 71 (8.1%) individuals in the groups with NGT, prediabetes, and diabetes, respectively. There was significant statistical difference by sex for the individuals in the NGT group (369 women and 152 men, $p = .02$), but not in the groups with prediabetes (219 women and 64 men, $p = .057$), and diabetes (57 women and 14 men, $p = .12$). Figs. 1 and 2 shows the flow STARD diagram for men and women.

Individuals in the NGT group were younger and exhibited lower BMI, WC, total body fat, and FyM index as well as lower fasting and 2 h post-load serum glucose levels than individuals with diabetes, IFG + IGT, IGT, and IFG, Table 1.

A total of 71 (8.1%), 85 (9.7%), 53 (6.0%), and 145 (16.6%), individuals were diagnosed with diabetes, IFG + IGT, IGT, and IFG, respectively. Interestingly, there were not significant differences by BMI, WC, and body fat between individuals in the different categories of GMD. Individuals with IFG showed lower total body fat and FyM index than individuals with IFG + IGT and diabetes, Table 1.

In both men and women with GMD, the Spearman correlation between FyM index with diabetes, IFG + IGT, IGT, and IFG, was stronger than correlation showed by other anthropometric measurements, Table 2.

In the overall population, the FyM index was strongly associated with prediabetes (OR 5.95; $_{95\%}$CI 3.3–10.6, $p < .005$) and diabetes (OR 6.6; $_{95\%}$CI 5.8–15.0, $p < .005$).

Stratified according sex, the FyM remained significant associated with prediabetes and diabetes in women (OR 4.2; $_{95\%}$CI 3.0–11.1 and OR 7.2; $_{95\%}$CI 2.0–15.2) and men (OR 2.6; $_{95\%}$CI 1.1–6.7 and OR 4.6; $_{95\%}$CI 1.4–15.1). In the overall population, the OR between FyM index with IGT, IFG, and IFG + IGT was 8.4 ($_{95\%}$CI 2.6–17.4), 5.2 ($_{95\%}$CI 2.6–10.6), and 6.1 ($_{95\%}$CI 1.8–9.5).

The logistic regression analysis between anthropometric measurements of obesity and GMD are shown in Table 3. The OR between FyM index and all categories of GMD was higher than the OR exhibited between other anthropometric measurements and GMD.

4. Discussion

Our results show that FyM index, as indicator of imbalance between total body fat and lean mass, is strongly associated to diabetes and all categories of prediabetes. Furthermore, as compared with other anthropometric measurements, the FyM index showed a higher correlation with all categories of GMD.

It has been reported that the imbalance between lean and fat masses is associated with chronic inflammation [14] and that the increase in fat deposition promotes intramyocellular lipid accumulation, resulting in the synthesis of bioactive lipid intermediates and lipid peroxides that activate the inflammatory response [15], disturbs the insulin signaling in peripheral tissues, and induce β-cell dysfunction [14], mechanism involved in the pathogenesis of insulin resistance and type 2 diabetes. In addition, the chronic low-grade inflammation is an important mediator in restraining myogenesis and/or accelerating muscle protein degradation [16] that leads to the loss of lean mass perpetuating the imbalance of lean and fat mass.

Skeletal muscle is importantly involved in insulin-mediated glucose uptake [17] so, the muscle mass variations exert an important role on glucose uptake, and thus, in serum glucose levels. With this regard, taking into account that obesity is characterized by excess of body fat and decrease of muscle mass [16,18], it would be expected that the FyM index mirror the risk of developing GMD. Our findings, showing a strong association between FyM index with all the categories of prediabetes as well as with diabetes, support the abovementioned statement.

It is important to take into account that women have more abdominal fat than men, which could be related with its increased risk of developing GMD; with this regard, although impedance does not discriminate between visceral and subcutaneous fat, the FyM was strongly associated with GMD in women and men.

Some limitations of our study should be mentioned. First, we use the bioelectrical impedance analysis, but not the gold standard test for measuring body components; however, three available consensus statements (European Working Group on Sarcopenia in Older People, Asian Working Group for Sarcopenia, and International Consensus for Cancer Cachexia) recommends the use of bioelectrical impedance analysis as an appropriate tool to assess total fat and skeletal muscle mass [13]. Second, because only Mexican individuals with average age 41.6 ± 12.3 were studied, our findings cannot be inferred to other ethnic groups or to younger or elderly patients; finally, we did not estimate visceral fat; hence we cannot determine the role of visceral fat

