Public University of Navarre

Department of Health Sciences

Cardiovascular Health, Muscular Strength and Body Composition in Colombian University Students

DOCTORAL THESIS

María Alejandra Tordecilla Sanders

June 2019

Supervisors:

Dr. Robinson Ramírez Vélez, Ph.D

Dr. Mikel Izquierdo, Ph.D

Table of Contents

Table Index

Figure Index

List of Abbreviations

AHA: American Heart Association

AUC: Area under the curve

BF: Body fat

BIA: Bioelectrical impedance analysis

BMI: Body mass index

CI: Confidence interval

CT: Computed tomography

CVD: Cardiovascular disease

CVH: Cardiovascular health

DXA: Dual-energy x-ray absorptiometry

FUPRECOL: Association between muscular strength and metabolic risk factors in Colombia

FMI: Fat mass index

HDL-C: High-density lipoprotein cholesterol

IDF: International diabetes federation

LDL-C: low-density lipoprotein cholesterol

LR (+): Positive likelihood ratio

LR (-): Negative likelihood ratio

MAP: Mean arterial pressure

MetS: Metabolic syndrome

MRI: magnetic resonance imaging

NGS: Normalized grip strength

OR: Odds Ratio

PA: Physical activity

ROC: Receiver operating characteristic

SD: Standard deviation

TEM: Technical error of measurement

WC: Waist circumference

WHO: World Health Organization

Summary

The current Ph.D. dissertation revolves around the components of the body composition and physical condition like body fat percentage (BF%), fat mass index (FMI) and muscular strength (normalized grip strength [NGS]) respectively, can be used to detect metabolic syndrome (MetS) in collegiate students from Colombia. Besides these components are related with the ideal cardiovascular health (CVH) in Colombian University Students. For these reasons, the current doctoral thesis is based on 3 scientific studies that have been published or submitted for publication in scientific international journals.

The first study (chapter 2), has the aim to explore thresholds of body fat percentage (BF%) and fat mass index (FMI) for the prediction of MetS among Colombian University students. The second study (chapter 3) to determine cut-off of normalized grip strength (NGS) for the detection of MetS in a large nonrepresentative sample of a collegiate student population from Colombia. The lastly study (chapter 4) has the purpose to investigate the relationship between handgrip strength, muscle mass, and ideal cardiovascular health (CVH) among Colombian college students.

Study 1

Percentage of Body Fat and Fat Mass Index as a Screening Tool for Metabolic Syndrome Prediction in Colombian University Students.

Ramírez-Vélez R; Correa-Bautista JE; Sanders-Tordecilla A; Ojeda-Pardo ML; Cobo-Mejía EA; Castellanos-Vega RDP; García-Hermoso A; González-Jiménez E; Schmidt-RioValle J; González-Ruíz K. (2017). Percentage of Body Fat and Fat Mass Index as a Screening Tool for Metabolic Syndrome Prediction in Colombian University Students. Nutrients 9(9). doi: 10.3390/nu9091009.

The first study we aimed to explore thresholds of body fat percentage (BF%) and fat mass index (FMI) for the prediction of MetS among Colombian University students. A cross-sectional study was conducted on 1687 volunteers (63.4% women, mean age=20.6 years). Weight, waist circumference, serum lipids indices, blood pressure, and fasting plasma glucose were measured. Body composition was measured by bioelectrical impedance analysis (BIA) and FMI was calculated. MetS was defined as including more than or equal to three of the metabolic abnormalities according to the International Diabetes Federation (IDF) definition. Receiver operating curve (ROC) analysis was used to determine optimal cut-off points for BF% and FMI in relation to the area under the curve (AUC), sensitivity, and specificity in both sexes. The overall prevalence of Mets was found to be 7.7%, higher in men than women (11.1% vs. 5.3%; $p<0.001$). BF% and FMI were positively correlated to MetS components ($p<0.05$). ROC analysis indicated that BF% and FMMI thresholds of 25.5% and 6.97 kg/m^2 in men, and 38.95% and 11.86 kg/m^2 in women, were found to be indicative of high MetS risk. Based on the IDF criteria, both indexes´ thresholds seem to be good tools to identify university students with unfavorable metabolic profiles.

Study 2

Muscle strength cut-off for the detection of metabolic syndrome in a nonrepresentative sample of collegiate students from Colombia

García-Hermoso A; Tordecilla-Sanders A; Correa-Bautista JE; Peterson MD; Izquierdo M; Quino-Avila AC; Sandoval-Cuellar C; González-Ruíz K; Ramírez-Vélez R. Muscle Strength cut-offs for the Detection of Metabolic Syndrome in Non-Representative Sample Collegiate Students from Colombia. Journal of Sport and Health Science. 2018 (In press). https://doi.org/10.1016/j.jshs.2018.09.004.

The aim of the second study was to determine cut-off of normalized grip strength (NGS) for the detection of MetS in a large nonrepresentative sample of a collegiate student population from Colombia. A cross-sectional study was conducted on 1795 volunteers (61.4% female, age=20.68±3.10 years, mean ±SD). Strength was estimated using a handheld dynamometer and normalized to body mass (handgrip strength (kg)/ body mass (kg)). Anthropometrics, serum lipids indices, blood pressure, and fasting plasma glucose were measured. Body composition was measured by bioelectrical impedance analysis (BIA). MetS was defined as including ≥ 3 of the 5 metabolic abnormalities according to the IDF definition. A metabolic risk score was computed from the following components: waist circumference, triglycerides, high-denstiy lipoprotein cholesterol, glucose, and systolic and diastolic blood pressure.

Receiver operating curve analysis showed significant discriminatory accuracy of NGS in identifying the thresholds and risk categories. Lower strength was associated with increased prevalence of MetS. In males, weak, intermediate, and strong NGS values at these points were <0.466, 0.466-0.615, >0.615, respectively. In females, these cut-offs points were <0.332, 0.332-0.437, >0.437, respectively. Our sex-specific cut-off of NGS could be incorporated into a clinical setting for identifying college students at cardiometabolic disease risk.

Study 3

Ideal Cardiovascular Health, Handgrip Strength and muscle mass among college students: The FUPRECOL Adults study

Garcia-Hermoso A; Correa-Bautista JE; Izquierdo M; Tordecilla-Sanders A; Prieto-Benavides D; Sandoval-Cuellar C; González-Ruíz K; Ramírez-Vélez R. Ideal Cardiovascular Health, Handgrip Strength, and Muscle Mass Among College Students: Results from the cross-sectional The FUPRECOL Adult Study. J Strength Cond Res. 2019 Jan 17. doi: 10.1519/JSC.0000000000003052. [Epub ahead of print].

The last study of the current Ph.D. dissertation has the purpose to investigate the relationship between handgrip strength, muscle mass, and ideal cardiovascular health (CVH) among Colombian college students. Data from 1835 college students were analyzed (1128 female). Muscular strength was estimated using a hand-hold dynamometer and normalized to body mass (normalized grip strength [NGS]). The percentage of body fat was determined for bioelectrical impedance analysis (BIA) using tetrapolar whole-body impedance. Ideal CVH was defined as meeting the ideal levels of 4 behaviors (smoking, body mass index, physical activity, and diet adherence) and 3 factors (total cholesterol, fasting glucose, and blood pressure). Higher levels of NGS and muscle mass (relative to body mass) were associated with a higher number of ideal CVH metrics scored on a continuous scale from 0 (all 7 poor) to 7 (all 7 ideal), a 1-metric increase was associated with reduced odds of weak NGS (33 and 36%) and low-medium muscle mass (28 and 34%) mass in men and women, respectively (all p<0.001). This study indicates that in Colombian college students, both handgrip strength and muscle mass are positively associated with the ideal CVH metrics. To reduce the possible future public health burden of muscular weakness, health professionals need to encourage the public to optimize lifestyle-related risk factors during the young adult stage.

Resumen

La actual disertación doctoral gira en torno a como los componentes de la composición corporal y la condición física, como el porcentaje de tejido graso (BF%- *Siglas en inglés body fat percentage)*, el índice de masa grasa (FMI- *Siglas en inglés fat mass index)* y la fuerza muscular (fuerza prensil ajustada- NGS- *Siglas en ingles normalized grip strength)* respectivamente, pueden utilizarse para detectar síndrome metabólico (MetS- *Siglas en inglés metabolic syndrome)* en estudiantes universitarios de Colombia. Además, estos componentes están relacionados con el índice de salud cardiovascular (CVH- *siglas en inglés cardiovascular health)* en estudiantes universitarios colombianos. Por estas razones, la presente tesis doctoral se basa en 3 estudios científicos que se han sido publicado o enviados para su publicación en revistas científicas internacionales.

El primer estudio (capítulo 2) tuvo como objetivo, fue explorar los valores de referencia del BF% y el FMI para la predicción de MetS en los estudiantes universitarios de Colombia. El objetivo del segundo estudio (capítulo 3) fue determinar los puntos de referencia de la NGS para la detección de MetS en una gran muestra no representativa de una población de estudiantes universitarios de Colombia. El último estudio (capítulo4) tuvo el propósito de investigar la relación entre la fuerza prensil, masa muscular y el índice de CVH en estudiantes universitarios de Colombia

Estudio 1

Porcentaje de grasa corporal y el índice de masa grasa como herramienta de detección para la predicción de síndrome metabólico en estudiantes universitarios colombianos.

Referencia:

Ramírez-Vélez R; Correa-Bautista JE; Sanders-Tordecilla A; Ojeda-Pardo ML; Cobo-Mejía EA; Castellanos-Vega RDP; García-Hermoso A; González-Jiménez E; Schmidt-RioValle J; González-Ruíz K. (2017). Percentage of Body Fat and Fat Mass Index as a Screening Tool for Metabolic Syndrome Prediction in Colombian University Students. Nutrients 9(9). doi: 10.3390/nu9091009.

El primer estudio tuvo como objetivo, fue explorar los valores de referencia del porcentaje de tejido graso (BF%- *Siglas en inglés Body fat percentage)* y el índice de masa grasa (FMI- *Siglas en inglés Fat mass index)* para la predicción de Síndrome metabólico (MetS- *Siglas en inglés Metabolic Syndrome)* en los estudiantes universitarios de Colombia. Se realizó un estudio transversal en 1687 voluntarios (63.4% mujeres, edad promedio=20.6 años). Se midió el peso, la circunferencia de cintura, los índices lipídicos, la presión arterial y la glucosa en plasma en ayunas. La composición corporal se midió a través de un analizador de impedancia bioeléctrica (BIA- *Siglas en inglés Bioelectrical impedance análisis)* y el FMI se calculó. El MetS se definió como la inclusión de más o equivalente a tres de las anomalías metabólicas según la definición de la Federación Internacional de Diabetes (IDF- *Siglas en inglés de International Diabetes Federation)*. El análisis de la Curva operativa del receptor (ROC- *Siglas en inglés de Receiver Operating Characteristic)* se utilizó para determinar los puntos de referencia óptimos para establecer el % de tejido graso y el FMI en relación al área bajo la curva (AUC-*Siglas en inglés Area Under the Curve)*, la sensibilidad y especificidad en ambos sexos, para la detección de síndrome metabólico. En toda la población evaluada se encontró una prevalencia del 7.7% se MetS, mayor en hombres que en mujeres (11.1% vs 5.3%, $p<0.001$). Se encontró una correlación positiva entre el % tejido graso y el FMI frente a los componentes de SM ($p<0.05$). Los análisis de la curva ROC indican que los puntos de referencia de %tejido graso y FMI de 25.55% y 6.97 kg/m^2 en hombres y 38.95% y 11.86 kg/m^2 en mujer, son indicativos de alto riesgo de SM. Teniendo en cuenta los criterios de la IDF, los puntos de referencia de los dos índices parecen

ser buenas herramientas para identificar perfiles metabólicos poco saludables en estudiantes universitarios.

Estudio 2

Puntos de corte de fuerza muscular para la detección de síndrome metabólico en una muestra no representativa de estudiantes universitarios de Colombia.

Referencia:

García-Hermoso A; Tordecilla-Sanders A; Correa-Bautista JE; Peterson MD; Izquierdo M; Quino-Avila AC; Sandoval-Cuellar C; González-Ruíz K; Ramírez-Vélez R. Muscle Strength cut-offs for the Detection of Metabolic Syndrome in Non-Representative Sample Collegiate Students from Colombia. Journal of Sport and Health Science. 2018 (In press). https://doi.org/10.1016/j.jshs.2018.09.004.

El objetivo del segundo estudio fue determinar los puntos de referencia de la fuerza prensil ajustada (NGS- *Siglas en ingles Normalized grip strength)* para la detección de síndrome metabólico (MetS- *Siglas en inglés Metabolic Syndrome)* en una gran muestra no representativa de una población de estudiantes universitarios de Colombia. Se realizó un estudio transversal en 1795 voluntarios (61.4% mujeres, edad= 20.68 ± 3.10 años, media ± DE). Se estimó la fuerza usando un dinamómetro manual y se ajustó por el peso de cada sujeto (fuerza prensil (kg)/ peso corporal (kg)). Se tomaron medidas antropométricas, índices del perfil lipídico, presión arterial, glucosa plasmática en ayunas. La composición corporal se midió a través de un analizador de impedancia bioeléctrica (BIA- *Siglas en inglés Bioelectrical impedance análisis)*. El MetS se definió como la inclusión de ≥ 3 de las 5 anomalías metabólicas según la definición de la Federación Internacional de Diabetes (IDF- *Siglas en inglés de International Diabetes Federation)*. Se calculó una puntuación de riesgo metabólico a partir de los siguientes componentes: circunferencia de cintura, triglicéridos, lipoproteínas de alta densidad (HDL-C: *Siglas en ingles de High density lipoprotein colesterol)*, glucosa y, presión arterial sistólica y diastólica.

Los análisis de la curva Operativa del receptor (ROC- *Siglas en inglés de Receiver Operating Characteristic)* evidenciaron como la fuerza ajustada identifica los puntos de referencia y las categorías de riesgo de forma precisa y significativa. Menor fuerza se asoció con mayor prevalencia de SM. En hombres, los valores de la fuerza ajustada categorizada en *débil, intermedia y fuerte* fue de <0.466, 0.466-0.615, >0.615, respectivamente. En mujeres estos puntos de corte fueron de >0.332, 0.332-0.437, >0.437, respectivamente. Los puntos de corte de la fuerza prensil ajustada pueden ser incorporadas en un entorno clínico para identificar riesgo cardiovascular en estudiantes universitarios.

Estudio 3

Salud Cardiovascular Ideal, fuerza muscular y masa muscular en estudiantes universitarios: Estudio FUPRECOL adultos*.*

Referencia:

Garcia-Hermoso A; Correa-Bautista JE; Izquierdo M; Tordecilla-Sanders A; Prieto-Benavides D; Sandoval-Cuellar C; González-Ruíz K; Ramírez-Vélez R. Ideal Cardiovascular Health, Handgrip Strength, and Muscle Mass Among College Students: Results from the cross-sectional The FUPRECOL Adult Study. J Strength Cond Res. 2019;33(3):747-754. doi: 10.1519/JSC.0000000000003052.

El último trabajo tuvo el propósito de investigar la relación entre la fuerza prensil, masa muscular y el índice de Salud Cardiovascular (CVH- *siglas en inglés Cardiovascular health)* en estudiantes universitarios de Colombia. Se analizaron datos de 1835 estudiantes universitarios (1128 mujeres). La fuerza muscular se estimó utilizando un dinamómetro manual y se ajustó por el peso del sujeto (NGS- *siglas en inglés Normalized grip strength*). El porcentaje de grasa corporal se determinó por el análisis de impedancia bioeléctrica (BIA-*siglas en ingles Bioelectrical impedance análisis)* usando una impedancia tetrapolar. El índice de CVH se definió como el cumplimiento de los niveles ideales de 4 comportamientos (tabaquismo, índice de masa corporal [IMC], actividad física y adherencia a la dieta) y 3 factores (colesterol total, glucosa en ayunas y presión arterial). Los niveles más altos de NGS y masa muscular (ajustada al peso corporal) se asociaron con un mayor cumplimiento de métricas del índice de CVH, puntuadas en una escala continua de 0 (los 7 parámetros deficientes) a 7 (los 7 parámetros saludables). un aumento de 1 métrica se asoció con una reducción de las probabilidades de presentar FPA débil (33 y 36%) y una masa muscular media-baja (28 y 34%) en hombres y mujeres respectivamente (todos valores $p<0.001$). Este estudio indica que, en estudiantes Universitarios de Colombia, tanto la fuerza prensil como la masa muscular son asociados positivamente con el índice de Salud Cardiovascular. Para reducir la posible futura carga de debilidad muscular en la salud pública, los profesionales de la salud deben alentar al público a mejorar los factores de riesgo relacionados con el estadio de vida durante la etapa de adulto joven.

Declaration

I, María Alejandra Tordecilla Sanders, do hereby declare that the research presented in this dissertation is based on 3 articles (Chapter 2 to 4) that have been published or submitted for publication in international peer-reviewed journals. To meet the stylistic requirements of a thesis, the formats of the papers have been adjusted accordingly throughout. These edits did not substantially change the content of the published articles. The role that I fulfilled within each of the publications is presented below.

This thesis describes the rationale, design, methodologies used and the results obtained in a cross-sectional study (The FUPRECOL Adults Study). We hypothesized that thresholds of Body fat percentage (%), Fat mass index (FMI) and normalized grip strength (NGS) predict of Metabolic Syndrome (MetS) among Colombian University students. Likewise, we hypothesized that Higher scores on 7 metrics for ideal Cardiovascular health (CVH), indicating better CHV, are associated with higher levels of handgrip strength and muscle mass in Colombian college students.

PhD student involvement:

- Data collection
- Data analysis
- Writing of the present thesis

Acknowledgments
Gratitude is expressed to the Center of Studies for Physical Activity Measurement *(CEMA)* for the technical and scientific support to conduct this thesis Project.

We thank the *Institución Universitaria Antonio José Camacho, Universidad Santo Tomás, Universidad Manuela Beltrán, and Universidad de Boyacá* for its contribution in obtaining data.

Finally, we also thank the volunteers for participated in the research project and for the confidence in the research team.

Financial support
The FUPRECOL Adults Study were design and funded by Ramirez-Velez Robinson (IP). Additionally, FUPRECOL has been partially supported by the Universidad del Rosario (Code N° FIUR DN-BG001), Institución Universitaria Antonio José Camacho (Code N° 111-02.01.48/16). Universidad Santo Tomás (Code N°2013004), Universidad Manuela Beltrán (Code N° FT201204), and Universidad de Boyacá (Code N° RECT60).

The funder had no role in the study design, data collection, data analysis and interpretation, preparation of the manuscript, or decision to publish.

List of publications and Conference Papers

Publications

1. Garcia-Hermoso A; Correa-Bautista JE; Izquierdo M; Tordecilla-Sanders A; Prieto-Benavides D; Sandoval-Cuellar C; González-Ruíz K; Ramírez-Vélez R. Ideal Cardiovascular Health, Handgrip Strength, and Muscle Mass Among College Students: Results from the cross-sectional The FUPRECOL Adult Study. J Strength Cond Res. 2019;33(3):747-754. doi: 10.1519/JSC.0000000000003052.

   JCR Impact Factor: 2,325 (Q2)

2. García-Hermoso A; Tordecilla-Sanders A; Correa-Bautista JE; Peterson MD; Izquierdo M; Quino-Avila AC; Sandoval-Cuellar C; González-Ruíz K; Ramírez-Vélez R. Muscle Strength cut-offs for the Detection of Metabolic Syndrome in Non-Representative Sample Collegiate Students from Colombia. Journal of Sport and Health Science. 2018 (In press). https://doi.org/10.1016/j.jshs.2018.09.004.

   JCR Impact Factor: *2,591 (Q2)*

3. Ramírez-Vélez R; Correa-Bautista JE; Sanders-Tordecilla A; Ojeda-Pardo ML; Cobo-Mejía EA; Castellanos-Vega RDP; García-Hermoso A; González-Jiménez E; Schmidt-RioValle J; González-Ruíz K. (2017). Percentage of Body Fat and Fat Mass Index as a Screening Tool for Metabolic Syndrome Prediction in Colombian University Students. Nutrients 9(9). doi: 10.3390/nu9091009.

   JCR Impact Factor: *4,196 (Q1)*

Conference papers

29 May to 2 Jun/2018. ACSM´s 65st Annual Meeting World Congress in Exercise, Minneapolis, Minnesota USA

1. González-Ruíz K, García-Hermoso A, Tordecilla-Sanders A, Correa-Bautista JE, Quino-Ávila AC, Sandoval-Cuellar, Ojeda-Pardo ML, Quintero AP, Ramírez-Vélez R. Normalized Grip Strength Thresholds for the Detection of Metabolic Syndrome inColom bian Collegiate Students. *Med Sci Sports Exerc. 2018;49(Supl.5):S180.*

2. Ramírez-Vélez R, Correa-Bautista JE, García-Hermoso A, Tordecilla-Sanders A, Prieto-Benavides DH, Sandoval-Cuellar C, González-Ruíz K, Cobo-Mejía EA, Castellanos-Vega RP. Muscular Strength Attenuates Adverse Effects Of Overweight On Cardiometabolic Risk Factors But Not In Its Counterparts With Higher Fat Among Collegiate Students. *Med Sci Sports Exerc.2018;49(Supl.5):S243*

Background

Cardiovascular disease (CVD) have been listed as the leading cause of death worldwide [1]. According to the American Heart Association (AHA) during the 2013 to 2016, more than 40% of the Hispanic population older than 20 years had CVD [2]. Several studies have stablished that in young adults who present risk factors for CVD, have a higher risk of developing coronary heart disease in later years and with atherosclerotic changes that persist into adulthood [3-5]. In this sense, the Metabolic Syndrome (MetS), defined by International Diabetes Federation (IDF) as a cluster of the most dangerous heart attack risk factors: diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure [6], is referred to as grouping of atherosclerotic CVD risk factor, that probably has more than one cause [7, 8].

It is estimate that 20-25% of the world´s adult population have the MetS and the prevalence is often more in the urban population of developing countries [6, 7]. The people, who has MetS are twice as likely to die form and three times as likely to have a heart attack or stroke compared with people without the syndrome [6]. Many experts have establishing that genetics, unhealthy lifestyle (physical inactivity and inadequate diet) [9], ageing, proinflammatory state and hormonal changes may also have a causal effect on the MetS and CVD develop, highlighting the insulin resistance and central obesity as significant factors [6, 9, 10, 11].