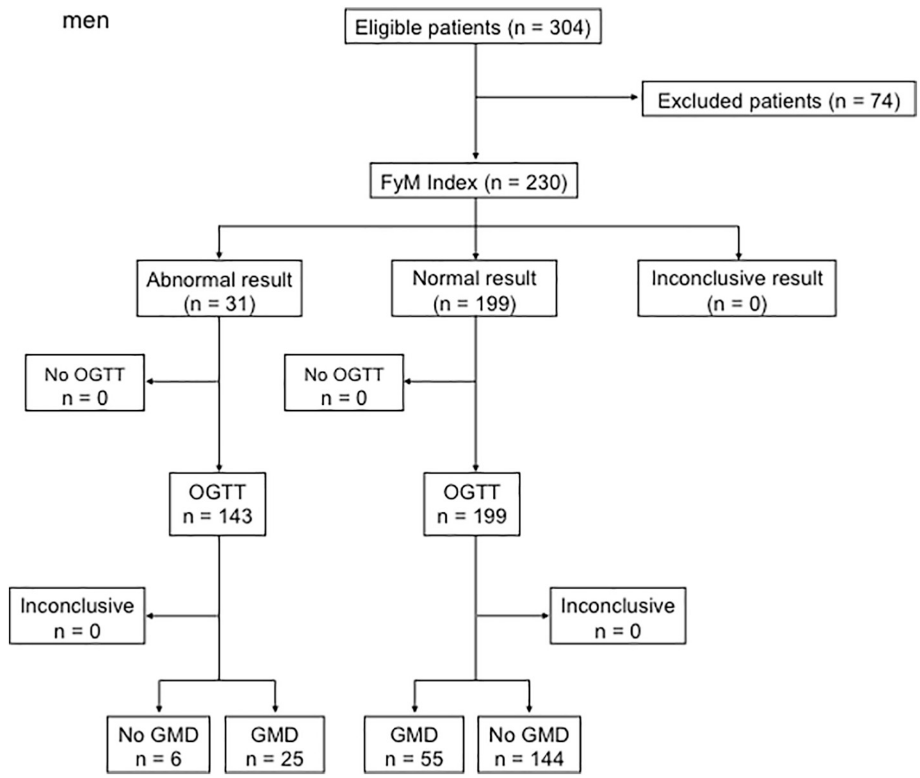

Fig 1. Flow STARD diagram for men.

versus total fat in the estimation of FyM index. Further studies including several ethnicities and age strata are warranted in order to confirm our findings.

5. Conclusion

The strong associations of FyM index with all categories of GMD supports the statement that it appropriately mirrors the imbalance between body fat and lean mass.

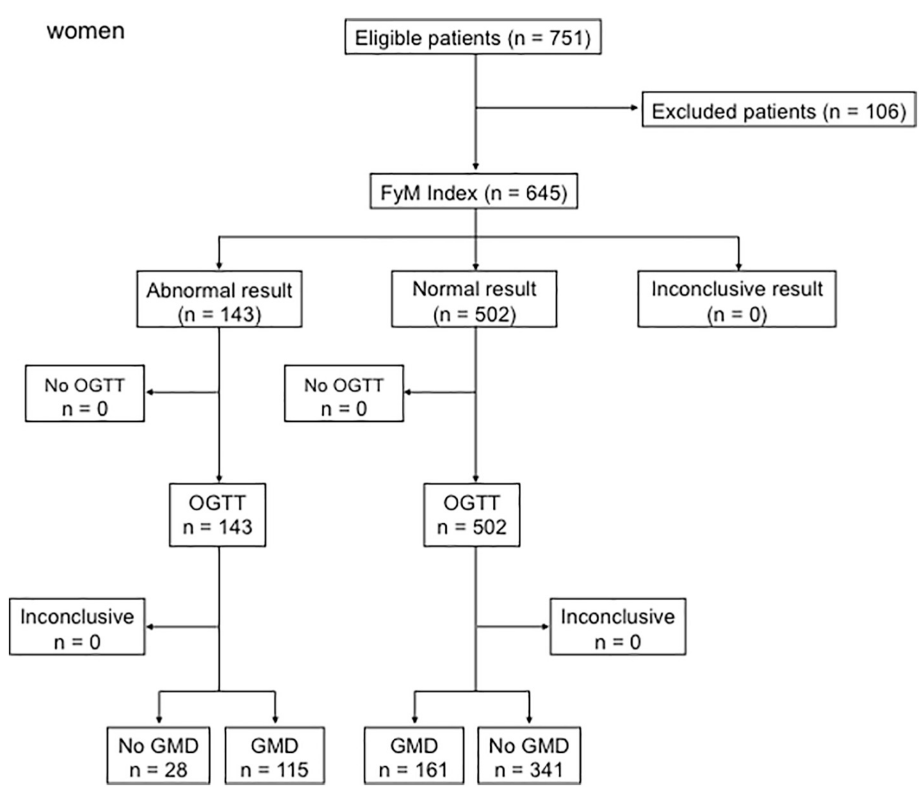

Fig. 2. Flow STARD diagram for women.

Table 1
Characteristics of individuals according glucose metabolic disturbance categories.