The excess of adiposity tissue is a risk factor for develop MetS and CVD [8]. Many studies have examined the role of body composition in health assessment and monitoring [11], using different methods like Bioelectric Impedance Analysis (BIA) and Fat Mass Index (FMI) as a predictive method of MetS by having a high correlation with the components of the MetS [12]. Likewise, the predictive role of other fitness components such as muscle strength [16,17] and cardiorespiratory fitness [18] have been described as independent and inverse association in the appearance of CVD and MetS in adolescents and adults [14-16].

Against this background, the AHA has designed new strategies with a global impact to reduce the occurrence of CVD, based on the new concept of Cardiovascular Health (CVH). This concept includes the adoption of 7 metrics comprise 4 healthy behaviors (current smoking, body mass index [BMI], physical activity and healthy diet score) and 3 physiological health factors (total cholesterol, blood pressure, and fasting plasma glucose levels). [2]

Several studies have established that young adults who reach middle age with favorable levels of cardiovascular risk factors (cholesterol, blood pressure and no cigarette consumption), have lower incidence of developing CVD and greater longevity [13-15], which highlights the importance of identifying and treating CVD risk factors at an early age. Recently works such as those made by Agostinis-Sobrinho C et al. [19] and Ramírez-Velez [20] describe how having high levels of CVH is associated with high levels of muscle strength in children and adolescents.

Based on the above, this thesis is an evidence on the determination of CVH in Colombian University students and its relationship with the muscular strength and body composition components. Therefore, this work describes the associations of physical fitness components such as muscular strength and body composition in university students with cardiovascular health. For these reasons, three cross-sectional design studies have been carried out that describe the muscular strength and body fat percentage reference value for the detection of metabolic syndrome (study 1 and 2) and the association of muscle strength and muscle mass with parameters of the CVH in collegiate students from Colombia.

References

[1] World Health Organization. Cardiovascular diseases (CVDs) [Internet]. Cardiovascular diseases. Disponible en: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

[2] Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation* 2018;137(12):e67-492.

[3] Navar-Boggan AM, Peterson ED, D'Agostino RB, Neely B, Sniderman AD, Pencina MJ. Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease. *Circulation* 2015;131(5):451-8.

[4] Pletcher MJ, Vittinghoff E, Thanataveerat A, Bibbins-Domingo K, Moran AE. Young Adult Exposure to Cardiovascular Risk Factors and Risk of Events Later in Life: The Framingham Offspring Study. *PLoS One* 2016;11(5): e0154288. Doi:10.1371/journal.pone.0154288.

[5] Tran D-MT, Zimmerman LM. Cardiovascular risk factors in young adults: a literature review. *J Cardiovasc Nurs* 2015;30(4):298-310.

[6] International Diabetes Federation. The IDF consensus worldwide definition of the Metabolic Syndrome. 2006

[7] Saklayen MG. The Global Epidemic of the Metabolic Syndrome. *Curr Hypertens Rep* 2018;20(2):12. Doi:10.1007/s11906-018-0812-z.

[8] Abdullah M. Metabolic syndrome and cardiovascular risk. *J Family Community Med* 2010;17(2):73-78. Doi:10.4103/1319-1683.71987

[8] Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu C-Y, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation* 2007;116(1):39-48.

[9] Ramírez-Vélez R, Correa-Bautista JE, González-Ruíz K, Vivas A, Triana-Reina HR, Martínez-Torres J, et al. Body Adiposity Index Performance in Estimating Body Fat Percentage in Colombian College Students: Findings from the FUPRECOL—Adults Study. *Nutrients* 2017;9(1):40

[10] Bener A, Yousafzai MT, Darwish S, Al-Hamaq AOAA, Nasralla EA, Abdul-Ghani M. Obesity index that better predict metabolic syndrome: body mass index, waist circumference, waist hip ratio, or waist height ratio. *J Obes* 2013;2013:269038.

[11] De Schutter A, Lavie CJ, Gonzalez J, Milani RV. Body Composition in Coronary Heart Disease: How Does Body Mass Index Correlate With Body Fatness?. *Ochsner J* 2011;11(3):220-5.

[12] Liu P, Ma F, Lou H, Liu Y. The utility of fat mass index vs. body mass index and percentage of body fat in the screening of metabolic syndrome. *BMC Public Health* 2014;14:341

[13] Stamler J, Stamler R, Neaton JD, Wentworth D, Daviglus ML, Garside D, et al. Low Risk-Factor Profile and Long-term Cardiovascular and Noncardiovascular Mortality and Life Expectancy: Findings for 5 Large Cohorts of Young Adult and Middle-Aged Men and Women. *JAMA* 1999;282(21):2012-8.

[14] Casagrande SS, Menke A, Cowie CC. Cardiovascular Risk Factors of Adults Age 20-49 Years in the United States, 1971-2012: A series of Cross-Sectional Studies. *PloS One.*2016;11(8): e0161770. Doi: 10.1371/journal.pone.0161770.

[15] Bucholz EM, Gooding HC, de Ferranti SD. Awareness of Cardiovascular Risk Factors in U.S. Young Adults Aged 18-39 Years. Am J Prev Med. 2018;54(4):e67-77.

[16] García-Hermoso A, Cavero-Redondo I, Ramírez-Vélez R, Ruiz JR, Ortega FB, Lee D-C, et al. Muscular Strength as a Predictor of All-Cause Mortality in an Apparently Healthy Population: A Systematic Review and Meta-Analysis of Data from Approximately 2 Million Men and Women. Arch Phys Med Rehabil. octubre de 2018;99(10):2100-2113.e5.

[17] García-Hermoso A, Tordecilla-Sanders A, Correa-Bautista JE, Peterson MD, Izquierdo M, Quino-Ávila AC, et al. Muscle strength cut-offs for the detection of metabolic syndrome in a nonrepresentative sample of collegiate students from Colombia. J Sport Health Sci [Internet]. 11 de septiembre de 2018 [citado 10 de marzo de 2019]; Disponible en: http://www.sciencedirect.com/science/article/pii/S2095254618300772

[18] Mandsager K, Harb S, Cremer P, Phelan D, Nissen SE, Jaber W. Association of Cardiorespiratory Fitness With Long-term Mortality Among Adults Undergoing Exercise Treadmill Testing. JAMA Netw Open. 5 de octubre de 2018;1(6):e183605.

[19] Agostinis-Sobrinho C, García-Hermoso A, Ramírez-Vélez R, Moreira C, Lopes L, Oliveira-Santos J, et al. Longitudinal association between ideal cardiovascular health status and muscular fitness in adolescents: The LabMed Physical Activity Study. Nutr Metab Cardiovasc Dis. 1 de septiembre de 2018;28(9):892-9.

[20] Ramírez-Vélez R, Tordecilla-Sanders A, Correa-Bautista JE, Peterson MD, Garcia-Hermoso A. Handgrip Strength and Ideal Cardiovascular Health among Colombian Children and Adolescents. J Pediatr. 1 de diciembre de 2016;179:82-89.e1.

Chapter 1: Theoretical background

Cardiovascular Disease (CVD) and Cardiovascular Health (CVH)

Cardiovascular disease (CVD) refers to the group of heterogeneous disorders of the heart and blood vessels, such as hypertension, coronary heart disease, cerebrovascular disease, heart failure, rheumatic heart disease, arrhythmia, congenital heart disease and cardiomyopathies; these include numerous problems that are most often related to a process called atherosclerosis, which is a condition that develops when plaque builds up in the walls of the arteries [1,2] This set of pathologies are chronic asymptomatic diseases that gradually evolve throughout life and advanced usually disease causes symptoms or sudden death. [3]

The number of deaths from CVD has increased globally during the past decade by 12.5%, and is now considered the number one cause of death worldwide. In 2015, 50% of deaths were attributed to ischemic heart disease and 35% to cerebrovascular disease [4]; it is estimated by 2030 that almost 23.6 million people will die of CVD, mainly from heart disease and stroke [1].

CVDs are caused by multiple factors that are invariable (age, gender, genetic heritage) and others that can be modifiable, like smoking tobacco, high blood pressure (HBP), dyslipidaemia, type 2 diabetes mellitus (T2DM), obesity, physical inactivity (PI) and poor eating habits [5]. Clinical studies, such as those by Framingham [6], INTERHEART [7] and the Multiple Risk Factor Intervention Trial [8], have shown that modifiable risk factors multiply CVD risk and myocardial infarction progressively. In this sense, different organisations and associations have established the importance of reducing CVD mortality, and managing modifiable risk factors in its diagnosis, monitoring and treatment [3].

Many studies have established an association between modifiable risk factors and the development of CVD, trying to explain the effect of certain factors on the heart and blood vessels [6-8]. One of these factors is smoking tobacco, which has demonstrated a dose effect and unfavourable interactions with other risk factors (total serum cholesterol, very-low density lipoprotein (VLDL), low density lipoprotein (LDL), and triglyceride serum concentrations) in the generation of atherosclerosis in narrowed vessels, thereby increasing the risk of thrombosis [9]. This has been shown for the effect of smoking in the reduction of flow-mediated dilatation (FMD) in systemic arteries, considering that altered FMD is a marker for vascular (endothelial) dysfunction [10].

The review by Messner and Bernhard determined the proatherogenic effect of smoking cigarettes, which generates reactive oxygen species (ROS), thereby inducing oxidative stress (OX), and is implicated in the increased expression of intracellular adhesion, vascular cell adhesion molecule, platelets and macrophages, reduced nitric oxide (NO) bioavailability within the cells and the subsequent loss of function of smooth muscle cells (SMC) in the vessel media from the activated endothelium. Endothelial cells release inflammatory and proatherogenic cytokines that cause endothelial cell loss by apoptosis or necrosis. Likewise, macrophages are activated by the expression of adhesion molecule receptors, which take up oxidised lipids produced by oxidative modification for increased ROS production and induce the formation of foam cells within the aortic wall; the death of foam cells induces the release of these lipids and the formation of lipid-rich aortic plaques (Figure 1) [10].

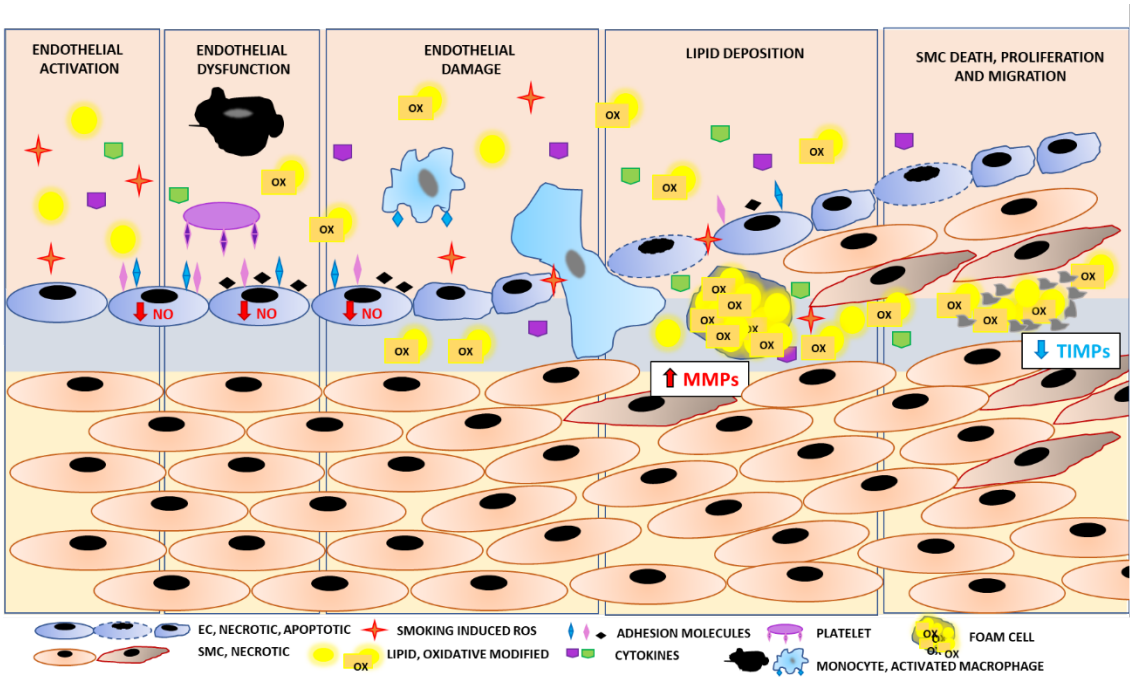

Figure 1. Schematic representation of smoking-induced signaling pathways in the vessel wall.

Figure modified from: *Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. Arterioscler Thromb Vasc Biol. 201;34(3):509-15. Doi: 10-1161/ATVBAHA.113.300156.*

In conclusion, smoking can cause direct physical damage to endothelial cells, resulting in remodelling and prothrombotic processes with the activation of systemic inflammatory signals that contribute to atherogenic vessel wall changes and subsequent cardiovascular disease [10].

HBP is commonly defined as persistent blood pressure (≥140/90 mm Hg) and is considered a modifiable CVD risk factor that affects more than 1 billion people worldwide; it is responsible for more than 10 million preventable deaths globally each year [11]. Numerous investigations have establishing that many interrelated factors contribute to raised blood pressure, like cardiac output, peripheral resistance, salt intake, obesity, insulin resistance, the renin-angiotensin system, the sympathetic nervous system and endothelial dysfunction [12].

The maintenance of normal blood pressure is dependent on the balance between cardiac output and peripheral vascular resistance, which is raised in patients with essential hypertension, specifically in the walls of the arterioles which contain SMC. The prolonged smooth muscle constriction increases the intracellular calcium concentration and induces structural changes like thickening of the arteriolar vessel walls mediated by angiotensin, which leads to an irreversible rise in peripheral resistance [12]. The most recent explanation for the pathophysiologic genesis of hypertension is based on the endothelial dysfunction associated with the overexpression of the vasoconstrictor peptide endothelin, the increased production of angiotensin II (Ang II) and aldosterone, and the reduced generation of vasodilators such as NO and prostacyclin, all increasing oxidative stress. Other factors associated with endothelial dysfunction are alterations in the expression of the kallikrein-kinin system that affects vascular tone, increased activity of the sympathetic nervous system, inappropriate renin

secretion with the resultant deficiencies of vasodilators such as prostacyclin, and renal salt handling (Figure 2) [13,14].

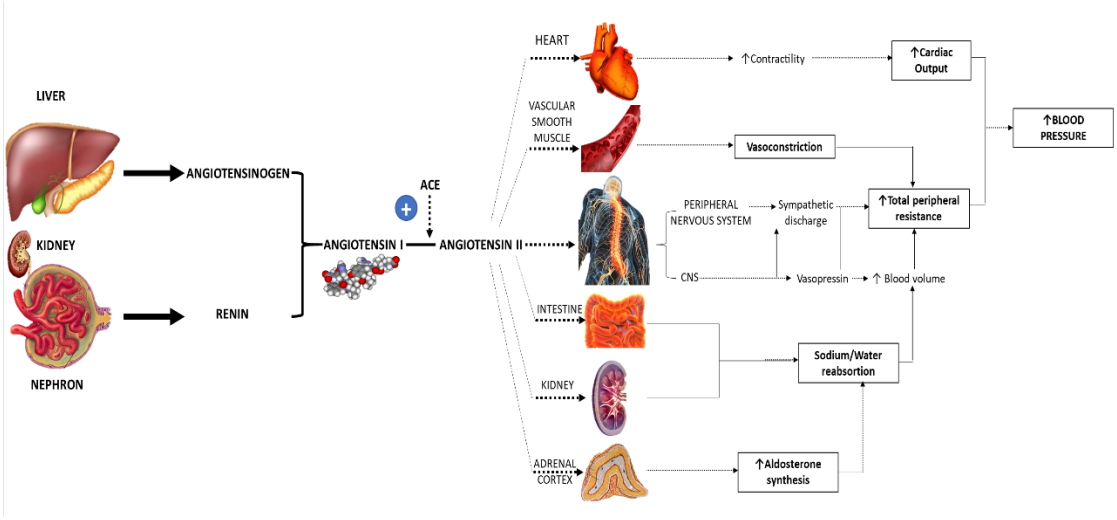

Figure 2. Pathophysiology factors for high blood pressure

Figure modified from: *DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG. Pharmacotherapy: a pathophysiologic approach. 9th ed. New York, USA: McGraw-Hill Education; 2014. 2586 pag.*

Other modifiable risk factors corresponding to the higher lipid burden associated with atherosclerosis and consequently CVD events [15] are the triad of high triglycerides, high low-density lipoprotein cholesterol (LDL-C) and low high-density lipoprotein cholesterol (HDL-C) levels, which are strongly associated with type 2 diabetes and metabolic syndrome (MetS) [16]. Disturbed lipid metabolism can also be the result of a genetic predisposition (hereditary dyslipidaemia), can be an integral part of other diseases (secondary dyslipidaemia) or can be the result of external factors (such as a diet rich in saturated fats and carbohydrates, reduced body activity, smoking, etc.) [3]. In this case, it is believed that dyslipidaemia, specifically high LDL-C levels (calculated using Friedewald´s formula ≥100 mg/dL), induces the formation of atherosclerotic lesions triggered by a local inflammation in the vascular wall [17,18]. Berneis and Krauss [19] suggested that the increased atherogenic potential of small dense LDL-C leads to the greater propensity for transport into the subendothelial space, increased binding to arterial proteoglycans, susceptibility to oxidative modification, increased levels of triglyceride rich lipoprotein remnants and reduced levels of HDL-C.

The process of the development of atherosclerotic lesions was described in six steps by Katakami [20]; this consists of the expression of adhesion molecules for OX as a result of vascular endothelial cell injury, which generates the release of cytokines and chemokines. These chemokines attract monocytes from the circulation to the injured area, which attach to the endothelium through interactions with adhesion molecules. Then, the monocytes penetrate into the subendothelial space and mature into macrophages that release cytokines. LDL-C is oxidised and infiltrates the subendothelial space (when the levels are high), before being retained in the intima. In this space, the macrophages take up and accumulate oxidised LDL-C, leading to foam cell formation and atherogenesis. Also, the oxidised lipids trigger the secretion of various growth factors by the endothelium. In this point, the vascular SMC of the media transform and migrate into the intima,

increasing the extracellular matrix, developing intimal thickening and sclerosis from the death of foam cells; this induces the release of these lipids and the formation of lipid-rich aortic plaques (atheroma) (Figure 3).

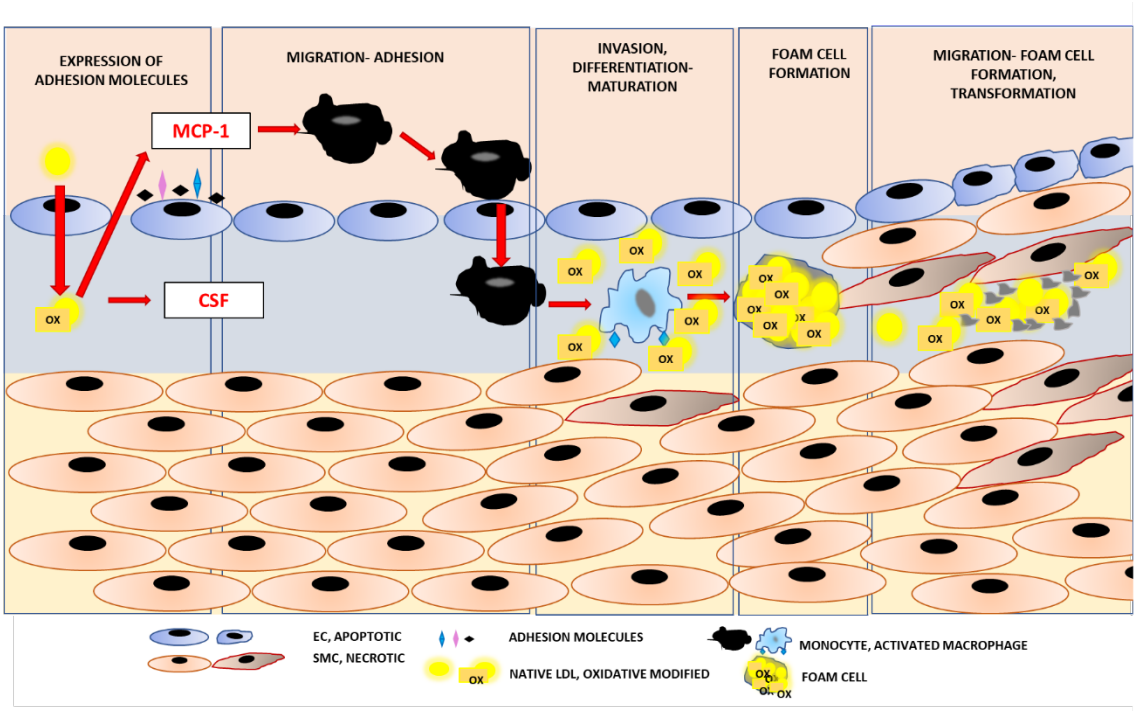

Figure 3. Process of the formation of atherosclerotic lesions

Figure modified from: *Katakami N. Mechanism of Development of Atherosclerosis and Cardiovascular Disease in Diabetes Mellitus. J Atheroscler Thromb. 2018; 25(1):27-39. Doi: 10.5551/jat.RV17014.*

As described previously, atherosclerotic lesions are formed for different and complex interactions of various factors that are accelerated in the presence of T2DM [20].

T2DM is defined by the International Diabetes Federation (IDF) as a chronic disease characterised by insulin resistance, because insulin cannot work properly, meaning that blood glucose levels keep rising and releasing more insulin, which triggers hyperglycaemia [21]. According to the World Health Organisation (WHO) and the American Diabetes Association (ADA) the diagnostic criteria of T2DM is glycated haemoglobin (HbA_{1c}) ≥6.5% and fasting plasma glucose 2-hour post-load plasma glucose ≥126 mg/dL [22]. Around 281,000 men and 317,000 women worldwide died with T2DM in 2011, so this is considered the sixth leading cause of disability worldwide [4, 22]. According to Rydén et al. [22], the increase in HbA_{1c} is associated with an increased CVD risk, and the relative risk of the occurrence of coronary artery disease (CAD) mortality is higher in patients with T2DM.

The pathophysiology of T2DM is initiated by β-cell dysfunction to regulate blood glucose concentrations, which results in fewer insulin effects on glucose disposal in the skeletal muscle and the suppression of endogenous glucose production in the liver. This change in insulin action is accompanied by the up-regulation of insulin secretion, which triggers increased compensation of the β-cell function and elevated concentrations of blood glucose. The increase in blood glucose concentration over time generates glucose toxicity, leading the production of ROS, which are known to enhance Nuclear Factor kB (NFkB) activity, which potentially induces β-cell apoptosis [23].

The association between T2DM and CVD can be explained by cumulative glucose exposure and non-enzymatic reactions with the amino groups of proteins; this is defined as protein glycation, which generates early-stage protein glycation products like haemoglobin A1c and glycoalbumin [20, 24, 25]. These products are submitted to complex reactions such as oxidation, dehydration and condensation creating advanced glycation end products (AGEs) that are involved in each step of atherosclerosis [20].

AGEs, through the interaction with cell surface receptors for AGEs (RAGE), evoke OX, and inflammatory, thrombotic and fibrotic reactions in vascular wall cells, which are involved in atherosclerotic CVD, as AGEs inhibit endothelial cell-derived NO production via suppression of endothelial NO synthase expression and increase the formation of peroxynitrite [24]. Likewise, AGEs have many functions, like eliciting the activation of NF-kB by promoting vascular inflammation, accelerating the migration of monocytes to the subendothelial space and its transformation to macrophages, leading macrophages to develop into foam cells, release cytokines, enhance vasoconstriction by increasing endothelin-1 levels and induce pathological neovascularisation in plaques (Figure 4) [24,25].

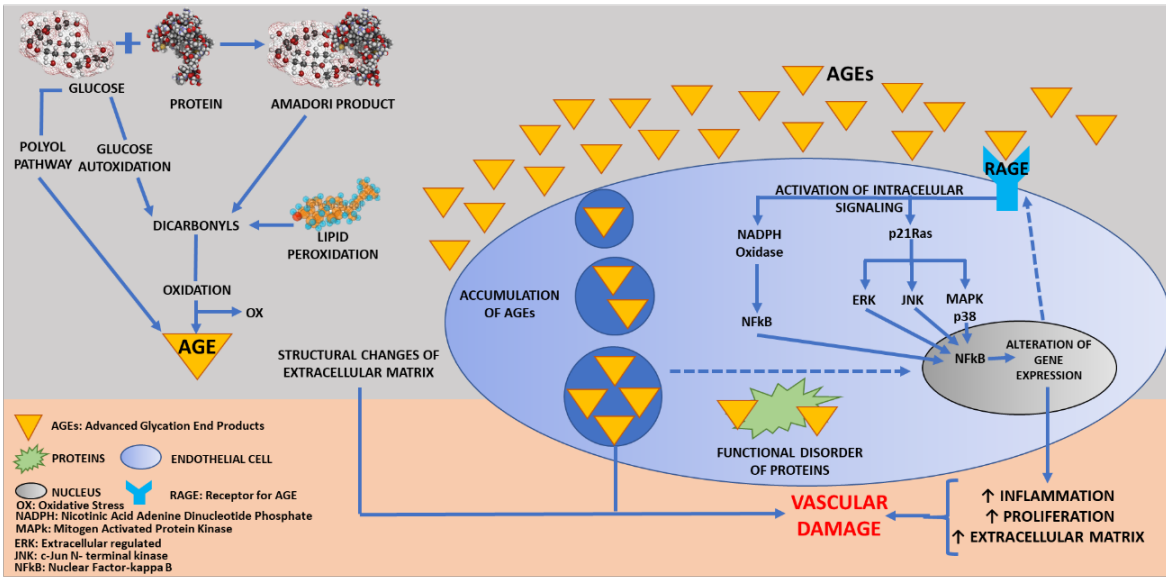

Figure 4. Role of AGEs in the vascular damage

Figure modified from: *Katakami N. Mechanism of Development of Atherosclerosis and Cardiovascular Disease in Diabetes Mellitus. J Atheroscler Thromb. 2018; 25(1):27-39. Doi: 10.5551/jat.RV17014.*

The fifth most important CVD risk factor for monitoring is obesity, which is defined as excessive fat accumulation, and is considered the most important preventable factor; it is associated with comorbidities (hypertension, T2DM, dyslipidaemia, obstructive sleep apnoea and certain cancers) and CVD mortality, which has been increasing in epidemic proportions in adults and children [3,26]. According to the WHO [27], almost 13% of the world´s adults aged 18 years and over were obese in 2016.

Obesity occurs when there is increased energy storage in the form of adipose tissue (AT), resulting from an imbalance between energy intake and energy expenditure over time [14]. This AT acts as an endocrine organ, which plays a substantial role in the chronic inflammatory cell infiltration processes,

cytokine production, and cell death that consequently induce insulin resistance, endothelial dysfunction, hypercoagulability and systemic inflammation, all of which are atherosclerosis promoters [26, 27]. This suggests that the adipokines released by AT interact and influence metabolic and immunologic cascades, such as vascular reactivity (leptin, TNF-α and adiponectin), inflammation (monocyte chemotactic protein 1 and IL-8) and coagulation (plasminogen activator inhibitor) [28,29].

The pathophysiology of obesity described by Rocha and Libby [28] involves the fatty acids and triglycerides that accumulate in the liver, muscle and adipose tissue. Excessive amounts of these lipids overload the oxidation and storage pathways in the hepatocytes or myocytes, leading to the accumulation of fatty acid intermediates (diacylglycerol and ceramide), which inhibit insulin function via the activation of serine kinase pathways, in particular the most potent proinflammatory cascades IkB kinase (IKK) and c-Jun *N*- terminal kinase (JNK) [28]. Likewise, free fatty acids might also bind toll-like receptors 4 or 13 (TLR4 or TLR13), which are present in adipocytes and macrophages, to activate the mitogen-activated protein kinase-activator protein 1 and nuclear factor kB (NF-kB) signalling pathways which are responsible for initiating an inflammatory gene response that generates insulin resistance (Figure 5) [28].

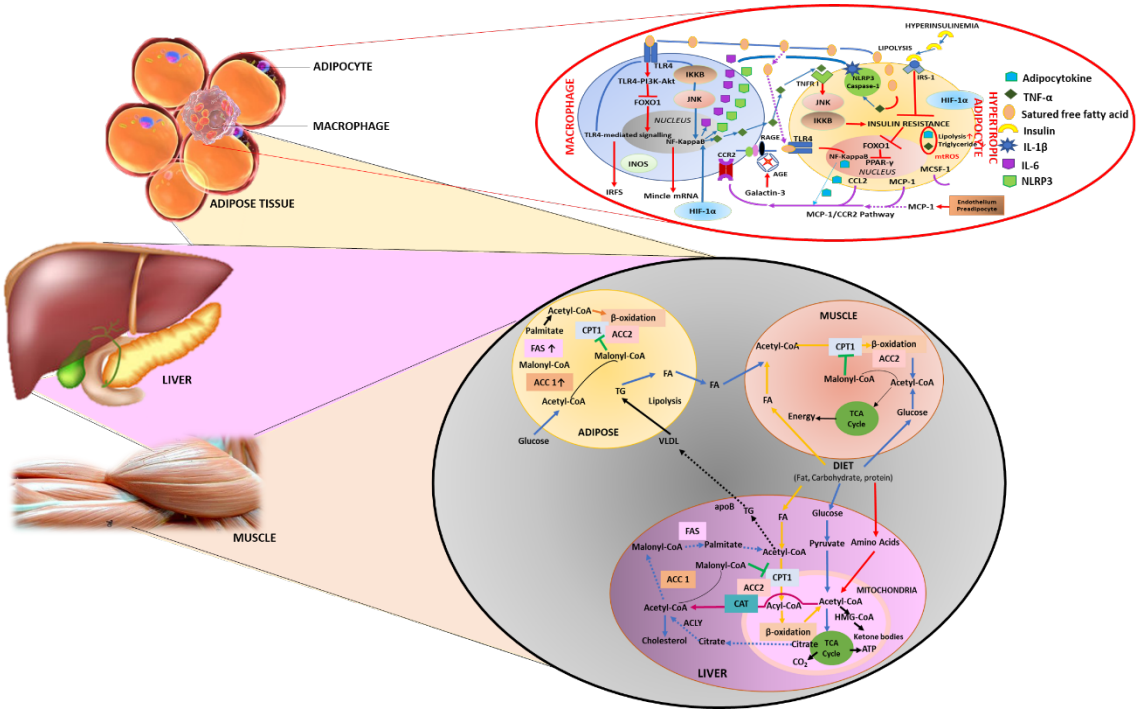

Figure 5. Effects of free fatty acids on various organs.

Figure modified from: *Rocha VZ, Libby P. Obesity, inflammation, and atherosclerosis. Nat Rev Cardiol. 2009;6(6):399-409. doi: 10.1038/nrcardio.2009.55.*

Another CVD risk factor corresponds to physical inactivity (PI), which is defined as <30 minutes of moderate-intensity physical activity on at least 5 days each week, or <20 minutes of vigorous-intensity physical activity on at least 3 days each week [4]. This factor causes 2 million deaths per year and 22% of all ischemic heart disease [3].

The review by Thijssen, Green and Hopman [30] suggests that PI leads to a rapid and dose-dependent inward remodelling of resistance arteries and to a thickening of the arterial walls, which is representative of endothelial dysfunction and favours atherosclerotic progression, for the up-

regulation of vasoconstrictor pathways, rather than the down-regulation of vasodilator pathways as an adaptation to PI.

Different studies have demonstrated that a 2 weeks reduction in daily activity level can generate changes in the expression of different genes involved in mitochondrial function, increasing insulin resistance in health subjects, in the same way as 9 days of strict bed rest [31,32]. Likewise, experimental evidence indicates that PI increases the production of vascular ROS, which contributes to endothelial dysfunction, the accumulation of visceral fat mass and impaired glucose and lipid metabolism [33,34]. This leads to the inflammation of ectopic fat, which is considered an important source of chronic systemic inflammation, promoting the development of insulin resistance, atherosclerosis, neurodegeneration and tumour growth and a rise in vascular lipid peroxidation as a global marker of OX, which implicates increased superoxide production for the activity of vascular NADPH oxidase [33,34].

The seventh most important CVD risk factor is poor eating habits (food rich in saturated fats and sucrose), related to traditional risk factors such as plasma lipids, blood pressure, or plasma glucose levels [4,35,36]. The review by Mozaffarian et al. [37] established that the increase in energy intake from trans fatty acids (TFA) (from hydrogenated oils) is associated with a 23% higher incidence of coronary heart disease.

The explanation for this has been established as the effect of TFA on fatty acid metabolism and the inflammatory responses of adipocytes, increased levels of soluble vascular-cell adhesion molecule 1 (sVCAM-1) and soluble intercellular adhesion molecule 1 (sICAM-1) identified on the nitric oxide-dependent endothelial dysfunction, the regulation of gene transcription, the activation of the kinase pathway (Jun N-terminal kinase; JNK), the generation of ROS, and the modulation of monocyte and macrophage activity by the increased production of inflammatory mediators; all of these increase the risk of atherosclerosis, plaque rupture, sudden death (from cardiac causes) and diabetes (Figure 6) [37].

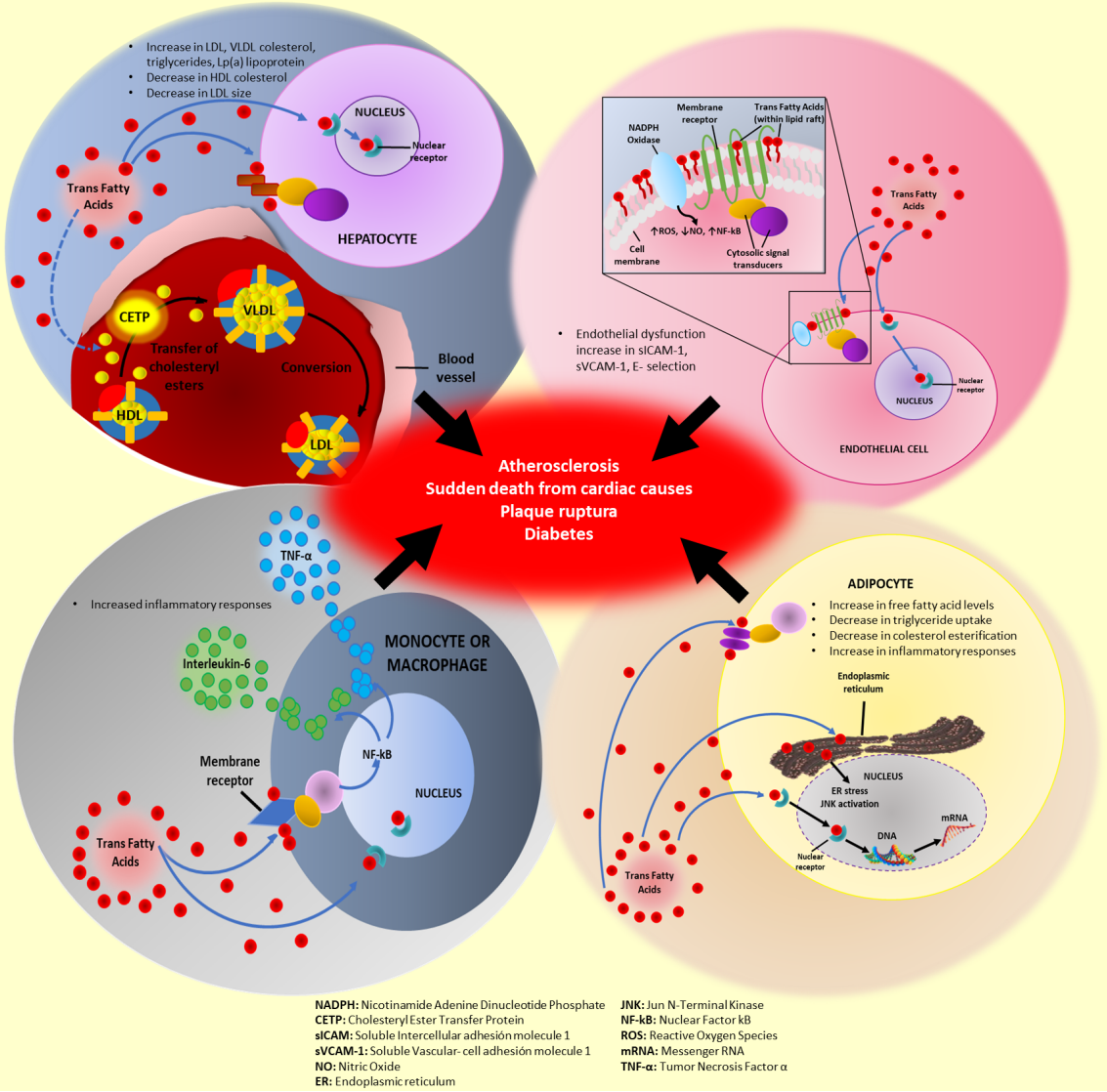

Figure 6: Potential physiological Effects of Trans Fatty Acids.

Figure modified from: *Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans Fatty Acids and Cardiovascular Disease. N Engl J Med. 2006;354(15):1601-13. Doi: 10.1056/NEJMra054035.*

With this background of the development of CVD risk factors, the American Heart Association (AHA) [38], establishing a new strategic impact goal, focused on reducing cardiac heart disease and stroke death rates and the prevalence of risk factors by 20%, as well as the improvement of cardiovascular health (CVH), which is determined as the factors needed to enhance general health. This uses the concept of *Ideal Cardiovascular Health*, which is defined as the adoption of seven metrics comprised of four healthy behaviours (abstinence from smoking, ideal body mass index [BMI], physical activity at goal and consumption of a healthy diet that promotes CVH) and three physiological health factors (untreated total cholesterol <200mg/dL, untreated blood pressure <120/<80 mm Hg, and absence of T2DM).

Several studies have established that young adults who reach middle age with some health behaviours and factors (cholesterol, blood pressure and no cigarette consumption), have a lower incidence of

developing CVD and greater longevity, which highlights the importance of identifying and treating CVD risk factors at an early age [39-41]. These results may be supported by the Ramirez-Vélez et al. [42] systematic review and meta-analysis which established that the incident CVD was lower (*HR=0.28, 95%CI: 0.23-0.33, p<0.001, I2=72.0%)* in individuals who had an ideal CVH profile (achieve 5-7 metrics) compared with individuals with a poor ideal CVH profile (meeting only 1-2 metrics).

Other studies, like those reported by Guo et al. [43] and Fernández-Alvira et al. [44], determined that adherence to ideal CVH may be a useful index in lowering the risk of atherosclerosis. In the same line, a prospective study of over 4000 participants has established that the number of ideal CVH metrics (accomplishment of 5-6 metrics) is inversely associated with the risk of developing subclinical atherosclerosis (represented by carotid plaques *(OR: 0.29, 95%CI: 0.18-0.49)*, increased carotid intima-media thickness *(OR: 0.44, 95%CI: 0.32-0.61)*, increased brachial-ankle pulse wave velocity *(OR: 0.20, 95%CI: 0.13-0.31)* and microalbuminuria (*OR:0.38, 95%CI: 0.17-0.87)*) and evaluated in the middle aged population [45]. The results can be explained by the fact that behaviours like moderate physical activity, smoking cessation and healthy diets had many beneficial effects on blood pressure, glucose homeostasis and dyslipidaemia, and consequently on the prevention of CVD events [35,46,47].

According to the systematic review by Calabrese et al. [35], changes in nutrient composition specifically replacing saturated fat, reducing salt intake, and implementing dietary patterns similar to the Mediterranean diet (MD) have been shown to be associated with a lower risk of CVD events. The results of randomised controlled trials (RCTs) and other systematic reviews have established that the replacement of saturated fatty acid with polyunsaturated fatty acid induces a 19% reduction of coronary heart disease *(RR= 0.81, 95CI: 0.70-0.95, p=0.008)* and CVD mortality of 27% *(HR: 0.73, 95CI:0.70-0.77)*, accompanied by a small reduction in serum total and LDL cholesterol. Likewise, this study concludes that the salt reduction generates a significant reduction of CVD incidence by 20% *(p<0.05)*.

With respect to the implementation of MD patterns, an umbrella review comprised 13 meta-analyses of observational studies and 16 meta-analyses of RCTs, with a total population of over 12,800,000 subjects; this established that a greater adherence to the MD determines a reduction of CVD risk *(p<0.01)*, for the beneficial effects of MD patterns on atherosclerotic risk factors like reduced weight, BMI and waist circumference, generating an anti-inflammatory effect in the vascular wall, inducing lower total cholesterol levels and blood pressure, and increasing HDL-cholesterol levels [48].

On the other hand, physical activity, especially exercise training (ET), has been considered a non-pharmacological therapy that improves arterial function, particularly the endothelium-dependent vasodilation for increased NO bioavailability and reduces OX in the microcirculation [49]. According to the Physical Activity Guidelines for Americans, adults should undertake at least 150 to 300 minutes a week of moderate-intensity or 75 to 150 minutes a week of vigorous-intensity aerobic physical activity, and include muscle-strengthening activities of moderate or greater intensity that involve all major muscle groups on 2 or more days a week for substantial health benefits [50].

From these recommendations, the protective effect of ET against the health risks factors associated with obesity is clearly established, independent of changes in body weight or composition [49]. In many systematic reviews and meta-analyses of intervention studies, there is a beneficial chronic effect (after 12 weeks) of ET on cardiovascular health due to an improved lipid profile, glycaemic control and cardiorespiratory fitness [51-54]. The evidence suggests that new modalities of ET like High-

Intensity Interval Training (HIIT) significantly improved maximal oxygen uptake *(VO_2 max, SMD: 1.20, 95%CI: 0.57 to 0.83, p<0.001),* systolic and diastolic blood pressure *(SBP, SMD: -0.35, 95%CI: -0.60 to -0.09, p<0.01; DBP, SMD:-0.38, 95%CI: -0.65 to -0.10, p<0.01)*, fasting glucose *(SMD:-0.35, 95%CI: -0.62to -0.09, p<0.01)*, waist circumference *(SMD: -0.20, 95%CI: -0.38 to -0.01, p<0.05)* and % body fat *(SMD: -0.40, 95% CI: -0.74 to -0.06, p<0.05)* in overweight/obese populations [53].

These beneficial effects of ET on CVH could be explained by the physiological pathway of the ET effect on vascular function, which implicates the increased shear stress in the vascular lumen, generating the activation of acetylcholine (Ach) signalling and phospholipase activity in endothelial cells, due to an increase in the intracellular release of Ca_2 and prostaglandin I2 (PGI2), and the relaxation of smooth muscle cells via the action of cyclic adenosine monophosphate (cAMP); also, it activates phosphoinositide 3-kinase (PI3K) for the vascular endothelial growth factor receptor 2 (VEGFR2) activity, which induces the phosphorylation of protein kinase B (AKT)-mediated nitric oxide synthase endothelium (eNOS) phosphorylation, leading to the increased production of NO (Figure 7) [55]

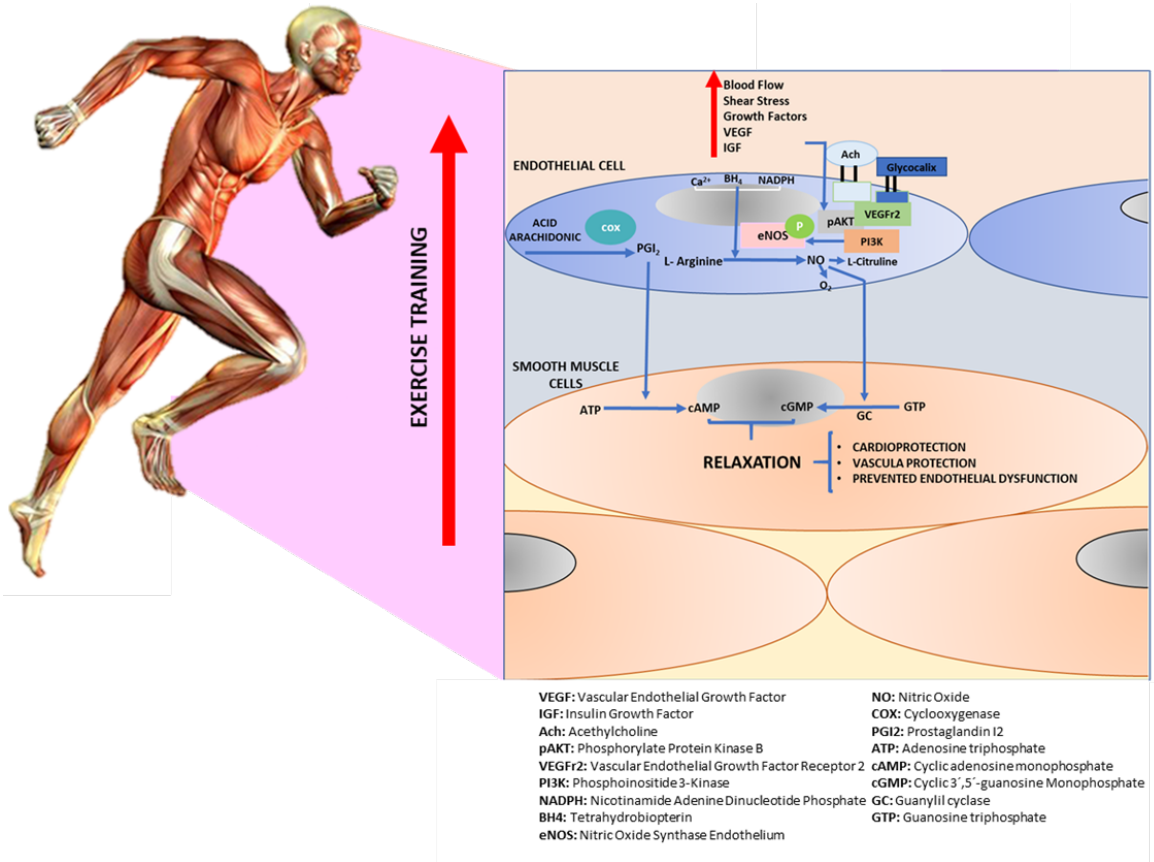

Figure 7. The effect of exercise training on the vascular endothelium.