	NGT	Type 2 diabetes	IFG + IGT	IGT	IFG	*p* value
	n = 521	*n* = 71	*n* = 85	*n* = 53	*n* = 145	
Age (years)	38.3 ± 12.3	49.0 ± 10.0	48.2 ± 9.9	44.7 ± 10.7	44.7 ± 11.2	0.006[*,†,‡]
Body mass index (Kg/m^2)	28.0 ± 6.3	32.9 ± 5.0	33.4 ± 6.0	32.6 ± 4.6	31.9 ± 6.2	0.04[‡]
Waist (cm)	91.9 ± 13.7	102.6 ± 12.1	103.6 ± 14.8	100.9 ± 10.9	100.8 ± 14.7	0.04[‡]
Total body fat, Kg	25.6 ± 9.7	35.7 ± 10.2	37.4 ± 13.4	35.0 ± 9.7	34.9 ± 14.8	0.03[‡]
Total lean mass, Kg	48.9 ± 10.0	48.0 ± 8.1	48.2 ± 7.2	49.1 ± 8.2	49.9 ± 8.7	0.59
FyM index	0.53 ± 0.19	0.74 ± 0.17	0.77 ± 0.22	0.71 ± 0.17	0.70 ± 0.30	0.03[‡]
Fasting glucose (mmol/L)	4.8 ± 0.5	7.9 ± 3.0	6.3 ± 0.7	5.1 ± 0.3	6.0 ± 0.5	< 0.005[**,†,‡]
2 h post-load glucose (mmol/L)	5.5 ± 1.2	14.5 ± 3.9	9.2 ± 0.9	8.8 ± 0.8	6.2 ± 1.0	< 0.005[*, **,†,‡]

Data are mean ± SD.
IGT, impaired glucose tolerance; IFG, impaired fasting glucose; NGT, normal glucose tolerance; FyM index, the Fat-to-Lean Mass index.
* $p < .05$ between the IFG and IFG + IGT.
** $p < .05$ between the IFG and IGT.
† $p < .05$ between the IFG and diabetes.
‡ $p < .05$ between the NGT with IFG, IGT, IFG + IGT, and Type 2 diabetes.

Table 2
Spearman correlations between the Fat-to-Lean Mass (FyM) index and glucose metabolic disorders in the population stratified according sex.

Women	Type 2 diabetes		IGT + IFG		IGT		IFG	
	R	*p* value	R	*p* value	R	*p* value	R	*p* value
	n = 57		*n* = 69		*n* = 45		*n* = 105	
Body mass index	0.181	0.04	0.208	0.01	0.178	0.04	0.210	0.04
Waist	0.164	0.04	0.194	0.04	0.152	0.04	0.184	0.04
Total fat	0.180	0.04	0.235	0.005	0.156	0.05	0.242	0.005
Total lean mass	−0.035	0.37	−0.083	0.34	−0.102	0.10	−0.014	0.09
FyM index	0.301	0.001	0.317	0.001	0.297	0.005	0.284	0.005
MEN	Type 2 diabetes		IGT + IFG		IGT		IFG	
	n = 14		*n* = 16		*n* = 8		*n* = 40	
Body mass index	0.155	0.04	0.148	0.04	0.034	0.83	0.077	0.65
Waist	0.170	0.04	0.153	0.04	0.027	0.69	0.110	0.06
Total fat	0.212	0.04	0.195	0.04	0.021	0.75	0.090	0.07
Total lean mass	−0.020	0.97	−0.105	0.11	−0.024	0.72	−0.098	0.14
FyM index	0.285	0.001	0.295	0.005	0.280	0.005	0.246	0.01

IGT, impaired glucose tolerance; IFG, impaired fasting glucose; NGT, normal glucose tolerance; FyM index, the Fat-to-Lean Mass index.

Table 3
Logistic regression analysis, adjusted by sex and age, showing the Odds Ratios (OR) between anthropometric measurements (independent variables) and the glucose metabolic disorders (dependent variables) in the overall population.

	Type 2 diabetes		IGT + IFG		IGT		IFG	
	OR	$_{95\%}$CI	OR	$_{95\%}$CI	OR	$_{95\%}$CI	OR	$_{95\%}$CI
Body mass index	1.06	1.03–1.1	1.05	1.03–1.1	1.03	1.01–1.12	1.02	1.01–1.09
Waist	1.04	1.01–1.05	1.03	1.01–1.06	1.01	1.005–1.04	1.01	1.006–1.04
Total fat	1.08	1.01–1.1	1.11	1.07–1.16	1.03	1.01–1.09	1.03	1.02–1.07
Total lean mass	0.99	0.96–1.02	0.98	0.96–1.01	1.01	0.97–1.03	1.02	0.99–1.03
FyM index	6.40	5.7–14.3	8.4	7.1–16.9	8.1	2.3–17.1	5.1	2.5–10.1

FyM index, the Fat-to-Lean Mass index.

Declaration interests

The authors declare no competing financial interests.

Funding

Mexican Social Security Institute (FIS/IMSS/PRIO/13/026).

Acknowledgements

We gratefully acknowledge the commitment and dedication of the physicians, chemists, and participant personnel of the Biomedical Research Unit of the Mexican Security Institute at Durango.

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