Figure modified from: *Fernandes T, Gomes-Gatto CV, Pereira NP, Alayafi YR, das Neves VJ, Oliveira EM. NO signaling in the Cardiovascular System and Exercise. Adv Exp Med Biol.2017;1000:211-245. Doi: 10.1007/978-981-10-4304-8 13.*

Metabolic Syndrome (MetS) and Cardiovascular Disease (CVD)

In the last 3 decades, a new concept has emerged that refers to metabolic disorder (specifically insulin resistance) which increases the risk of developing CVD (three times) and diabetes (five times), known as metabolic syndrome (MetS) [56,59]. MetS is defined as a cluster of interconnected factors (central obesity, elevated blood pressure, impaired glucose tolerance and atherogenic dyslipidaemia) that increase the risk of coronary heart disease, stroke and type 2 diabetes [57,58].

According to the International Diabetes Federation (IDF) [60], the diagnosis of MetS occurs when a person has three or more of the following risk factors: a) Central obesity: defined as waist circumference for Latin American ethnic ≥90 cm for males and ≥80 cm for females, b) raised triglycerides ≥150 mg/dL (1.7 mmol/L), c) reduced HDL-cholesterol: <40 mg/dL (1.03 mmol/L) in males and <50 mg/dL (1.28 mmol/L) in females, d) raised blood pressure: systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg, and e) raised fasting plasma glucose: ≥100 mg/dL (5.6 mmol/L); it is estimated that over a billion people in the world had MetS, one-quarter to one-third of which are adults [57,61].

The relationship between MetS and the development of CVD, understanding CVD as the heart and blood vessel disorders that include hypertension, coronary heart disease, cerebrovascular and other pathologies associated with it, which are most often related to an atherosclerosis process [1,2], is the multiple risk factors referred to its appearance, like atherogenic dyslipidaemia, high blood pressure (HBP), obesity, diabetes and physical inactivity [5, 61].

The predominant underlying risk factors of MetS appear to be insulin resistance and obesity as a result of behavioural factors like physical inactivity and excess food fat intake, which generates excess energy and is stored as subcutaneous or visceral fat [57,59]. The visceral adipose tissue, specifically comprised of white adipose tissue, is metabolically active and secretes dozens of hormones, free fat acids (FFA), adipocytokines and inflammatory factors (TNF-α, interleukin 6, angiotensinogen, PAI-1, resistin) [61,62,63]. In this sense, the excess of fat accumulation generates a destructive effect on glucose metabolism, like insulin resistance and pancreatic beta cell dysfunction, defined lipotoxicity, characterised by impaired glucose oxidation, glycogen synthesis and decreased glucose transport-phosphorylation as result of the fat accumulation of intracellular toxic metabolites of FFA such as triacylglycerol (TAG) [57,64,65].

Increased plasma FFA concentrations can lead to insulin resistance in the muscle and liver, inhibiting insulin signalling, and stimulating an increase in hepatic gluconeogenesis and decreased glucose myocellular disposal; over time, this generates decompensation of pancreatic β-cells due to the increased need for insulin to overcome myocellular and hepatic insulin resistance [14,57]. The pathophysiological explanation of these effects has been determined in many investigations such as those by Yazici et al. [64] and Van Pelt et al. [65]; these groups established that FFA promotes insulin resistance by activating inflammatory pathways like toll-like receptor 4 (TRL-4) signalling from the protein kinase C and JNK-1 pathways in adipocytes, macrophages and skeletal cells. These signalling pathways stimulate levels of diacylglycerol, ceramide, LCFA-CoA (long-chain fatty acyl COAs), acylcarnitines and oxidative radicals, which reduce GLUT4 translocation to the muscle membrane (Figure 8).

As previously described, insulin resistance also leads to a change in the balance between the phosphoinositide 3-kinase (PI3K) and mitogen-activated protein (MAP) kinase pathways. As PI3k leads to a reduction in endothelial NO production, resulting in endothelial dysfunction and a reduction in GLUT 4 translocation, causing decreased skeletal muscle and fat glucose uptake, and continued

ET-1 (endothelin-1) production for the expression of vascular cell adhesion molecules and mitogen stimulus to vascular smooth muscle cells [66, 67]

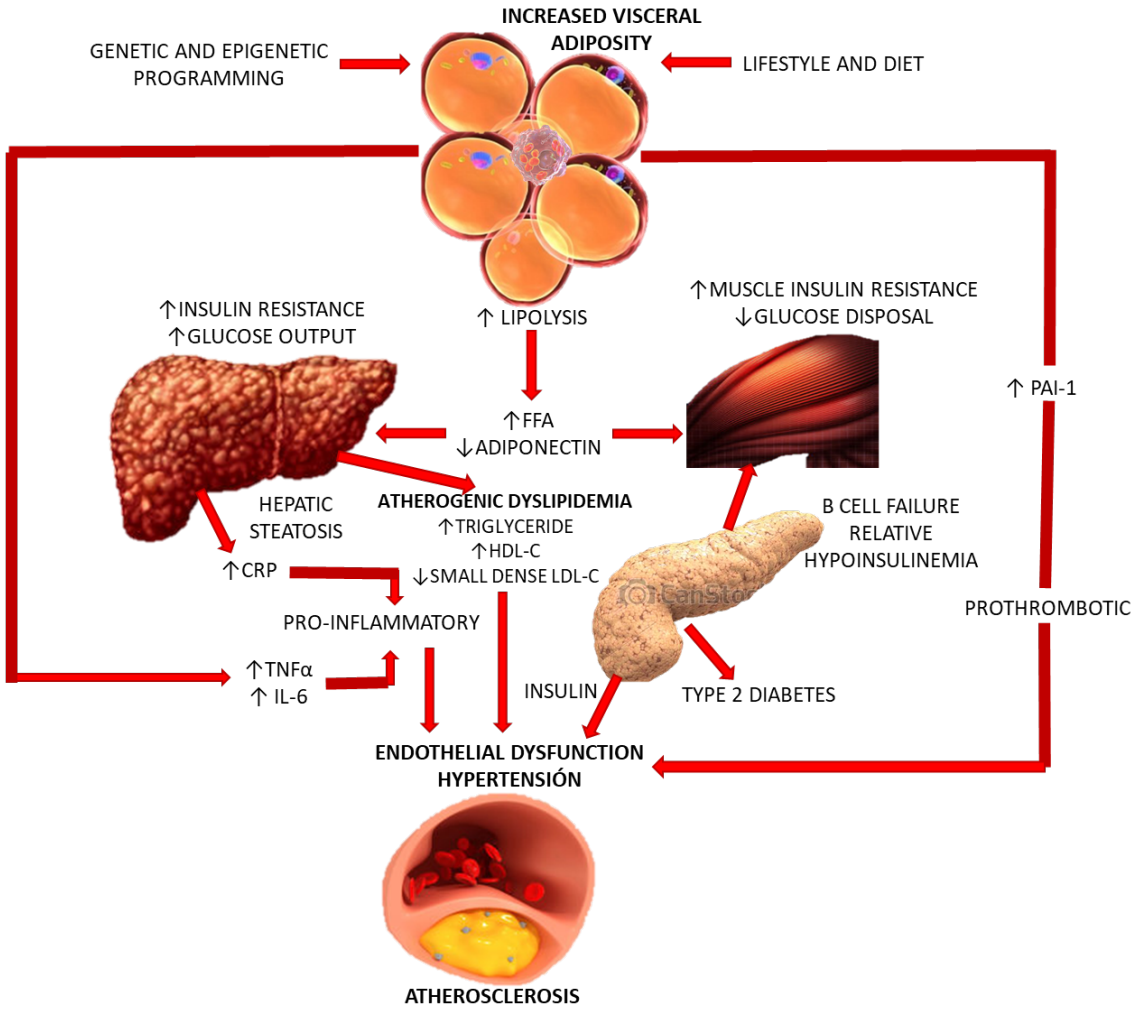

Figure 8. Clustering of MetS characters and the increased risk of T2DM and CVD.

Figure modified from: *Samson SL, Garber AJ. Metabolic Syndrome. Endocrinol Metab Clin North Am. 2014;43(1):1-23. Doi: 10.1016/j.ecl.2013.09.009.*

According to the above, MetS is a major health risk of CVD and T2DM; therefore, its management is recommended as a primary intervention, especially in a healthy lifestyle, including moderated calorie restriction (CR) to achieve a 5-10% loss of body weight in the first year, moderate increase in physical activity and change in dietary composition [60,68].

CR is a non-pharmacological dietary intervention known to reduce metabolic rate and oxidative damage, improve markers of age-related disease, and alter neuroendocrine activities from the weight loss effect [69]. The significant decrease in whole-body adiposity and central adiposity measures indicate a potential reduction of fat stores and delays the development of age-associated diseases (such as type 2 diabetes) for the improvement in β-cell responsiveness to glucose and insulin sensitivity, as well as reducing LDL-C and triacylglycerol levels, suggesting a beneficial effect of CR in chronic disease risk reduction [69,71].

Some interventional studies such as the CALERIE study [70,71] established that 2 years of 13% calorie restriction (reduction in calorie intake from 2467 kcal to 2170 kcal, based on energy requirements estimated from doubly-labelled water) significantly reduced multiple cardiometabolic risk factors in young, non-obese adults, such as LDL-cholesterol (-0.23 ± 0.04 mmol/L, *p<0.0001)*, triglycerides (-0.27±0.04, *p=0.0002),* systolic (-2.20 ± 0.82 mm Hg*, p<0.0011)* and diastolic (-3.40 ± 0.62 mm Hg*, p<0.0001)* blood pressure, and an improvement in C-reactive protein (-0.068±0.018 mmol/L, *p=0.012)*, insulin sensitivity index (0.099 ± 0.015, *p<0.0001),* and metabolic syndrome score (-2.669 ± 0.193, *p<0.0001)*, and body composition components like weight (-7.6±0.3 kg, *p<0.001*), waist circumference (-6.2±0.4 cm *p<0.001*), fat mass (-5.4±0.3 kg, *p<0.001*) and fat free mass (-2.0±0.2 kg, *p*<0.001).

Combined interventions of CR and exercise have been shown to generate healthy effects on cardiovascular risk factors when 3 to 6 months of treatment were reached, by reducing triacylglycerol (-22 ± 8 mg/dL, *p<0.01*), LDL-C (-16.0±5.1 mg/dL, *p<0.05*) and diastolic blood pressure (-4.0±2.1 mm Hg, *p<0.05*) levels and decreasing the estimated 10-year CVD risk by 38% (p<0.001) [72]. Also, modest weight loss (3.0% to 4.9%) achieved with exercise is known to enhance insulin activity, improve carotid vascular function and atherosclerosis risk factors, and reduce inflammatory biomarkers and lipids [73-75].

The beneficial effect of exercise and CR on health has been determined by the induced reduction in fatty acid availability and decrease in the activation of the inflammatory JNK and IKK-NFkB pathways, decrease in plasminogen activator inhibitor-1 (PAI-1), tumour necrosis factor receptor-II (TNFRII) and HOMA-IR, and increase plasma levels of adiponectin, resistin and sex hormone binging globulin (SHBG); these later generate increases in vascular function and regression of the burden of atherosclerosis [65,75]. These healthy effects are a result of the training in muscle fibre composition to increase the muscle insulin receptor expression, GLUT 4 expression and capacity for muscle mitochondria to oxidise fatty acids, which might reduce the accumulation of cytosolic lipid molecules and stimulate the mitochondrial biogenesis improving the insulin sensitivity. [74,76,77]

Muscular strength (MS), MetS and CVH

Physical fitness is catalogued as one of the strongest predictors of individual future health status, characterised by the ability to perform daily activities with vigour, through capacities that are associated with a low risk for the development of chronic diseases and premature death, especially cardiorespiratory fitness and muscular strength (MS) [78,79]. The MS is defined by Artero EG et al. [78] as the ability of a specific muscle or muscle group to generate force, for resist repeated contractions over time and/or to maintain the contraction of muscle fibres over a short period of time.

Based on the meta-analysis of Kodoma et al. [80], achieving better cardiorespiratory fitness is associated with a lower risk of all-cause mortality and CVD in healthy men and women. In the same way, it has been established that reduced muscular strength (MS) increases the risk of mortality for all-cause, cardiovascular death and CVD for its association with insulin resistance and β-cell dysfunction, independent of cardiorespiratory fitness and adiposity [81-83]. Against this, different researchers have suggesting the importance of increasing MS through exercise from childhood for which the MS is considered capable of predicting adult MetS outcomes independent of childhood cardiorespiratory fitness [82]. As mentioned previously, it has been recognised that handgrip strength (HGS) is a simple inexpensive measure of overall MS and useful prognostic indicator of mortality; when corrected by body mass, this is associated with a higher prevalence of MetS in adults,

independent of age and body size, and is considered to reflect muscle mass as an important health indicator [84,85].

The study by Peterson et al. study [86] established that low normalised handgrip strength (NHS) was associated with cardiometabolic disease and physical disabilities in middle-age to older men and women; for the loss of every 0.05 kg of MS, the odds of diabetes increases by 49%, of hyperglycaemia by 46%, of hypertriglyceridemia by 15%, of low HDL-cholesterol by 22%, of hypertension by 19%, and the odds of disability status in American adults by 36% (all $p<0.01$). Similar works as those presented by Ramírez-Vélez et al. [87], who determined the association between the new ratio of NHS and increased visceral fat level mass (MVF), and the prevalence of MetS and Ideal CVH, found that subjects with lower MVF ratio (Q1) is associated with worse CVH metrics (accomplishment 0-2 metrics) and a higher prevalence of MetS (32.2%, $p<0.0001$) in early Colombian adults.

In this sense, resistance training has been determined as part of the physical activity recommendations for the primary and secondary prevention of MetS and associated chronic diseases in adults, with a role of skeletal muscle in the metabolism of glucose and triglycerides [78,88].

Several studies have elucidated the health impact of the physical activity and exercise to increase mitochondrial oxidative capacity and skeletal muscle capillarisation, while generating anti-inflammatory effects, which contribute to improved insulin signalling, glucose uptake and metabolic flexibility [89]. The interventional study Tomeleri et al. [90] has shown that 12 weeks of resistance training reduce MetS components (glucose: -20.4%, waist circumference: -1.5% and systolic blood pressure: -6.2%, all $p<0.05$) and inflammatory biomarkers (CRP: -28.6%, TNF-α: -21.6%, all $p<0.05$), can generate different body composition and physical fitness parameters, like reduced body fat (-6.0%, $p<0.01$), increased skeletal muscle mass (+6.1 kg, $p<0.01$) and MS (+14.0, $p<0.001$) in older women.

In this sense, the mechanism responsible for the improvement in MetS parameters is speculated, identifying multiple factors, such as the IL-6 released by muscle contraction, which has anti-inflammatory properties and stimulates the production of anti-inflammatory cytokines such as IL-1ra and IL-10; together, these lead to the reduction of FFA, suppress TNF-α expression, down-regulate TLR 4 expression and reduce the activation of NF-kB signalling and cytokine production, consequently improving glucose homeostasis [90, 91]. IL-6 is a myokine produced by skeletal muscle during physical activity in the muscle which is activated through the gp130 receptor, AMP-kinase (in charge of stimulates fatty acid oxidation) and PI3-kinase to increase glucose uptake and fat oxidation, besides when the IL-6 is released peripherally with different effects in organs like the liver and adipose tissue, thus increasing hepatic glucose output and lipolysis during exercise, respectively (Figure 9) [92-94].

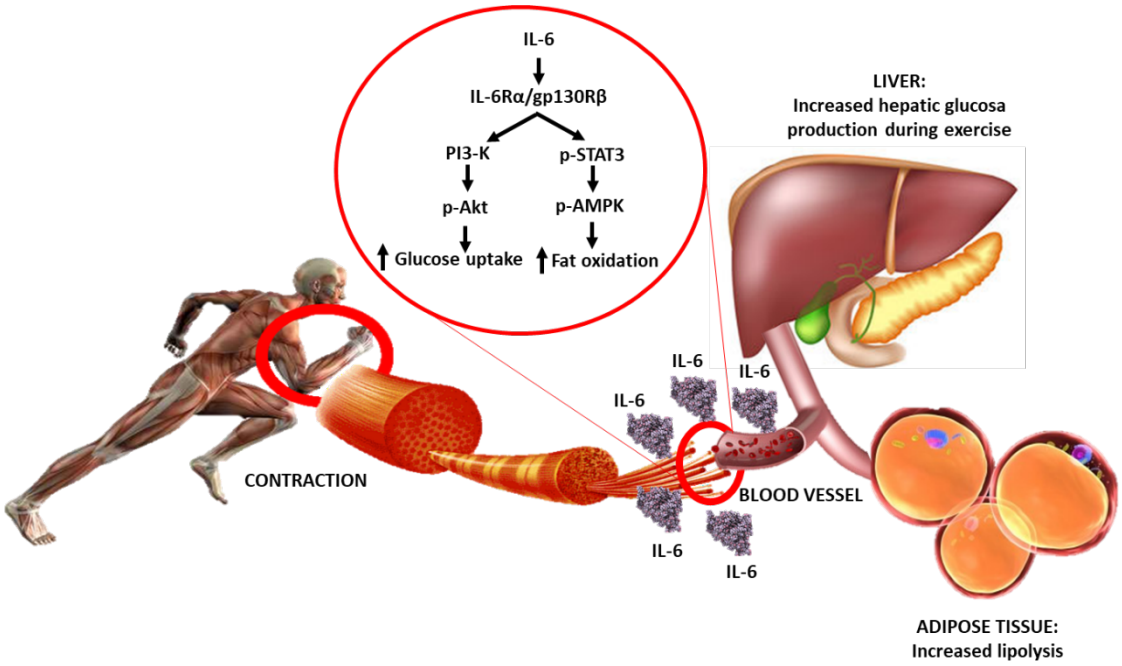

Figure 9. Biological role of contraction-induced IL-6.

Figure modified from: *Pedersen BK, Febbraio MA. Muscle as an endocrine organ: focus on muscle-derived interleukin-6. Physiol Rev. 2008;88(4):1379-406. Doi: 10.1152/physrev.90100.2007.*

References

[1] World Health Organization. Cardiovascular disease. [internet]. 2017 [cited 2019 Jun]. Available from: https://www.who.int/cardiovascular_diseases/about_cvd/en/

[2] American Heart Association. Cardiovascular disease. [internet]. 2017 [cited 2019 Jun]. Available from: https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease

[3] Francula-Zaninovic S, Nola IA. Management of Measurable Variable Cardiovascular Disease´ Risk Factors. *Curr Cardiol Rev.*2018;14(3):153-163. Doi:10.2174/1573403X14666180222102312

[4] Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, et al. Reducing the Global Burden of Cardiovascular Disease, Part 1: The Epidemiology and Risk Factors. *Circ Res.* 2017; 121:677-694. DOI: 10.1161/CIRCRESAHA.117.308903.

[5] Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The fifth joint Task Force of the European Society of Cardiology and other Societies on Cardiovascular Disease Prevention in Clinical practice (constituted by representatives of nine societies and by invited experts). *Eur Heart J.*2012; 33(13):1635-701. Doi: 10.1093/eurheartj/ehs092.

[6] Mahmood SS, Levy D, Vasan RS, Wang TJ. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet.* 2014;383(9921):999-1008. Doi:10.1016/S0140-6736(13)61752-3.

[7] Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (The INTERHEART study): case-control study. *Lancet*. 2004;364(9438):937-52

[8] Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. Multiple Risk Factor Intervention Trial Research Group. *Arc Intern Med.* 1992;152(1):56-64.

[9] Burns DM. Epidemiology of smoking-induced cardiovascular disease.*Prog Cardiovasc Dis.* 2003; 46(1):11-29.

[10] Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. *Arterioscler Thromb Vasc Biol.* 201;34(3):509-15. Doi: 10-1161/ATVBAHA.113.300156.

[11] Patel P, Ordunez P, DiPette D, Escobar MC, Hassell T, WyssF, et al. Improved Blood Pressure Control to Reduce Cardiovascular Disease Morbidity and Mortality: The Standardized Hypertension Treatment and Prevention Project. *Rev Panam Salud Publica.* 2017;41:1

[12] Beevers G, Lip GYH, O´Brien E. ABC of hypertension: The pathophysiology of hypertension. BMJ. 2001;322 (7291):912-916.

[13] Black HR, Elliot WJ. Hypertension: A companion to Braunwald´s Heart Disease. 1st ed. Philadelphia,PA,USA: Saunders Elsevier; 2007.615 pages.

[14] DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG. Pharmacotherapy: a pathophysiologic approach. 9th ed. New York, USA: McGraw-Hill Education; 2014. 2586 pages.

[15] European Association for Cardiovascular Prevention & Rehabilitation, Reiner Z, Catapano AL, De Backer G, Graham I, Taskinen MR, et al. ESC/EAS Guidelines for the management of dyslipidemias: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Eur Heart J.* 2011;32(14):1769-818. Doi: 10.1093/eurheartj/ehr158.

[16] Payne RA. Cardiovascular risk. *Br J Clin Pharmacol.* 2012;74(3):396-410. Doi: 10.1111/j.1365-2125. 2012.04219.x

[17] Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. *Circulation*. 2002;105(9):1135-43.

[18] Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. *Nature*. 2011;473(7347):317-25. Doi: 10.1038/nature10146.

[19] Berneis KK, Krauss RM. Metabolic origins and clinical significance of LDL heterogeneity. *J Lipid Res.* 2002;43(9):1363-79

[20] Katakami N. Mechanism of Development of Atherosclerosis and Cardiovascular Disease in Diabetes Mellitus. *J Atheroscler Thromb. 2018; 25(1):27-39. Doi: 10.5551/jat.RV17014.*

[21] International Diabetes Federation. Diabetes: Type 2 diabetes. [Internet]. 2019 [Cited 2019 Jun]. Available from: https://www.idf.org/aboutdiabetes/type-2-diabetes.html

[22] Task Force on diabetes, prediabetes, and cardiovascular diseases of the European Society of Cardiology (ESC), European Association for the Study of Diabetes (EASD), Rydén L, Grant PJ, Anker SD, et al. ESC guidelines on diabetes, prediabetes, and cardiovascular diseases developed in collaboration with the EASD- summary. *Diab Vasc Dis Res*. 2014;11(3):133-73. Doi: 10.1177/1479164114525548.

[23] Stumwall M, Goldstein BJ, Van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. *Lancet*. 2005;365:1333-46.

[24] Yamagishi S, Matsui T. Role of hyperglycemia-induced Advanced Glycation End Product (AGE) Accumulation in Atherosclerosis. *Ann Vas Dis*. 2018;11(3):253-258. Doi: 10.3400/avd.ra.18-00070.

[25] Fishman SL, Sonmez H, Basman C, Singh V, Poretsky L. The role of advanced glycation end-products in the development of coronary artery disease in patients with and without diabetes mellitus: a review. *Mol Med.* 2018;24(1):59. Doi: 10.1186/s10020-018-0060-3.

[26] Lavie CJ, Milani RV, Ventura HO. Obesity and Cardiovascular Disease: Risk factor, paradox, and impacto of weight loss. *J Am Coll Cardiol.* 2009;53(21):1925-32. Doi:10.1016/j-jacc.2008.12.068.

[27] World Health Organization. Obesity and overweight. [internet]. 2017 [cited 2019 Jun]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

[28] Rocha VZ, Libby P. Obesity, inflammation, and atherosclerosis. *Nat Rev Cardiol.* 2009;6(6):399-409. Doi: 10.1038/nrcardio.2009.55.

[29] Mandviwala T, Khalid U, Deswal A. Obesity and Cardiovascular Disease: a risk factor or a risk marker? *Curr Atheroscler Rep.* 2016:18:21. Doi:10.1007/s11883-016-0575-4

[30] Thijssen DH, Green D, Hopman MT. Blood vessel remodeling and physical inactivity in humans. *J Appl Physiol.*2011;111(6):1836-45. Doi: 10.1152/japplphysiol.00394.2011.}

[31] Lammers G, Poelkens F, Van Duijnhoven NTL, Pardoel EM, Hoenderop JG, Thijssen DHJ, Hopman MTE. Expression of genes involved in fatty acid transport and insulin signaling is altered by physical inactivity and exercise training in human skeletal muscle. *Am J Physiol Endocrinol Metab.* 2012;303:E1245-E1251. Doi: 10.1152/ajpendo.00356.2012.

[32] Alibergovic AC, Sonne MP, Hojbjerre L, Bork-Jensen J, Jacobsen S, Nilsson E, et al. Insulin resistance induced by physical inactivity is associated with multiple transcriptional changes in skeletal muscle in young men. *Am J Physiol Endocrinol Metab*. 2010;299:E752-E763.

[33] Laufs U, Wassmann S, Czech T, Munzel, Eisenhauer M, Bohm M, Nickening G. Physical Inactivity Increases Oxidative Stress, Endothelial Dysfunction, and Atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2005;25(4):809-14. Doi: 10.1161/01.ATV.0000158311.24443.af

[34] Pedersen BK. The diseasome of physical inactivity- and the role of myokines in muscle-fat cross talk. *J Physiol*. 2009;587:5559-68. Doi: 10.1113/jphysiol.2009.179515.

[35] Calabrese I, Riccardi G. Effectiveness of Changes in Diet Composition on Reducing the Incidence of Cardiovascular Disease. *Curr Cardiol Rep.* 2019;21(9):88. Doi: 10.1007/s11886-019-1176.

[36] Kromhout D, Menotti A, Alberti-Fidanza A, Puddu PE, Hollman P, Kafatos A, et al. Comparative ecologic relationships of saturated fat, sucrose, food groups, and a Mediterranean food pattern score to 50-year coronary heart disease mortality rates among 16 cohorts of the Seven Countries Study. *Eur J Clin Nutr.* 2018;72(8):1103-1110. Doi: 10.1038/s41430-018-0183-1.

[37] Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans Fatty Acids and Cardiovascular Disease. *N Engl J Med.* 2006;354(15):1601-13. Doi: 10.1056/NEJMra054035.

[38] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association´s strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121(4):586-613. Doi:10.1161/CIRCULATIONAHA.109.192703.

[39] Stamler J, Stamler R, Neaton JD, Wentworth D, Daviglus ML, Garside D, et al. Low Risk-Factor Profile and Long-term Cardiovascular and Noncardiovascular Mortality and Life Expectancy: Findings for 5 Large Cohorts of Young Adult and Middle-Aged Men and Women. *JAMA* 1999;282(21):2012-8.

[40] Casagrande SS, Menke A, Cowie CC. Cardiovascular Risk Factors of Adults Age 20-49 Years in the United States, 1971-2012: A series of Cross-Sectional Studies. *PloS One.*2016;11(8): e0161770. Doi: 10.1371/journal.pone.0161770.

[41] Bucholz EM, Gooding HC, de Ferranti SD. Awareness of Cardiovascular Risk Factors in U.S. Young Adults Aged 18-39 Years. Am J Prev Med. 2018;54(4):e67-77.

[42] Ramírez-Vélez R, Saavedra JM, Lobelo F, Celis-Morales CA, Pozo-Cruz BD, García-Hermoso A. Ideal Cardiovascular Health and Incident Cardiovascular Disease Among Adults: A Systematic Review and Meta-analysis. *Mayo Clin Proc.* 2018;93(11):1589-1599. Doi: 10.1016/j.mayocp.2018.05.035.

[43] Guo L, Cheng L, He W, Ju Y, Zhao X. Ideal Cardiovascular Health and Incidence of Carotid Plaque among Middle-Aged and Elderly Adults. *J Stroke Cerebrovasc Dis.* 2018;27(2):391-396. Doi: 10.1016/j.jstrokecerebrovasdis.2017.09.013.

[44] Fernández-Alvira JM, Fuster V, Pocock S, Sanz J, Fernández-Friera L, et al. Predicting subclinical Atherosclerosis in Low-Risk Individuals: Ideal Cardiovascular Health Score and Fuster-BEWAT Score. *J Am Coll Cardiol.* 2017;70(20):2463-2473. Doi: 10.1016/j.jacc.2017.09.032.

[45] Wang L, Niu JY, Zhao ZY, Li M, Xu M, Lu JL, et al. Ideal Cardiovascular Health is Inversely Associated with Subclinical Atherosclerosis: A prospective Analysis. *Biomed Environ Sci.* 2019;32(4):260-271. Doi: 10.3967/bes2019.036.

[46] Bull ER, Dombrowski SU, McCleary N, Johnston M. Are interventions for low-income groups effective in changing healthy eating, physical activity and smoking behaviors? A systematic review and meta-analysis. *BMJ Open.* 2014;4(11):e006046. Doi: 10.1136/bmjopen-2014-006046.

[47] Berra K, Rippe J, Manson JE. Making physical activity counseling a priority in clinical practice: the time for action is now. *JAMA*. 2015;314(24):2617-8. Doi: 10.1001/jama.2015.16244.

[48] Dinu M, Pagliai G, Casini A, Sofi F. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomized trials. *Eur J Clin Nutr.* 2018;72(1):30-43. Doi: 10.1038/ejcn.2017.58.

[49] Phillips SA, Mahmoud AM, Brown MD, Haus JM. Exercise interventions and peripheral arterial function: implications for cardiometabolic disease. *Prog Cardiovasc Dis.* 2015;57(5):521-34. Doi: 10.1016/j.pcad.2014.12.005.

[50] Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The Physical Activity Guidelines for Americans. *JAMA*. 2918;320(19):2020-2028. Doi: 10.1001/jama.2018.14854.

[51] Lin X, Zhang X, Guo J, Roberts CK, McKenzie S, Wu WC, et al. Effects of Exercise Training on Cardiorespiratory Fitness and Biomarkers of Cardiometabolic Health: A systematic Review and Meta- Analysis of Randomized Controlled Trials. *J Am Heart Assoc.* 2015;4(7). Pii: e002014. Doi: 10.1161/JAHA.115.002014.

[52] Pan B, Ge L, Xun YQ, Chen YJ, Gao CY, Han X, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. *Int J Behav Nutr Phys Act.*2018;15(1):72. Doi: 10.1186/s12966-018-0703-3.

[53] Batacan RB Jr, Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. *Br J Sports Med.* 2017;51(6):494-503. Doi: 10.1136/bjsports-2015-095841.

[54] Hollings M, Mavros Y, Fresston J, Fiatarone Singh M. The effect of progressive resistance training on aerobic fitness and strength in adults with coronary heart disease: A systematic review and meta-analysis of randomized controlled trials. *Eur J Prev Cardiol.* 2017;24(12):1242-1259. Doi: 10.1177/20474873177133229.

[55] Fernandes T, Gomes-Gatto CV, Pereira NP, Alayafi YR, das Neves VJ, Oliveira EM. NO signaling in the Cardiovascular System and Exercise. *Adv Exp Med Biol.*2017;1000:211-245. Doi: 10.1007/978-981-10-4304-8_13.

[56] American Heart Association. Metabolic Syndrome. [internet]. 2016 [cited 2019 Jun]. Available from: https://www.heart.org/en/health-topics/metabolic-syndrome/about-metabolic-syndrome

[57] Samson SL, Garber AJ. Metabolic Syndrome. *Endocrinol Metab Clin North Am.* 2014;43(1):1-23. Doi: 10.1016/j.ecl.2013.09.009.

[58] Alshehri AM. Metabolic Syndrome and cardiovascular risk. *J Family Community Med.* 2010;17(2):73-78.

[59] O´Neill S, O´Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev.* 2015;16(1):1-12. Doi: 10.1111/obr.12229.

[60] International Diabetes Federation. The IDF consensus worldwide definition of the Metabolic Syndrome. Brussels, Belgium. 2006.

[61] Saklayen MG. The Global Epidemic of the Metabolic Syndrome. *Curr Hypertens Rep.* 2018;20(2):12. Doi: 10.1007/s11906-018-0812-z.

[62] Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab.* 2004;89(6):2548-56. Doi: 10.1210/jc.2004-0395.

[63] Carobbio S, Pellegrinelli V, Vidal-Puig A. Adipose tissue function and expandability as determinants of lipotoxicity and the Metabolic Syndrome. *Adv Exp Med Biol.* 2017;960:161-196. Doi: 10.1007/978-3-319-48382-5_7

[64] Yazici D, Sezer H. Insuline resistance, Obesity and Lipotoxicity. *Adv Exp Med Biol.*2017;960:277-304. Doi: 10.1007/978-3-319-48382-5_12.

[65] Van Pelt DW, Newsom SA, Schenk S, Horowitz JF. Relatively low endogenous fatty acid mobilization and uptake helps preserve insulin sensitivity in obese women. *Int J Obes. (Lond).* 2015;39(1):149-55. Doi: 10.1038/ijo.2014.70.

[66] Bódis K, Roden M. Energy metabolism of white adipose tissue and insulin resistance in humans. *Eur J Clin Invest.* 2018;48:c13017. Doi: 10.1111/cc13017.

[67] Huang PL. A comprehensive definition for metabolic syndrome. *Dis Model Mech*. 2009; 2(5-6):231-237. Doi: 10.1242/dmm.001180.

[68] Pérez-Martínez P, Mikhailidis DP, Athyros VG, Bullo M Couture P, et al. Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation. *Nutr Rev*. 2017;75(5):307-326.

[69] Redman LM, Ravussin E. Caloric restriction in humans: impact on physiological, psychological, and behavioral outcomes. *Antioxid Redox Signal. 2011;14(2):275-87. Doi: 10.1089/ars.2010.3253.*

[70] Kraus WE, Bhapkar M, Huffman KM, Pieper CF, Krupa Das S, Redman LM. 2 years of calorie restriction and cardiometabolic risk (CALERIE): exploratory outcomes of a multicenter, phase 2, randomized controlled trial. *Lancet Diabetes Endocrinol.* 2019;7(9):673-683. Doi: 10.1016/S2213-8587(19)30151-2.

[71] Das SK, Roberts SB, Bhapkar MV, Villareal DT, Fontana L, et al. Body-composition changes in the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE)-2 study: a 2-y randomized controlled trial of calorie restriction in nonobese humans. *Am J Clin Nutr.*2017;105(4):913-927. Doi: 10.3945/ajcn.116.137232.

[72] Lefevre M, Redman LM, Heilbronn LK, Smith JV, Martin CK, Rood JC, et al. Caloric restriction alone and with exercise improves CVD risk in healthy non-obese individuals. *Atherosclerosis.*2009;203(1):206-13. Doi: 10.1016/j.atherosclerosis.2008.05.036.

[73] Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Blair SN, Church TS. Effects of clinically significant weight loss with exercise training on insulin resistance and cardiometabolic adaptations. *Obesity (Silver Spring).* 2016;24(4):812-9. Doi: 10.1002/oby.21404.

[74] Mora-Rodríguez R, Ortega JF, Ramirez-Jimenez M, Moreno-Cabañas A, Morales-Palomo F. Insulin sensitivity improvement with exercise training is mediated by body weight loss in subjects with metabolic syndrome. *Diabetes Metab.* 2019. Pii:S1262-3636(19)30086-2. Doi: 10.1016/j.diabet.2019.05.004.

[75] Ahmadi N, Eshaghian S, Huizenga R, Sosnin K, Ebrahimi R, Siegel R. Effects of intense exercise and moderate caloric restriction on cardiovascular risk factors and inflammation. *Am J Med.* 2011;124(10):978-82. Doi: 10.1016/j.amymed.2011.02.032.

[76] Stuart CA, South MA, Lee ML, McCurry MP, Howell ME, Ramsey MW, Stone MH. Insulin responsiveness in metabolic syndrome after eight weeks of cycle training. *Med Sci Sports Exerc.* 2013;45(11):2021-9. Doi: 10.1249/MSS.0b013e31829a6ce8.

[77] Pedersen LR, Olsen RH, Jurs A, Anholm C, Fenger M, Haugaard SB, Prescott E. A randomized trial comparing the effect of weight loss and exercise training on insulin sensitivity and glucose metabolism in coronary artery disease. *Metabolism.* 2015;64(10):1298-307. Doi: 10.1016/j.metabol.2015.07.007.

[78] Artero EG, Lee DC, Lavie CJ, España-Romero V, Sui X, Chruch TS, Blair SN. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev.* 2012;32(6):351-8. Doi: 10.1097/HCR.0013e3182642688.

[79] Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*. 2015;386(9990):266-73. Doi: 10.1016/S014-6736(14)62000-6.

[80] Kodoma S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*. 2009;301(19):2024-35. Doi: 10.1001/jama.2009.681.

[81] Fraser BJ, Huynh QL, Schmidt MD, Dwyer T, Venn AJ, Magnussen CG. Childhood Muscular Fitness Phenotypes and Adult Metabolic Syndrome. *Med Sci Sports Exerc.* 2016; 48(9):1715-22. Doi: 10.1249/MSS.0000000000000955.

[82] Ruiz JR, Castro-Piñero J, Artero EG, Ortega FB, Sjostrom M, Suni J, Castillo MJ. Predictive validity of health-related fitness in youth: a systematic review. *Br J Sports Med.* 2009;43(12):909-23. Doi: 10.1136/bjsm.2008.056499.

[83] Kim Y, Windaele K, Lee DC, Sharp SJ, Wareham N, Brage S. Independent and joint associations of grip strength and adiposity with all-cause and cardiovascular disease mortality in 403,199 adults: The UK Biobank study. *Am J Clin Nutr.* 2017;106(3):773-782. Doi: 10.3945/ajon.117.156851.

[84] Jurca R, Lamonte MJ, Barlow CE, Kampert JB, Church TS, Blair SN. Association of muscular strength with incidence of metabolic syndrome in men. *Med Sci Sports Exerc.* 2005;37(11):1849-55. Doi: 10.1249/01.mss.0000175865.17614.74

[85] Byeon JY, Lee MK, Yu MS, Kang MJ, Lee DH, Kim KC, et al. Lower Relative Handgrip Strength is Significantly Associated with a higher prevalence of the Metabolic Syndrome in Adults. *Metab Syndr Relat Disord.* 2019;17(5):280-288. Doi: 10.1089/met.2018.0111.

[86] Peterson MD, Duchowny K, Meng Q, Wang Y, Chen X, Zhao Y. Low Normalized Grip Strength is a Biomarker for Cardiometabolic Disease and Physical Disabilities Among U.S. and Chinese Adults. *J Gerontol A Biol Sci Med Sci.* 2017;72(11):1525-1531. Doi:10.1093/Gerona/glx031.

[87] Ramírez-Vélez R, Correa-Rodríguez M, Izquierdo M, Schmidt-RioValle J, González-Jiménez E. Muscle fitness to visceral fat ratio, metabolic syndrome and ideal cardiovascular health metrics. *Nutrients.* 2018;11(1). Pii.E24. Dooi: 10.3390/nu11010024.

[88] Stump CS, Henriksen EJ, Wei Y, Sowers JR. The metabolic syndrome: a role of skeletal muscle metabolism. *Ann Med*. 2006;38(6):389-402. Doi: 10.1080/07853890600888413.

[89] Wijndaele K, Duvigneaud N, Matton L, Duquet W, Thomis M, Beunen G, et al. Muscular strength, aerobic fitness, and metabolic syndrome risk in Flemish adults. *Med Sci Sports Exerc.* 2007:39(2):233-40. Doi: 10.1249/01.mss.0000247003.32589.ag

[90] Tomeleri CM, Souza MF, Burini RC, Cavaglieri CR, Ribeiro AS, Antunes M, et al. Resistance training reduces metabolic syndrome and inflammatory markers in older women: A randomized controlled trial. *J Diabetes.* 2018;10(4):328-337. Doi: 10.1111/1753-0407.12614.

[91] Rada I, Deldioque L, Francaux M, Zbinden-Foncea H. Toll like receptor expresión induced by exercise in obesity and metabolic syndrome: a systemic review. *Exerc Immunol Rev.* 2018;24:60-71.

[92] Pedersen BK. Exercise-induced myokines and their role in chronic diseases. *Brain Behav Immun.* 2011;25(5):811-6. Doi: 10.1016/j.bbi.2011.02.010.

[93] Pedersen BK, Fischer CP. Physiological roles of muscle-derived interleukin-6 in response to exercise. *Curr OPin Clin Nutr Metab Care.* 2007;10(3):265-71. Doi: 10.1097/MCO.0b013e3280ebb5b3.

[94] Pedersen BK, Febbraio MA. Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiol Rev.* 2008;88(4):1379-406. Doi: 10.1152/physrev.90100.2007.

Aims and layouts of the thesis

Study 1 (Chapter 2)

Tittle: Percentage of body fat and fat mass index as a screening tool for metabolic syndrome (MetS) prediction in Colombian university students

Research aim: To explore thresholds of body fat percentage (BF%) and fat mass index (FMI) for the prediction of MetS among Colombian University students.

Hypothesis: thresholds of BF% and FMI predict of MetS among Colombian University students.

Study 2 (Chapter 3)

Tittle: Muscle strength cut-off for the detection of metabolic syndrome in a nonrepresentative sample of collegiate students from Colombia

Research aim: to determine cut-offs of normalized grip strength (NGS) for the detection of MetS in a large nonrepresentative sample of a collegiate student population from Colombia.

Hypothesis: thresholds of normalized grip strength predict of MetS in a sample of a collegiate student population from Colombia

Study 3 (Chapter 4)

Tittle: Ideal cardiovascular health, handgrip strength, and muscle mass among college students: The FUPRECOL Adults Study.

Research aim: To determinate the relationship between handgrip strength, muscle mass, and ideal Cardiovascular Health among Colombian college students.

Hypothesis: Higher scores on 7 metrics for ideal CVH, indicating better CVH, are associated with higher levels of handgrip strength and muscle mass in Colombian college students.

Chapter 2: Percentage of body fat and Fat Mass Index as a screening tool for Metabolic Syndrome prediction in Colombian University Students.

1. Introduction

With increasing prevalence worldwide, obesity has become a significant public health issue [1]. Obesity has been linked to a number of cardiovascular disease (CVD) risk factors including metabolic syndrome (MetS) [2]. In Colombia, it is estimated that over 50% of adults are overweight or obese and the obesity epidemic has been associated with obesogenic factors, such as an intake of energy-dense diets, a sedentary lifestyle, and low levels of physical activity [3,4].

In this context, there is growing evidence that suggests that the way in which fat is distributed contributes different effects on the cardiometabolic risk associated with obesity [3-5]. In addition, measures of central body obesity, such as waist circumference and waist-hip ratio, have been suggested as being more strongly related to MetS risk compared to body mass index (BMI) [4,5]. Aside from age or sex, excess body fat is the strongest determinant of an individual´s risk of developing countries such as Colombia [2,11]. Recently, more research has examined the potential role of body composition measurements in health monitoring [12,13]. Bioelectrical impedance analysis (BIA) is the method that is most frequently used to assess body composition and calculate BF% in clinical practice, given its accuracy, simplicity, low cost, and excellent correlation with DCA, CT, or magnetic resonance image (MRI) [14,15].

Alternative simple and inexpensive approaches for assessing body adiposity have been suggested. A recen study highlighted the usefulness of the fat mass index (FMI), measured as kg/m2, as an indicator of the function of adipose tissue as a surrogate marker of cardiovascular risk in young adults [16]. However, BF% and FFM are known to change with height, weight, sex and age. Along this line, Valitallie et al. [16] proposed an FMI that considers an individual´s height. FMI, like BMI except that it uses a two-compartment model, merits reappraisal and appears to be of interest in the classification of overweight, obese and underweight patients [17]. Previous research has evaluated the applicability of FMI in the prediction of MetS and has highlighted its close relation with the components of MetS [17]. However, only a few studies have focused on the differential impact adiposity levels [18-24] in young adults when examining the link between fat and the risk of MetS.

Understanding the specific fat distribution associated with MetS risk is important to improve the interventions that are currently more focused on overall weight loss [5,6]. Our study proposes a gender-specific fat index based on BIA as a way of estimating the fat mass and body adiposity dysfunction associated with MetS. Apart from the study of Liu et al. [17], this is the first study in Colombian young adults (university students) to investigate the association between fat mass by BIA and MetS components. Based on the IDF definition of MetS [2], the aim of the study was to explore thresholds of BF% and FMI for the prediction of MetS among Colombian university students.

2. Methods

2.1 Study Design and Sample Population

During the 2014-2017 academic years, we reviewed a cross-sectional component of the FUPRECOL study that investigated the association between muscular strength and metabolic risk factors in Colombian collegiate students. The FUPRECOL study aimed to establish the general prevalence of cardiovascular risk factors, including anthropometric and metabolic markers, in the study population

and to examine the relationships between physical fitness levels, body compositions, and cardiometabolic risk factors. We recently published a complete description of the FUPRECOL study design, methods, and primary outcomes for our current cohort [2]. The sample consisted of adults (men: *n*=107; women: *n*=1128). We removed cases due to missing (*n*=37, 2.0%) or erroneous data entry (*n*=83, 4.5%) and those which had neither age nor a valid date of birth recorded (*n*= 28, 1.5%), limiting the analytical sample to 1687 volunteers, which was 63.4% women and a mean age of 20.6 years. The subjects, whose ages ranged from 18 to 35 years, were all of low to middle socioeconomic status (SISBEN levels: 1-4 on a scale of 1-6 as defined by "The System of Identifying Potential Beneficiaries of Social Programs", called SISBEN). The system takes into account sociodemographic characteristics including family composition, employment status, family income, and educational level; living conditions, including construction type and materials; and access to public utilities, which involves sewers, electricity, potable water, and garbage collection. They were enrolled in public or private universities in the capital district of Bogota, Boyacá, and Cali, Colombia.

Exclusion criteria included the following: medical or clinical diagnosis of a major systemic disease including malignant conditions such as cancer, type 1 or 2 diabetes, high blood pressure, hypothyroidism or hyperthyroidism; a history of drug or alcohol abuse; regular use of multivitamins; chronic inflammatory conditions including rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis; infectious conditions; and a BMI $\geq$ 35kg/m^2. Volunteers received no compensations for their participation.

2.2 Data collection

Subjects were screened for inclusion in the study via personal interviews. Interview questions collected consisted of health status, medical history, CVD risk factors, and lifestyle. After completing another general information questionnaire, participants were instructed to wear shorts and a T-shirt to the physical exam. They were also required to remove all worn jewelry and metal objects. Once the subjects were barefoot and in their underwear, their body weight (kg) was measured using an electric scale (Model Tanita® BC- 418®, Tokyo, Japan) with a range of 0-200 kg and with an accuracy of within 100 g. Height was measured with a portable stadiometer with a precision of 0.1 cm and a range of 0-2.5 m (Seca ® 274, Hamburg, Germany). BMI was calculated by using the formula proposed by the Quetelet where BMI= body mass (kg)/ height (m^2). Body mass index status was evaluated according to the World Health Organization (WHO) criteria [24]. The waist circumference (WC) (cm) was measured as the narrowest point between the lower costal border and the iliac crest. When this point was not evident, it was measured at the midpoint between the last rib and the iliac crest, using a metal tape measures (Lufkin W606PM®, Parsippany, NJ, USA), in accordance with the International Society for the Advancement of Kinanthropometry guidelines [25]. The evaluation process was carried out by a team of professionals (four physical therapy professors) with extensive experience in anthropometric measurement. Two percent of the sample was measured twice in order to ensure quality of measures. The technical error of measurement (TEM) values was less than 2% for all anthropometric variables.

BF% and FMI were determined for Bia by a tetrapolar whole body impedance (Tanita Model BC-418®, Tokyo, Japan). A detailed description of the BIA technique can be found in a previous study [2]. For the calculation of intra-inter observer TEM, at least 50 subjects needed to be measured (30 men, 20 women, aged 22.3 ± 2.1 years). The corresponding intra-observer technical error (% reliability) of the measurements was 95%. FMI was then calculated by dividing each subject´s fat mass (kg) by the square of his or her height (m), as previously described [17]. In a sub-sample (48 adults, 54% women, range mean age = 20 to 40 years old), we verified the validity of BIA for

predicting BF% in Colombian adults using DXA as a reference. Our analysis showed a strong agreement between the two methods, as reflected in the range of BF% (Lin´s concordance correlation coefficient= 0.943 (95%CI= 0.775 to 0.950, *p*= 0.041) and bias- 0.6 (SD 2.2; 95% CI= -5.0 to 3.7). In line with our findings, a previously study has shown a high correlation between fat mass determined by BIA and that obtained by a CT scan and DXA [14,15,26]. Thus, these results show that BIA and DXA are comparable methods for measuring body composition with lower/higher body fat percentage.

2.3 Metabolic Syndrome diagnosis

After the subjects had fasted for 10-12 h, blood samples were obtained from capillary sampling between 6:00 a.m. and 9:00 a.m. Participants were asked not to engage in prolonged exercise in the 24 h prior to testing. The biochemical profile included the following: (i) high-density lipoprotein cholesterol (HCL-C); (ii) triglycerides; (iii) low-density lipoprotein cholesterol (LDL-C); (iv) total cholesterol; (v) glucose fasting by enzymatic colorimetric methods (CardioChek PA®, Polymer Technology Systems, PTS, Indianapolis, IN, USA). The inter-assay reproducibility (coefficient of variation) was determined from 16 replicate analyses of 8 capillary blood pools over a period of 15 days. The percentages obtained were 2.6% for triglycerides; 2.0% for total cholesterol, 3.2% for HDL-C, 3.6% for LDL-C, and 1.5% for fasting glucose.

Blood pressure was taken on the left arm at the heart level with an automatic device Omron M6 Comfort (Omron® Healthcare Europe B.B., Hoofddorp, The Netherlands) while the participants were sitting still. The Blood pressure monitor cuff was placed two to three fingers-widths above the bend of the arm and a two-minute pause was allowed between the first and second measurements with a standard cuff for an arm circumference of 22-32 cm.

MetS was defined in accordance with the updated harmonized criteria of the IDF [2]. Participants were considered to have MetS if they showed three or more of the following: (1) abdominal obesity for individuals (WC ≥ 80 cm in women and ≥ 90cm in men) [27]; (2) hypertriglyceridemia (≥ 150 mg/dL); (3) low HDL-C (<50 mg/dL in women and <40 mg/dL in men): (4) high blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85mmHg); (5) high fasting glucose (≥100 mg/dL).

2.4 Lifestyle co-variables

A standardized questionnaire, FANTASTIC lifestyle, was used to collect comprehensive information about substance use via a personal interview with participants [28]. Alcohol consumption and smoking status were defined as subjects how had consumed any alcoholic beverage ≥ 1 times per week, and those who had smoked ≥ 10 cigarettes per week, for at least six months, as previously described by Ramírez-Vélez et al. [28]. Participants who exercised three or more times a week for > 30 min were categorized as physical active (PA), and those who exercised less than three times a week were considered insufficiently physically active. The accuracy of information about lifestyle co-variables obtained from the FANTASTIC questionnaire has been validated by different cross-sectional studies and described in detail elsewhere [28,29].

2.5 Ethics statement

Informed consent was obtained from each participant. The protocol was based on the Helsinki Declaration Accord (World Medical Association for Human Subjects). Moreover, ethical approval was obtained from the Universidad Manuela Beltrán (UMB N° 01-1802-2013).

2.6 Statistical Analysis

Participants´ characteristics obtained were given as mean values and standard deviation (SD). Histograms and Q-Q plots were used to verify the normality of the selected variables. Independent two-tailed *t*-test for continuous variables, and chi-square (x^2) test for categorical variables, were used to examine sex differences or MetS grouping. The relationships between BF%, FMI and MetS components were tested by means of partial correlation coefficients. This analysis was adjusted by age, sex, tobacco, and alcohol consumption, and PA levels. To predict MetS with BF% and FMI, we used area under the curve (AUC), ranging between 0 and 1 (a Worthless and a perfect test, respectively), which is a global indicator of diagnostic performance, and represents the ability of the test to correctly classify participants with high risk MetS by *p*-values <0.01 and an AUC >0.80. The positive likelihood ratio LR (+) and the negative likelihood ratio LR (-) were also determined. Cutoff points were chosen based on the highest Youden index, i.e., the point on the receiver operating characteristic curve (RPC) that is farthest from the line of equality [30]. Data analysis was performed using the Statistical Package for the Social Sciences for Windows SPSS, version 21.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

3. Results

3.1 Descriptive characteristics

Descriptive characteristics of the participants are presented in Table 1. The final sample had a mean age of 20.6 years (SD 3.0; range 19-24 years) with 63.4% of participants being women. Women were found to have significantly lower height, WC, blood pressure, triglycerides, and PA than men ($p<0.05$). The prevalence of MetS was higher in men than in women at 11.2% vs 5.3% ($p<0.001$).

Table 1. Characteristics among a sample of college students from Colombia (mean ± SD) or frequency (%)

Characteristic	Mean (n=617)	Women (n=1070)	*P Value*
Anthropometric			
Age (years)	20.6 ± 2.2	20.6 ± 2.0	0.843
Weight (kg)	58.9 ± 10.0	69.9 ± 12.4	<0.001
Height (cm)	159.8 ± 6.1	172.5 ± 6.7	<0.001
WC (cm)	78.4 ± 9.5	71.5 ± 7.9	<0.001
BMI (Kg/m2)	23.2 ± 3.7	23.2 ± 3.7	0.356
Body fat (%)	15.7 ± 6.7	27.0 ± 7.2	0.028
FMI (kg/m^2)	3.9 ± 2.3	6.5 ± 2.7	<0.001
Body mass index status n (%) *			
Underweight	34 (5.5)	71 (6.7)	<0.001
Normal weight	425 (68.8)	725 (57.8)	<0.001
Overweight	128 (20.8)	220 (20.5)	<0.001
Obese	31 (5.0)	54 (5.0)	<0.001
Blood pressure			
Systolic blood pressure (mmHg)	120.83 ± 13.0	111.28 ± 11.1	<0.001
Diastolic blood pressure (mmHg)	74.83 ± 11.4	71.78 ± 9.3	<0.001
Mean arteria pressure (mmHg)	97.83 ± 10.8	91.53 ± 8.9	<0.001
Metabolic biomarkers			
Total cholesterol (mg/dL)	132.26 ± 30.8	146.27 ± 33.3	0.212
Triglycerides (mg/dL)	93.01 ± 8.7	88.10 ± 43.7	0.011
LDL-C (mg/dL)	38.92 ± 10.4	43.98 ± 12.8	<0.001

HDL-C (mg/dL)	81.89 ± 26.5	87.85 ± 26.2	0.589
Glucose (mg/dL)	84.36 ± 12.2	85.99 ± 11.6	0.002
Metabolic Syndrome *n* (%) * Yes	73 (11.2)	59 (5.3)	0.001
Life-style n (%) *			
Tobacco (≥10 cigarettes per week)	183 (29.7)	213 (19.9)	0.289
Alcohol (≥ 1 times per week)	294 (47.6)	381 (35.6)	0.358
PA (Three or more times a week for > 30 min)	213 (34.5)	228 (21.3)	0.011

*Continuous variables are reported as mean values (standard deviations) and categorical variables are reported as numbers and percentages in brackets. Significant between-sex differences (t-tests or * chi-square test χ2). WC: waist circumference; BMI: body mass index; FMI: fat mass index; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; PA: physical activity.*

At least one MetS component was found in 818 participants (48.5%), two MetS components were present in 341 participants (20.2%), three MetS components were found in 126 participants (7.7%), and four or more components of MetS were present in 80 participants (4.7%) (Figure 1)

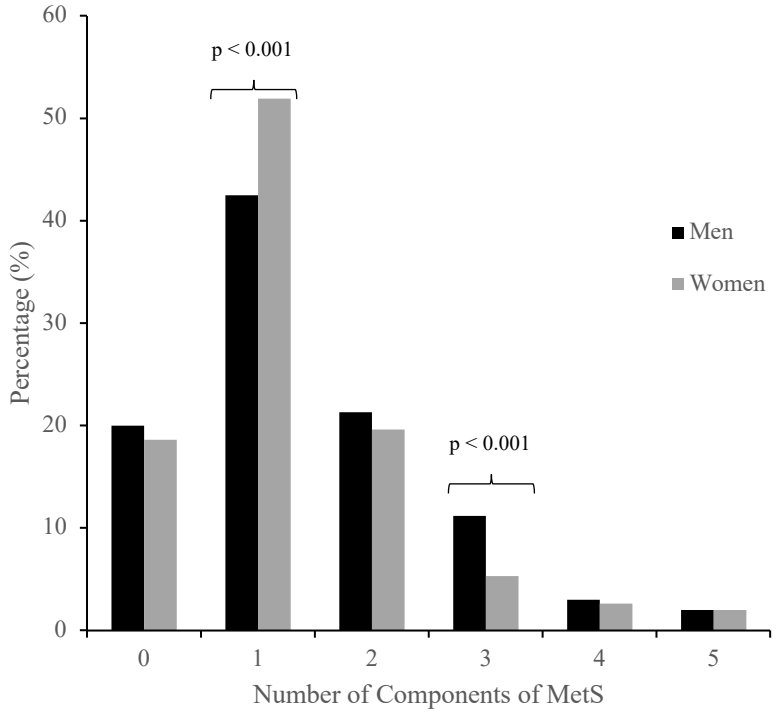

Figure 10. Distribution of the prevalence of metabolic syndrome components according to sex.

3.2 Clinical characteristics and distribution by MetS status

Independent of sex, participants with MetS had significantly higher weight, body mass index, WC, BF%, FMI, and total cholesterol and triglyceride levels (p<0.01) (Table 2). Furthermore, participants without MetS were more active (34.5% vs. 17.8% for men, and 21.1% vs. 6.8% for women, p<0.01)

Table 2. The descriptive characteristics of participants with and without MetS in both sexes.

Variable	Men (*n*= *617*)			Women (*n*= 1070)		
	MetS (*n* = 73)	**Non-MetS (*n* = 544)**	***P* Value**	**MetS (*n* = 59)**	**Non-MetS (*n* = 1011)**	***P* Value**
Anthropometric						
Age (years)	21.7 ±3.4	20.4±3.1	0.229	22.3±3.8	20.5±2.8	<0.001
Weight (kg)	80.8±15.8	67.3±10.7	<0.001	76.4±13.8	57.4±8.8	<0.001
Height (cm)	172.7±7.5	172.1± 6.6	0.129	161.1±5.6	158.9±5.8	0.902
WC (cm)	89.5±11.6	76.7±8.0	<0.001	84.9±8.8	70.5±7.1	0.145
BMI (Kg/m2)	27.0±4.7	22.6±3.1	<0.001	29.3±4.7	22.7±3.3	<0.001
Body fat (%)	23.5±7.5	14.5±5.7	0.005	37.3±6.0	26.2±6.8	0.234
FMI (kg/m^2)	6.6±3.1	3.4±1.8	<0.001	11.2±3.4	6.1±2.4	<0.001
Body mass index status n (%) *						
Underweight	4 (0.6)	30 (5.0)	<0.001	0.00 (0.0)	71 (6.6)	<0.001
Normal weight	16 (2.6)	408 (66.1)	<0.001	8 (0.8)	717 (67.0)	<0.001
Overweight	37 (6.0)	91 (14.8)	<0.001	23 (2.1)	197 (18.4)	<0.001
Obese	16 (2.6)	15 (2.4)	<0.001	28 (2.6)	26 (2.4)	<0.001
Blood pressure						
Systolic blood pressure (mmHg)	131.0±11.9	119.3±12.4	0.461	123.5±11.0	110.3±10.6	0.809
Diastolic blood pressure (mmHg)	83.6±10.8	73.5±10.1	0.160	81.6±13.8	71.1±8.6	0.237
Mean arteria pressure (mmHg)	107.3±10.2	96.4±10.1	0.176	102.6± 9.2	90.7±8.4	0.518
Metabolic biomarkers						
Total cholesterol (mg/dL)	146.0±39.6	130.2±29.1	<0.001	153.4±33.7	145.7±33.3	0.955
Triglycerides (mg/dL)	163.0±75.9	83.0±33.7	<0.001	139.8±66.6	84.9±40.2	<0.001
LDL-C (mg/dL)	31.3±5.9	40.1±10.6	<0.001	36.5±9.04	44.5±12.8	0.002
HDL-C (mg/dL)	86.0±30.8	81.3±26.1	0.077	89.6±28.4	87.6±26.2	0.571
Glucose (mg/dL)	92.4±13.4	83.1±11.6	0.063	92.6±14.4	85.5±11.4	0.142
Life-style n (%) *						
Tobacco (≥10 cigarettes per week)	19 (26.0)	155 (28.5)	0.769	5 (8.5)	198)19.6)	0.088
Alcohol (≥ 1 times per week)	36 (49.3)	294 (54.0)	0.563	22 (37.3)	394 (38.7)	0.378
PA (Three or more times a week for > 30 min)	13 (17.81)	188 (34.5)	0.005	4 (6.8)	213 (21.0)	0.018

*Continuous variables are reported as mean values ± standard deviations and categorical variables are reported as numbers(percentages). Significant between-sex differences (t-tests or*chi-square test χ2). WC: waist circumference; BMI: body mass index; FMI: fat mass index; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; PA: physical activity. The mean blood pressure was calculated using the following formula: (systolic blood pressure + (2×diastolic blood pressure))/3.*

Table 3 shows the partial correlation between BF%, FMI and MetS components. Overall, BF% and FMI were weakly positively correlated with all MetS parameters (all $p<0.05$), except HDL, which was negatively correlated.

Table 3. Results of the partial correlation analysis between body fat percentage (BF%), fat mass index (FMI), and MetS components.

Variable	Glucose (mg/dL)	HDL-C (mg/dL)	Triglycerides (mg/dL)	Total Cholesterol (mg/dL)	MAP (mmHg)	WC (cm)	FMI (kg/m^2)
Body fat (%)	0.188*	-0.239**	0.230**	0.279**	0.276**	0.827**	0.960**

FMI (kg/m2)	0.113**	-0.256**	0.230**	0.162*	0.272**	0.860**	1
WC (cm)	0.106*	-0.219	0.248	0.858**	0.271**	1	
Mean blood pressure (mmHg)	0.004	-0.022**	0.179**	0.259**	1		
Total cholesterol (mg/dL)	-0.008	-0.341**	0.241**	1			
Triglycerides (mg/dL)	0.125**	-0.170**	1				
HDL-C (mg/dL)	-0.158**	1					
Glucose (mg/dL)	1						

*Analysis adjusted by co-variables: age, sex, tobacco, alcohol, and physical activity. *p< 0.05; **p<0.01. WC: waist circumference; FMI: fat mass index; HDL-C: high-density lipoprotein cholesterol; MAP: mean arterial pressure. The mean blood pressure was calculated using the following formula (Systolic blood pressure + (2 x diastolic blood pressure))/3*

3.3 Optimal cut-off values in the screening of MetS

The ROC analysis showed that BF% and FMI parameters could be used to detect MetS according to the IDF criteria among Colombian university students (Table 4; Figure 2). Since multiple levels of risk were desired, the selection of the resulting cut-off values was based on multiple combinations of sensitivity. The focus was on higher sensitivity for the BF% and FMI thresholds in an effort to identify the majority of cases of MetS according to the IDF criteria. In men, the cut-off point values of 25.5% for BF% provided a sensitivity of 96.1%, an LR (+) value of 2.3, a specificity of 57.5%, and an LR (-) value of 0.06. For FMI, the cut-off value of 6.9 kg/m^2 provided a sensitivity of 95-8%, an LR (+) value of 2.2, a specificity of 56.2%, and an LR (-) value of 0.07. With respect to BF% among the women in the study population, the cut-off point value of 38.9% provided a sensitivity of 97.4%, an LR (+) value of 2.2, a specificity of 55.9%, and an LR (-) value of 0.04. The ROC curve for FMI was also obtained, using a cut-off value of 11.8 kg/m^2, a sensitivity of 97.6%, an LR (+) of 2.2, a specificity of 56.9%, and an LR (-) of 0.04.

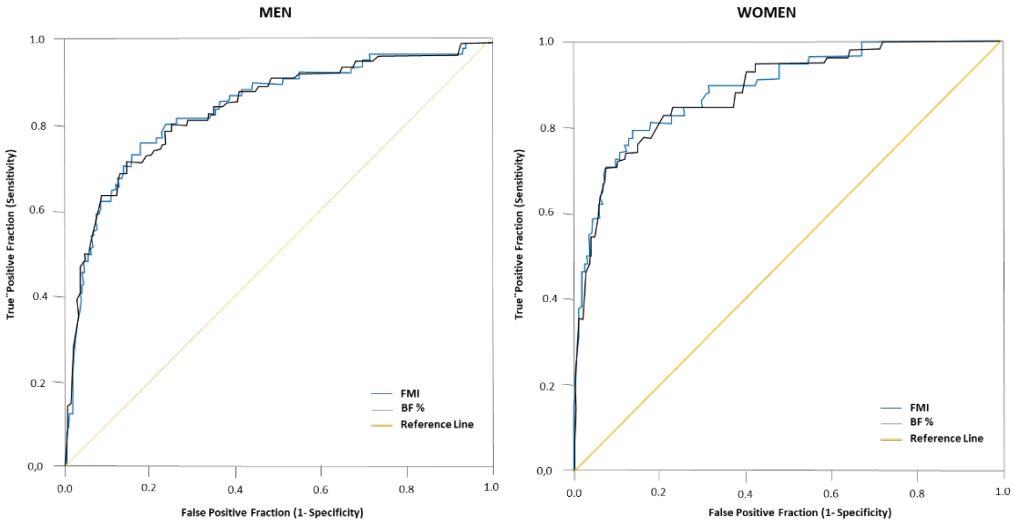

Figure 11. ROC curves for BF% and FMI for prediction of the prevalence of MetS according to IDF criteria in men and women.

Table 4. Parameters of the ROC curves analysis for the diagnostic performance of body fat percentage (BF%) and fat mass index (kg/m^2) in identifying high risk of MetS according to the IDF criteria in men and women.

Parameter			BF%	FMI
High risk of MetS	Men	AUC	0.835	0.838
		95% CI	0.779-0.891	0.779-0.892
		P Value	<0.001	<0.001
		Cut-off	25.5	6.9
		Sensitivity (%)	96.1	95.8
		Specificity (%)	57.5	56.2
		LR (+)	2.3	2.2
		LR (-)	0.06	0.07
	Women	AUC	0.887	0.889
		95% CI	0.842-0.932	0.844-0.933
		P Value	<0.001	<0.001
		Cut-off	38.9	11.9
		Sensitivity (%)	97.4	97.6
		Specificity (%)	55.9	56.9
		LR (+)	2.2	2.2
		LR (-)	0.04	0.04

AUC: area under the curve; CI: confidence interval; LR (+): positive likelihood ratio; LR (-): negative likelihood ratio.

4. Discussion

In our study, we found that the MetS prevalence was higher in men than in women (11,2% vs 5.3%, $p<0.001$), which is an intermediate value compared to those reported in local and international studies, ranging from 2 to 13% [31-33], that BF% and FMI were positively correlated to MetS components ($p<0.05$), and that the ROC analysis showed that both the BF% and FMI had a moderate discriminatory power in the identification of MetS among Colombian university students.

The higher prevalence of MetS, at 11.2%, seen in male subjects in our results does not coincide with Ruano-Nieto et al. [34] who found that the estimated prevalence of MetS was 8.4% for women and 6.1% for men in a population of Ecuadorian university students. The overall prevalence of MetS in our study, at 7.7%, was also greater than that in other Latin American countries such as Chile at 4.9% and Argentina at 4.1% [35,36]. Clearly, the prevalence of MetS could differ between studies depending on the MetS cluster used, the design method, and the target population. In this study, we used the IDF and AHA/NHLBI [2] joint statement, as it was an international attempt to harmonize the definition of MetS; central obesity is not an obligatory component of this definition and it is ethnic-specific.

Of those components, abdominal obesity, the most prevalent manifestation of MetS, is a marker of dysfunctional adipose tissue, and is of central importance in clinical diagnosis [37-41]. Our results show correlation between BF%, FMI and all of the cardiometabolic biomarkers analyzed, including mena arterial pressure, glucose, HDL-C, LDL.C, triglycerides, and total cholesterol ($p<0.05$ for all). These findings agree with Knowles et al. [19], who studied a population of young Peruvian adults and found significant correlations between the fat parameters and the above-mentioned cardiometabolic biomarkesr. Blood lipid disorders and adipose tissue are the key etiologic defects that define MetS; we found all fat indices used in this study were associated with BF%. In contrast,

other researchers such as Schuster et al. [40], who studied a sample of 444 young adults in Brazil, only found correlations between the BF% and glucose, HDL-C, and triglycerides. Our result may be different due to degree and the prevalence varying on the basis of ethnicity, genetic susceptibility, lifestyle, and geographic location. In addition, our results showed lower values of weight, height, and WC in women compared to men. This aligns with Liu et al. [17], who studied a population of 1698 adults in China. In all likelihood, these differences in body composition were due to sexual dimorphism [31] and diet [34]. Sex-specific hormones are another possible explanation. For example, the triglyceride levels and blood pressure were also lower among women in comparison to men. In this context, much of the risk of MetS associated with sex can be explained by the change is steroid hormone levels and the metabolism of carbohydrates and lipids [39]. An increase in total fat and the distribution of central fat, resulting from alterations in biomarker-disease, such as fasting glucose triglycerides, and ferritin, which are mediators of MetS, has been reported in female Hispanic/Latino adults [40]. This coincides with previous research, in which this finding was correlated with lower cardiovascular morbidity and dysfunctional adipose tissue in women [39,41]. Furthermore, the observation of ongoing changes in body composition by sex and its relationship with obesity has demonstrated that obesity affects individuals no matter their muscle mass, fat mass, height, and weight [41].

The AUC values for the MetS ROC analysis, at 0.835 for men and 0.838 for women, indicate that BF% has moderate diagnostic capabilities to identify subjects with MetS (≥3 risk factors). Interestingly, when considering MetS in our study, FMI showed the greatest AUC to predict MetS risk in women compared to men. Results show that metabolic disorders are present in young adult independent of age, smoking, physical activity, or fitness levels [42]. There is a growing interest in suggesting cut-off points for body fat levels for the early detection of CVD risk. Future longitudinal studies should be carried out to understand the role of different levels of adiposity on CVD risk stratification within a college population.

In contrast, another study carried out by Mohammadreza et al. [43] among Iranian adults found that BF% was not as effective a parameter for predicting MetS as other anthropometric indexes such as BMI, waisto-to height ratio, and waist-to hip ratio. In this same line, Mousa et al. [44] studied a population of young adults and found that the predictive power of BF% and BMI for screening Mets was limited. This discrepancy in result could be explained by the heterogeneity of the sample population. Consequently, the applicability and usefulness of BF% and FMI in the prediction of MetS require further studies of different populations and ethnic groups. These results are partially consistent with previous studies that showed BF% was positively correlated with single metabolic risk factors, such as BMI and triglycerides, and negatively correlated with HDL cholesterol in men, but not in women [45,46].

To our knowledge, few studies have explored the use of FMI as a proxy of obesity. In a study of 538 Mexican American college students (373 women and 165 men), the validity of FMI and BMI against BF% with BIA as the reference method was evaluated [47]. Correlations between FMI and BF% resulted in correlation coefficients of 0.976 in men (p<0.001) and 0.992 in women (p<0.001). However, similar to our findings, the correlations between FMI and PBF were higher (r= 0.960, p<0.01). In a study of 2986 healthy white men and 2649 white women, age 15 to 98 years in Switzerland, the men FMI in the overall age group was 4.9 (1.) kg/m^2 in men and 6.6 (2.4) kg/m^2 in women [48], compared to our results, of 6.6(3.1)kg/m^2 in men and 11.2 (3.4)kg/m2 in women without MetS. This difference can be explained by the fact that FMI cutoffs in the Swiss group were derived from BMI and not from MetS cutoff. On the other hand, in the Petz et al. study [47], the median FMI

in the overall age group was 7.3 (interquartile range 4.5) kg/m^2 in men and 9.0 (interquartile range 5.9) kg/m^2 in in women. Our FMI means fell within the lower range of the Mexican American normal FMI ranges in both men and women. This was expected, as South Americans have a lower percentage of body fat across all age groups when compared to non-Hispanic whites, Mexican American, and non-Hispanic blacks [49]. In a subsequent study from the same group (5635 apparently healthy adults from a mixed non-randomly selected Caucasian population) in Switzerland, obesity was defined as an FMI greater than 8.2 kg/m^2 in men and 11.8 kg/m^2 in women [50], which are similar than our FMI cutoffs of ≥6.9 kg/m^2 in men and ≥11.8 kg/m^2 in women in our study. These findings, although limited, show an interesting agreement with our results, which collectively contribute to the concepts of developing one set of recommended ranges that are not affected by height.

Our results have public health and clinical implications as college populations have been reported as a period in life when several behavioral and metabolic changes occur. These changes, in addition to the adoption of a Western lifestyle and diet, have led to a rise in the prevalence of overweight and obese Colombians, particularly among university students [32,51]. Further studies are needed to identify clinical characteristics in young adults that could be used in screening tests to predict MetS risk in adulthood.

Th principal limitation of this study was the use of cross-sectional data. Furthermore, it is also true that the hydration status of the participants could have modified the results of the BF% measured with BIA. Most BIA prediction equations assume that the fat mass and fat-free mass consist of 73% water [52]. These major limitations of the BIA method remain unresolved. Secondly, the assessment of other biomarkers, such as insulin, adiponectin, and c-reactive protein levels, which could have shown additional information about prognostic assessment, was not performed. These and other questions deserver further investigations by future well-designed longitudinal studies.

The main strength of our study is the fact that our study compared the predictive power of both BF% and FMI while providing cut-off values for the prediction of MetS in university students from Colombia. Considering the wide use of BIA methods and their extension to assess body composition, our study has important implications for evaluating CVD and metabolic risks in high-risk subjects, such as those with MetS.

5. Conclusions

In conclusion, BF% and FMI had a moderate discriminatory power in the identification of MetS in Colombian university students. Apart from the differences between our cut-off points and those reported in other research in geographically different populations, this study reports the first cutoff points for identification of MetS by BF% and FMI in Colombian young adults. We demonstrated that a BF% ≥ 38.9% in women and ≥25.5% in men, and an FMI ≥11.8 kg/m^2 in women and ≥ 6.9 kg/m^2 in men, are thresholds that could be used to predict Colombian young adults at high risk of MetS.

Financial support

The FUPRECOL Adults Study were design and funded by Ramirez-Velez Robinson (IP). Additionally, FUPRECOL has been partially supported by the Universidad del Rosario (Code N° FIUR DN-BG001), Institución Universitaria Antonio José Camacho (Code N° 111-02.01.48/16). Universidad Santo Tomás (Code N°2013004), Universidad Manuela Beltrán (Code N° FT201204), and Universidad de Boyacá (Code N° RECT60). The funder had no role in the study design, data collection, data analysis and interpretation, preparation of the manuscript, or decision to publish.

6. Reference

[1] Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, Ahmed M, Aksut B, Alam T, Alam K, et al. Global, regional and national burden of cardiovascular Diseases for 10 causes, 1990 to 2015. *J Am Coll Cardiol* 2017;70:1-25

[2] Alberti KG, Echel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC, et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-1645.

[3] Ramírez-Vélez R, Correa-Bautista JE, González-Ruíz K, Vivas A, Triana-Reina HR, Martínez-Torres J, Prieto-Benavides DH, Carrillo HA, Ramos-Sepúlveda JA, Villa-González E, et al. Body Adiposity Index performance in Estimating Body Fat Percentage in Colombian College Students: Findings from the FUPRECOL Adults Study. *Nutrients* 2017;9:40

[4] González-Muniesa P, Martínez-González MA, Hu EB, Després JP, Matsuzawa Y, Loos RJF, Moreno LA, Bray GA, Martínez JA. Obesity. *Nat Rev Dis Prim* 2017;3:17034

[5] Bener A, Yousafzai MT, Darwish S, Al-HAmaq AO, Nasralla EA, Abdul-Ghani M. Obesity index that better predict metabolic syndrome: Body mass index, waist circumference, waist hip ratio, or waist height ratio. *J Obes* 2013;2013:269038

[6] Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, Vasan RS, Murabito JM, Meigs JB, Cupples LA et al. Abdominal visceral and subcutaneous adipose tissue compartments: Association with metabolic risk factors in the Framingham Heart Study. *Circulation* 2007, 116:39-48.

[7] Wellens RI, Roche AF, Khamis HJ, Jackson AS, Pollock MI, Siervogel RM. Relationships between the body mass index and body composition. *Obes Res* 1996;4:35-44

[(] Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A critical review. *Nutr Today* 2015; 50:117-128.

[9] Baumgartner RN, Heymsfield SB, Roche AF. Human body composition and the epidemiology of chronic disease. *Obes Res.* 1995;3:73-95.

[10] Rollins KE, Javanmard-Emamghissi H, Awwad A, Macdonald IA, Fearon KCH. Lobo DN. Body composition measurement using computed tomography: Does the phase of the scan matter?. *Nutrition* 2017;41:37-44.

[11] González-Ruíz K, Correa-Bautista JE, Ramírez-Vélez R. Body adiposity and its relationship of metabolic syndrome components in Colombian adults. *Nutr Hosp* 2015;32:1468-1475.

[12] De Shutter A, Lavie CJ, González J, Milani RV. Body composition in coronary heart disease: How does body mass index correlate with body fatness?. *Ochsner J* 2011; 11:220-225.

[13] Mazzoccoli G. Body composition: where and when. *Eur J Radiol* 2016;85:1456-1460.

[14] Jeong DLS, Min H, Kim Y, Choi S, Kim Y. Measuring performance evaluation of body fat measuring instrument applying body measuring value method. *Korean J Health Promot Dis Prev* 2006;6:79-87.

[15] Xu L, Cheng X Wang J, Cao Q, Sato T, Wang M, Zhao X, Liang W. Comparisons of body-composition prediction accuracy: a study of 2 biolectric impedance consumer devices in healthy Chinese persons using DXA and MRI as criteria methods. *J Clin Densitom* 2011;14:458-464.

[16] VanItallie TB, Yang MU, Heymsfiedl SB, Funk RC, Boileau, RA. Height-normalized indices of the body´s fat-free mass and fat mass: Potentially useful indicators of nutritional status. *Am J Clin Nutr* 1990;52:953-959.

[17] Liu P, Ma F, Lou H, Liu Y. The utility of fat mass index vs. body mass index and percentage of body fat in the screening of metabolic syndrome. *BMC Public Health* 2014;14:341.

[18] Amato MC, Giordano C. Visceral adiposity index: An indicator of adipose tissue dysfunction. *Int J Endocrinol* 2014,2014:730827

[19] Knowles KM, Paiva LL, Sanchez SE, Revilla L, Lopez T, Yasuda MB, Yanez ND, Gelaye B, Williams MA. Waist circumference, body mass index, and other measures of adiposity in predicting cardiovascular disease risk factors among Peruvian adults. *Int J Hypertens* 2011;2011:1-10.

[20] Techatraisak K, Wongmeerit K, Dangrat C, Wongwananuruk T, Indhavivadhana S. Measures of body adiposity and visceral adiposity index as predictors of metabolic syndrome among Thai women with PCOS. *Gynecol Endocrinol* 2016;32:276-280.

[21] Li L, Wang C, Bao Y, Peng L, Gu H, Jia W. Optimal body fat percentage cut-offs for obesity in Chinese adults. *Clin Exp Pharmacol Physiol* 2012;39:393-398.

[22] Cho YG, Song HJ, Kim JM, Park KH, Paek YJ, Cho JJ, Caterson L, Kang JG. The estimation of cardiovascular risk factors by body mass index and body fat percentage in Korean male adults. *Metabolism* 2009; 58:765-771.

[23] Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, Galluzzo A, AlkaMeSy Study Group. Visceral Adiposity Index: A reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* 2010;33:920-922.

[24] World Health Organization. *Obesity: Preventing and Managing the Global Epidemic:* Report of a WHO Consultation on Obesity,3-5 June 1997, WHO/NUT/NCD/98.1 1997; WHO; Geneva, Switzerland, 1997.

[25] Marfell-Jones M, Olds T, Stewart A. *International Standards for Anthropometric Assessment;* ISAK: Potchefstroom, South Africa, 2006.

[26] Yamakaga H, Ito R, Tochya M, Muranaka K, Tanaka M, Matsuo Y, Odori S, Kono S, Shimatsu A, Satoh-Asahara N. The utility of dual bioelectrical impedance analysis in detecting intra-abdominal fat area in obese patients during weight reduction therapy in comparison with waist circumference and abdominal CT. *Endocr J* 2014;61:807-819.

[27] Cornier MA, Després JP, Davis N, Grossniklaus DA, Klein S, Lamarche B, Lopez-Jimenez F, Rao G, St-Onge MP, Towfighi A, et al. Assessing adiposity: A scientific statement from the American Heart Association. *Circulation* 2011;124:1996-2019.

[28] Ramírez-Vélez R, Agredo RA. The Fantastic instrument´s validity and reliability for measuring Colombian adult´s life-style. *Rev Salud Publica (Bogota)* 2012, 14:226-237.

[29] Silva AM, Brito Ida S, Amado JM. Translation, adaptation and validation of the Fantastic Lifestyle Assessment questionnaire with students in higher education. *Cienc Saude Colet*2014;19:1901-1909.

[30] Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. *Biom J* 2005;47:458-472.

[31] Ruíz AJ, Aschner PJ, Puerta MF, Cristancho RA. IDEA study (International Day for the Evaluation of Abdominal Obesity): Primary care study of the prevalence of abdominal obesity and associated risk factors in Colombia. *Biomedica* 2012;32:610-616.

[32] Fonseca-Camacho DF, Hernández-Fonseca JM, González-Ruíz K, Tordecilla-Sanders A, Ramírez-Velez R. A better self-perception of physical fitness is associated with lower prevalence of metabolic syndrome and its components among university students. *Nutr Hosp* 2014;31:1254-1263.

[33] Li CI, Kardia SI, Liu CS, Lin WY, Lin CH, Lee YD, Sung FC, Li TC, Lin CC. Metabolic syndrome is associated with change in subclinical arterial stiffness: A community-based Taichung community health study. *BMC Public Health* 2011;11-808.

[34] Rauno-Nieto CI, Melo-Pérez JD, Mogrovejo-Freire L, De Paula-Morales KR, Espinoza-Romero CV. Prevalence of metabolic síndrome and associated risk factors in Ecuadorian university students. *Nutr Hosp* 2015;31:1574-1581.

[35] Martínez MA, Leiva AM, Sotomayor C, Victoriano T, Von Chrismar AM, Pineda S. Factores de riesgo cardiovascular en estudiantes de la Universidad Austral de Chile. *Rev Med Chile* 2012;140:426-435.

[36] Gotthelf SJ. Prevalencia de síndrome metabólico según definición de la International Diabetes Federetion (IDF) en adolescentes escolarizados de la provincia de Salta, Argentina. *Rev Fed Argent Cardiol* 2013;42:119-126.

[37] Wang X, Strizich G, Hua S, Sotres-Alvarez D, Buelna C, Gallo LC, Gellman MD, Mossavar-Rahmani Y, O´Brien MJ, Stoutenberg M, et al. Objetively measured sedentary time and cardiovascular risk factor control in US Hispanics/ Latinos with diabetes mellitus: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *J Am Heart Assoc* 2017;6:e004324.

[38] Macias N, Quezada AD, Flores M, Valencia ME, Denova-Gutiérrez E, Quintero-Trenado M. Gallegos-Carrillo K, Barquera S, Salmerón J. Accuracy of body fat percent and adiposity indicators cut off values to detect metabolic risk factors in a sample of Mexican adults. *BMC Public Health* 2014;14:341.

[39] Murphy MO, Loria AS. Sex-specific effects of stress on metabolic and cardiovascular disease: Are women at higher risk?. *Am J Phisiol Regul Integr Comp Physiol* 2017;313:R1-R9.

[40] Schuster J, Vogel P, Eckhardt C, Morelo SD. Applicability of the visceral adiposity index (VAI) in predicting components of metabolic syndrome in young adults. *Nutr Hosp* 2014;30:806-812.

[41] Chumlea WC, Sun SS. Bioelectrical Impedance Analysis. In Human Body Composition; Heymsfield SB, Lohman TC, Wang ZM, Going SB. Ed. Human Kinetics: Champaign, IL, USA, 2005; pp. 79-88.

[42] Zhu S, Wang Z, Shen W, Heymsfield SB, Heshka S. Percentage body fat ranges associated with metabolic syndrome risk: Results based on the third National Health and Nutrition Examination Survey (1988-1994). *Am J Clin Nutr* 2003;78:228-235.

[43] Mohammadreza B, Farzad H, Davoud K, Fereidoun AF. Prognostic significance of the complex "Visceral Adiposity Index" vs. simple anthropometric measures: Tehran lipid and glucose study. *Cardiovasc Diabetol* 2012;11:20.

[44] Mousa U, Kut A, Bozkus Y, Cicek Demir C, Anil C, Bascil Tutuncu N. Performance of abdominal bioelectrical impedance analysis and comparison with other known parameters in predicting the metabolic syndrome. *Exp Clin Endocrinol Diabetes* 2013, 121, 391-396.

[45] Wang J, Rennie KL, Gu W, Li H, Yu Z, Lin X. Independent associatios of body-size adjusted fat mass and fat-free mass with the metabolic syndrome in Chinese. *Ann Hum Biol* 2009;36:110-121-

[46] Kim JY, Oh S, Chang MR, Cho YG, Park KH, Paek YJ, Yoo SH, Cho JJ, Caterson LD, Song HJ. Comparability and utility of body composition measurement vs anthropometric measurement for assessing obesity related health risks in Korean men. *Int J Clin Pract* 2013;67:73-80.

[47] Peltz G, Aguirre MT, Sanderson M, Fadden MK. The role of fat mass index in determining obesity. *Am J Hum Biol* 2010; 22: 639-647.

[48] Kyle UG, Shutz Y, Dupertuis YM, Pichard C. Body composition interpretation. Contributions of the fat-free mass index and the body fat mass index. *Nutrition* 2003;19:597-604.

[49] Johnson Stoldossa CA, Forhan M, Padwal RS, González MC, Prado CM. Practical considerations for body Composition assessment of Adults with Class II/III Obesity Using Bioelectrical impedance analysis or Dual-Energy X-Ray Absorptiometry. *Curr Obes Rep* 2016;5:389-396.

[50] Schutz Y, Kyle U, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasions aged 18-98 years. *Int J Obes* 2002;26:953-960.

[51] Martínez-Torres J, Correa-Bautista JE, González-Ruíz K, Vivas A, Triana-Reina HR, Prieto-Benavidez DH, Carrillo HA, Ramos-Sepúlveda JA, Villa-González E, García-Hermoso A, et al. A Cross-sectional study of the prevalence of Metabolic syndrome and associated factors in Colombian Collegiate Students: The FUPRECOL- Adults Study. *Int J Environ Res Public Health* 2017;14:233.

[52] Jaffrin MY, Morel H. Body fluid volume measurements by impedance: A review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. *Med Eng Phys* 2008;30:1257-1269.

Chapter 3: Muscle strength cut-offs for the detection of Metabolic Syndrome in a nonrepresentative sample of collegiate students from Colombia.

1. Introduction

Muscular weakness, as determined with the use of a handgrip dynamometer, is recognized as a marker of health risk, similar to that observed for conventional risk factors. [1-3] López-Martínez et al. [3] demonstrated that muscle strength is negatively associated with metabolic syndrome (MetS) in young adults. Additionally, in a prospective study (follow-up in young adulthood for 20 years), Fraser et al. [4] showed that those in the lowest third tertile of strength were independently associated with adult MetS. Similarly, our group [5,6] and other investigators [7-9] have shown an independent and inverse association between low strength and cardiometabolic risk clustering among adolescents and adults. The contribution of muscular weakness to the progression of sedentary behavior with aging and/or cardiometabolic risk factors (e.g., obesity, MetS, insulin resistance) is equally unequivocal, and recent national effort to identify cut-offs or thresholds for clinically relevant weakness among young people [10] will help clinicians screen individuals at greatest risk. [11,12].

Senechal et al. [11] determined low muscle strength cut-offs for the prediction of MetS among middle-aged and older males using a composite score of normalized strength from chest press and leg press from a sample of 5685 men aged<50 years and 1541 men aged ≥ 50 years. However, at this time, thresholds derived from handgrip muscle strength, a clinically relevant strength measure, among Latin-American college students remains to be determined. Moreover, even though there is scientific evidence regarding the role of muscle strength preservation for prevention against cardiometabolic risk in several populations, no studies have stablished the minimum strength capacity associated with the risk of MetS among Latin-American college students. Clinically relevant handgrip strength cut-off for detecting MetS have been stablished for youths [6], adults [11], and older adults [7,8].

However, Leong et al. [13] reported considerable heterogeneity in median handgrip strength among 125,456 healthy adults aged 35-70 years from 21 countries in the Prospective Urban Rural Epidemiology study. This finding is important because it has been reported that handgrip strength is predictive of mortality and cardiovascular disease (CVD) independently of country income [14]. Therefore, from a public health perspective, the inclusion of handgrip strength measures in health surveillance system is clearly justifiable. For example, moderate weight gain from early to middle adulthood is associated with significantly increased risk of major chronic diseases and mortality. [2] Therefore, young adults may also be a good population for monitoring fitness, identifying risk factors, and offering interventions among those at high cardiometabolic risk. For that, cut-offs to determine young adults at cardiometabolic risk are required and to be used later to promote muscular strength and to lower CVD risk in later life.

Thus, our study aimed to determine cut-offs of grip strength for the detection of MetS in a large collegiate student population from Colombia. Such evidence could serve as proof of a concept for the development of broad normative reference test standards for clinical, academic, and community settings.

2. Methods

2.1 Participants and study design

Data were from a cross-sectional component of the FUPRECOL (in Spanish, Asociación de la Fuerza Prensil con Manifestaciones Tempranas de Riesgo Cardiovascular en Adultos Colombianos) study conducted during the 2014-2017 academic years. We recently published a complete description of

the FUPRECOL study design, methods, and primary outcomes for our current cohort. [9] A convenience sample comprised 1795 volunteers (61.4% female, aged=20.68 ± 3.10 years, mean ± SD) between ages 18 and 30 years of low to middle socioeconomic status, which was evaluated in accordance with the following Colombian government classification: stratum 1-2= low, stratum 3-4= middle, and stratum 5-6= high). The sample comprised students enrolled in public or private universities from 3 distinct areas of Colombia: the capital district of Bogota (Cundinamarca), Tunja (Boyacá), and Santiago de Cali (Valle del Cauca).

Exclusion criteria included medical or clinical diagnosis of a major system disease, including malignant conditions such as cancer, type 1 or 2 diabetes, high blood pressure, and hypothyroidism or hyperthyroidism; a history of drug or alcohol abuse; regular use of multivitamins; chronic inflammatory conditions including rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis; infectious conditions; or a body mass index (BMI) ≥ 35 kg/m^2. Volunteers were not compensated for their participation. Informed consent was obtained from each participant. All participants provided written consent, and each study was approved by the local authorized institutional review boards (Bogota UMB Code N° 01-1802-2013, UR Code N° CEI-ABN026-000010; Cali UNIAJC Code N° 111-01.01.48/16; Tunja Code N° RECT 60) and complied with the Declaration of Helsinki (World Medical Association for Human Subjects). The students who agreed to participate and who had signed the informed consent form were given appointments for the procedures described in the following.

2.2 Physical examination

Subjects were screened for inclusion in the study via personal interviews, Interview questions included queries about health status, medical history, CVD risk factors, and lifestyle. After completing another general information questionnaire, participants were instructed to wear shorts and t-shirts to the physical examination. They were also required to remove all jewelry and metal objects. Once the subjects were barefoot and, in their underwear, their body weight (kg) was measured using an electric scale (Tanita model BC-418, Tanita Corp., Tokyo Japan) with a range of 0-200 kg and with an accuracy within 100 g. Height was measured with a portable stadiometer with a precision of 0.1 mm and a range of 0.2.50 m (Seca 274, Vogel and Halke, Hamburg, Germany). BMI was calculated by using the following formula: body mass (kg)/ height (m^2). BMI status was evaluated according to the World Health Organization criteria.[15] The waist circumference (WC) was measured in cm as the narrowest point between the lower costal border and the iliac crest. When this point was not evident, it was measured at the midpoint between the last rib and the iliac crest, using a meta tape measure (Lufkin W606PM; Cooper Tools, Parsippany, NJ, USA). The evaluation process was carried out by a team of professionals (4 physical therapy professors) with extensive experience in anthropometric measurement. Measurements for 2% of the sample was carried out twice to ensure quality of measures. The technical error of measurement (TEM) values were <2% for all anthropometric variables.

Body fat percentage (BF%) and fat mass index (FMI) were determined for bioelectrical impedance analysis (BIA) by a tetrapolar whole-body impedance (Tanita Model BC-418; Tanita Corp.,). For the calculation of intra-and inter-observer TEM, at least 50 subjects needed to be measured (30 males, 20 females, aged 22.3 ± 2.1 years). The Tanita Model BC-418 is a reliable system that has good agreement with laboratory-based methods of assessment (hydrostatic weighing: r= 0.81, p<0.05; error of 1.68 BF% or DXA: r=0.87, p< 0.001) [16,17] The corresponding intraobserver technical error (% relatability) of the measurements was 95%. A detailed description of the BIA technique can be found elsewhere. [18]

Before testing, participants were required to adhere to the BIA manufacturer's instructions (http://www.tanita.com/es/bc-418/), including no to (i) eat or drink within 4 h of the test; (ii) consume caffeine or alcohol within 12 h of the test; (iii) take diuretics within 7 days of the test; (iv) do physical exercise within 12 h of the test, and (v) urinate within 30 min of the test. FMI was calculated by dividing each subject´s fat mass (kg) by the square of his or her height $(m)^2$, as described previously. [19]

2.3 Muscular strength

Handgrip strength was assessed using an adjustable digital handgrip dynamometer (T-18 TKK SMEDLY III; Takei Scientific Instruments Co., Ltd., Niigata, Japan). Participants watched a brief demonstration of the technique and were given verbal instructions on how to perform the test. The dynamometer was adjusted according to the subjects´ hand size based on a predetermined protocol. [20] The best score for each hand was recorded in kg. The handgrip strength was calculated as the average of the left and right hand. Because there is substantial covariance between strength and both physical function and chronic health is directly mediated by the proportion of strength relative to body mass, handgrip strength was a normalized grip strength (NGS) per body mass-for instance, handgrip strength (kg)/body mass (kg). The reproducibility of our data was R= 0.96. Intra-rater reliability was assessed by determining the intra-class correlation coefficient (0.98, 95% confidence interval (CI): 0.97-0.99, n=20, median age= 22.88 ± 1.41 years, 66.2 ± 5.41 kg, 1.75 ± 0.1 m, 24.91 ± 3.12 kg/m^2)

2.4 MetS diagnosis

After the subjects had fasted for 10-12 h, blood samples were obtained from capillary sampling from 6:00-10:00 a.m. Participants were asked not to engage in prolonged exercise in the 24 h prior to testing. The biochemical profile included the following: (i) high-density lipoprotein cholesterol (HDL-C), (ii) triglycerides, (iii) low-density lipoprotein cholesterol (LDL-C), (iv) total cholesterol, and (v) glucose fasting by enzymatic colorimetric methods. Inter-assay reproducibility (coeffient of variation) was determined from 80 replicate analyses of 8 plasma pools over a period of 15 days. The percentages obtained were 2.6% (triglycerides), 2.0% (total cholesterol), 3.2% (HDL-C), 3.6% (LDL-C), and 1.5% (fasting glucose)

Blood pressure was taken on the left arm at the heart level with the automatic device Omron M6 Comfort (Omron Healthcare Europe B.V., Hoofddorp, The Netherlands) while the participants were sitting still. The blood pressure monitor cuff was placed 2-3 finger- widths above the bend of the arm, and a 2-min pause was allowed between the first and the second measurement with a standard cuff for an arm circumference of 22-32 cm. The mean arterial pressure (MAP) was calculated using the following formula: MAP= (systolic blood pressure + (2 x diastolic blood pressure))/3.

Participants were considered to have diagnoses of the MetS if they had ≥ 3 of the following: (i) abdominal obesity (WC ≥ 80 cm in females and WC ≥ 90 cm in males), (ii) hypertriglyceridemia (≥150 g/dL), (iii) low HDL-C (<50 mg/dL in females and <40 mg/dL in males), (iv) high blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg) or MAP ≥ 100 mmHg, and (v) high fasting glucose (≥100 mg/dL). MetS was defined in accordance with the updated harmonized criteria of the International Diabetes Federation (IDF). [21]

We calculated a composite MetS score that reflects a continuous score of the 5 MetS risk factors. The MetS score was calculated from the individual subjects´ data, based on the IDF [21], and the standard deviations were calculated using data from the entire subject cohort at baseline. The equation used was MetS score=((HDL-C: male ≤40 mg/dL or female ≤ 50 mg/dL)/SD: female=1.04 or male = -

0.19) + ((triglycerides (TG): 150mg/dL)/SD: female= 0.99 or male=0.97)+((fasting glucose: 100 mg/dL)/SD: female= 0.98 or male=1.02)+((WC: male≥94 cm or female ≥ 80 cm)/SD: female=0.99 or male=0.94)+((MAP: 100 mmHg)/SD: female= 0.88 or male= 1.07). The mean of this continuously distributed MetS score was therefore 0 by definition.

2.5 Lifestyle covariates

A standardized questionnaire, the "FANTASTIC" lifestyle (family, physical activity (PA), nutrition, tobacco toxins, alcohol, sleep/stress, personality type, insight, and career), was used to collect comprehensive information about substance use via a personal interview with participants. Alcohol consumption and smoking status were defined as subjects who had consumed any alcoholic beverage ≥1 time per week and those who had smoked ≥10 cigarettes per week for at least 6 months, respectively, as previously described by Ramírez-Vélez et al. [22] Participants who exercised ≥3 times a week for >30 min were categorized as "physically active", and those who exercised <3 times a week were considered "physically inactive. [22]

2.6 Statistical analysis

Descriptive characteristics are provided as means, SDs, and is percentages. Histograms and Q-Q plots were used to verify the normality of the selected variables. Independent 2-tailed *t* tests for continuous variables and X^2 tests for categorical variables were used to examine sex differences or the MetS group. Analysis of covariance adjusted for age, tobacco, alcohol, and PA levels (owing to the relationship with MetS) was used to determine the main effects for NGS (weak, intermediate, and strong) and anthropometrics, blood pressure, metabolic biomarkers, and muscle strength outcomes. We calculated standard indices, including sensitivity, specificity, area under the curve (AUC), and receiver operating characteristic (ROC) curve analysis, to establish weak, intermediate, and strong handgrip cut-off scores for subjects (male and female). Such cut-off could be used to predict MetS according to the IDF criteria. Sensitivity was defined as the probability of classifying correctly those college students presenting MetS (true positives), whereas specificity was defined as the probability of classifying correctly those participants presenting non-MetS (true negatives). The shortest distance is the ROC curve was calculated using the function √(1-sensitivity[2])+(1-specificity[2] by maximizing the Youden index. The positive likelihood ratio (LR(+)) and the negative likelihood ratio (LR(-)) were used to analyze the potential diagnostic accuracy of the NGS to discriminate among weak, intermediate, and strong for MetS. Locally weighted scatterplot smoothing curves were used to illustrate the shape of the relationship between the NGS and MetS score. Conditional inference tree analyses were used as an alternative method for determining weak, intermediate, and strong risk thresholds of normalized strength for detection of the high-risk cardiometabolic phenotype, as described previously [23]. Data were analyzed with SPSS version 24.0 for windows (IBM Corp., Armonk, NY, USA.) and freely available statistical software R version 3.2.3 (RStudio Team, Boston, MA, USA). A p value<0.05 denoted statistical significance.

3. Results

The 1795 volunteers included 1103 females (61.4%). Their mean age was 20.68 ± 3.10 years. Overall, males had greater body weight, WC, blood pressure, high triglycerides, and PA levels than females ($p \leq 0.001$), whereas females had lower handgrip and NGS ($p \leq 0.001$). The prevalence of overweight and obesity was 21.31% and 5.53% in females, respectively ($p \leq 0.001$) (Table 5).

Table 5. Characteristics among a sample of college students from Colombia (mean ± SD, n=1795).

Characteristics	Male (*n=692)*	Female (n=1103)	*p*
Anthropometric			
Age (year)	20.51 ± 3.22	20.59 ± 2.99	0.097
Weight (kg)	68.91 ± 12.22	58.79 ± 10.36	<0.001
Height (cm)	172.30 ± 6.65	159.09 ± 5.86	<0.001
WC (cm)	78.23 ± 9.32	71.53 ± 8.02	<0.001
High WC *n* (%)	75 (10.84)	151 (13.69)	0.069
BMI (kg/m2)	23.17 ± 3.60	23.21 ± 3.77	0.089
Body fat (%)	15.61 ± 6.54	27.03 ± 7.26	0.002
FMI (kg/m2)	3.81 ± 2.24	6.50 ± 2.75	< 0.001
Body mass index status, n (%)			
Underweight	38 (5,49)	72 (6.52)	< 0.001
Normal weight	477 (68.93)	735 (66.64)	< 0.001
Overweight	144 (20.81)	235 (21.31)	< 0.001
Obese	33 (4.77)	61 (5.53)	< 0.001
Blood pressure			
Systolic (mmHg)	120.28 ± 12.97	111.29 ± 11.15	< 0.001
Diastolic (mmHg)	74.19 ± 11.45	71.74 ± 9.35	< 0.001
MAP (mmHg)	97.23 ± 10.90	91.51 ± 8.92	< 0.001
Hypertension, *n* (%)	282 (40.75)	187 (16.95)	< 0.001
Cardiometabolic parameters			
Total cholesterol (mg/dL)	132.75 ± 30.23	146.39 ± 33.33	0.081
High total cholesterol, *n* (%)	21 (3.03)	62 (5.62)	0.007
Triglycerides (mg/dL)	93.74 ± 48.54	88.50 ± 45.34	0.017
High triglycerides, *n* (%)	54 (7.80)	127 (11.51)	<0.001
LDL-C (mg/dL)	81.07 ± 26.09	87.92 ± 26.15	0.386
High LDL-C, *n* (%)	272 (39.31)	638 (61.92)	<0.001
HDL-C (mg/dL)	39.55 ± 10.67	43.97 ± 12,80	<0.001
Low HDL-C, *n* (%)	383 (55.35)	798 (72.35)	< 0.001
Glucose (mg/dL)	84.81 ± 11.99	86.05 ± 11.57	0.010
High glucose, *n* (%)	61 (8.82)	90 (8.16)	0.629
MetS score	-3.85 ± 2.95	-3.94 ± 2.66	0.008
MetS, *n* (%)	84 (12.14)	82 (7.43)	0.001
Lifestyle, n (%)			
Tobacco (≥10 cigarettes per week)	199 (28.76)	210 (19.04)	0.548
Alcohol (≥1 time per week)	378 (54.62)	430 (38.98)	0.451
Physical activity levels (≥150 min per week)	243 (35.12)	222 (20.13)	0.001
Muscular strength			
Handgrip (kg)	39.42 ± 7.14	24.07 ± 4.95	< 0.001
NGS*	0.58 ± 0.11	0.42 ± 0.09	< 0.001

**NGS measured as handgrip strength (kg)/ body mass (kg).*

Notes: values are presented as mean ± SD unless otherwise noted.

Abbreviations: BMI= body mass index; FMI= fat mass index; HDL-C= high-density lipoprotein cholesterol; MAP= mean arterial pressure; MetS= metabolic syndrome; NGS= normalized grip strength; WC=waist circumference.

In males, the prevalence of overweight and obesity was 20.81% and 4.77%, respectively ($p< 0.001$). It was observed that 40.75% of males had high blood pressure. Total cholesterol, and LDL-C levels were significantly higher in females than in males ($p< 0.05$).

Table 6 depicts ROC curve analysis for the diagnostic performance NGS in identifying weak, intermediate, and strong risk of MetS. Since multiple levels of risk were desired, the selection of the resulting cut-off values was based on multiple combinations of sensitivity and specificity. In males, NGS values for weak, intermediate, and strong were < 0.466, 0.466-0.615, and >0.615, respectively (Table 6)

Table 6. Parameters of the ROC curves analysis for the diagnostic performance of NGS identifying weak, intermediate, and strong risk of MetS according to the IDF criteria in males and females.

Parameters		Weak	Intermediate	Strong
Male	AUC	0.720	0.740	-
	95%CI	0.679-0.802	0.679-0.802	-
	p	<0.001	<0.001	-
	Cut-off	<0.466	0.466-0.615	>0.615
	Sensitivity (%)	89.0	86.9	84.3
	Specificity (%)	57.8	56.8	58.7
	LR (+)	2.11	2.10	2.04
	LR (-)	0.19	0.23	0.26
	Percentile	≤14	15-62	≥63
Female	AUC	0.725	0.728	-
	95%CI	0.670-0.780	0.660-0.777	-
	p	<0.001	<0.001	-
	Cut-off	<0.332	0.332-0.437	>0.437
	Sensitivity (%)	84.9	85.0	86.6
	Specificity (%)	58.5	58.3	57.9
	LR (+)	2.04	2.02	2.05
	LR (-)	0.25	0.24	0.23
	Percentile	≤17	18-60	≥61

Notes: NGS is measured as grip strength (kg)/body mass (kg).
Abbreviations: AUC= area under the curve; CI= confidence interval; IDF= International Diabetes Federation; LR (+) = positive likelihood ratio; LR (-) = negative likelihood ratio; MetS= metabolic syndrome; NGS= normalized grip strength; ROG= receiver operating characteristic curve.

Mean difference in anthropometrics, cardiometabolic risk, and muscle strength parameters according to NGS categories are shown in Table 7. In males and females, analysis of variance adjusted for age, tobacco, alcohol, and PA levels showed that there were differences in body weight, FMI, and muscle strength (all $p<0.05$).

Table 7. Sex threshold for weak, intermediate, and strong NGS with anthropometric, blood pressure, metabolic biomarkers, and muscle strength.

Variables	Male (*n*= 692)						Female (*n*=1103)					
	Weak (*n*=101)	**Intermediate (*n*=326)**	**Strong (*n*=265)**	***F***	***P***	n^2_p	**Weak (*n*=188)**	**Intermediate (*n*=466)**	**Strong (*n*=265)**	***F***	***P***	n^2_p
Anthropometric												
Weight (kg)	80.0 ± 15.8	70.6 ± 11.2	63.5 ± 8.6	91.53	<0.001	0.241	67.5 ± 13.5	59.6 ± 10.1	52.5 ± 6.3	116.01	<0.001	0.227
WC (cm)	87.6 ± 12.7	79.5 ± 8.6	74.3 ± 6.0	100.45	<0.001	0.231	77.0 ± 9.0	72.1 ± 7.3	67.0 ± 5.5	98.05	<0.001	0.199
Body fat (%)	22.2 ± 7.9	16.6 ± 5.7	12.9 ± 4.5	109.76	<0.001	0.247	32.5 ± 7.2	28.1 ± 6.9	22.5 5.9	112.58	<0.001	0.223
FMI (kg/m^2)	6.3 ± 3.4	4.1 ± 1.9	2.8 ± 1.2	117.16	<0.001	0.259	8.9 ± 3.4	6.8 ± 2.6	4.9 ± 1.8	128.13	<0.001	0.241
Blood pressure (mmHg)												
Systolic	123.9 ±13.8	122.9±12.3	119.4 ± 11.0	12.66	< 0.001	0.136	111.7 ± 10.4	111.4 ± 11.4	110.4 ± 10.7	1.46	0.232	0.004
Diastolic	78.6 ± 10.1	76.4 ± 11.0	72.9 ± 9.6	8.83	< 0.001	0.026	73.3 ± 9.3	71.7 ± 10.1	72.2 ± 9.8	1.91	0.147	0.005
MAP	101.3 ± 10.3	99.6 ± 10.3	96.1 ± 9.3	13.98	< 0.001	0.040	92.5 ± 8.6	91.5 ± 9.3	91.3 ± 8.7	1.42	0.240	0.004
Cardiometabolic biomarkers												
Total cholesterol (mg/dL)	133.4 ± 27.6	142.3 ± 29.8	140.6 ± 26.1	3.24	0.039	0.010	150.0 ± 32.3	148.5 ± 28.6	148.3 ± 28.5	0.02	0.978	0.001
Triglycerides (mg/dL)	113.6 ± 54.6	103.9 ± 47.2	95.3 ± 40.8	9.83	<0.001	0.029	98.5 ± 42.9	94.0 ± 37.7	86.8 ± 34.9	6.65	0.001	0.017
HDL-C (mg/dL)	38.1 ± 10.2	39.9 ± 10.6	41.5 ± 9.5	4.84	0.008	0.014	38.0 ± 11.7	41.9 ± 11.7	45.2 ± 12.4	15.63	<0.001	0.039
LDL-C (mg/dL)	74.0 ± 23.0	82.7 ± 27.0	81.5 ± 25.3	4.09	0.017	0.016	93.2 ± 27.6	88.4± 25.3	85.9 ± 22.9	1.87	0.155	0.006
Glucose (mg/dL)	87.4 ± 11.5	85.5 ± 11.7	82.8 ± 12.1	5.76	0.003	0.017	89.1 ± 8.6	87.6 ± 11.3	85.2 ± 12.5	6.09	0.002	0.017
MetS score	-1.742 ± 3.160	-3.252 ± 2.762	-4.684 ± 2.369	51.60	<0.001	0.135	-2.191± 2.689	-3.437± 2.525	-4.729 ± 2.125	54.01	<0.001	0.125
Muscle strength												
Handgrip (kg)	32.0 ± 6.1	38.4 ± 5.9	43.7 ± 6.4	135.94	<0.001	0.288	19.7 ± 3.8	23.1 ± 3.9	26.5 ± 3.7	161.13	<0.001	0.125
NGS*	0.403 ± 0.052*	0.546 ± 0.042	0.691 ± 0.069	132.83	< 0.001	0.764	0.294 ± 0.032	0.388 ± 0.028	0.507 ± 0.054	109.09	<0.001	0.771

**NGS is measured as handgrip strength (kg)/body mass (kg). F values and partial eta-squared (n^2_p) calculated from analysis of variance adjusted for age, tobacco, alcohol, and physical activity levels.*

Notes: values are presented as mean ± SD unless otherwise noted.

Abbreviations: FMI= fat mass index; HDL-C= high- density lipoprotein cholesterol; LDL-C= low- density lipoprotein cholesterol; MAP= mean arterial pressure; MetS= metabolic syndrome, NGS= normalized grip strength; WC= waist circumference.

Conditional inference trees predicting probability of the high-risk cardiometabolic phenotype (MetS according to the IDF criteria) confirmed different low strength thresholds between males and females. Figure 3 provides results for the primary definition. The first cut-off point identified in males was based on having NGS <0.466 *vs.* ≥ 0.466. within the group of subjects with NGS ≥0.466, a second cut-off point was identified as an NGS >0.615. Among the weakest males (NGS<0.466), 34.6% had MetS, as compared with 10.7% among males with intermediate NGS (0.466-0.615), and only 4.9% among males with the highest NGS (>0.615). Among females, the first identified cut-off point was based on having an NGS ≥0.332 *vs.* <0.332. Within the group of subjects with an NGS < 0.332, a second cut-off point was identified as an NGS ≥ 0.332. Among the weakest females (NGS <0.332), 18.0% had MetS as compared with 7.9% among females with intermediate NGS (0.332-0.437) and only 2.4% among females with the highest NGS (>0.437).

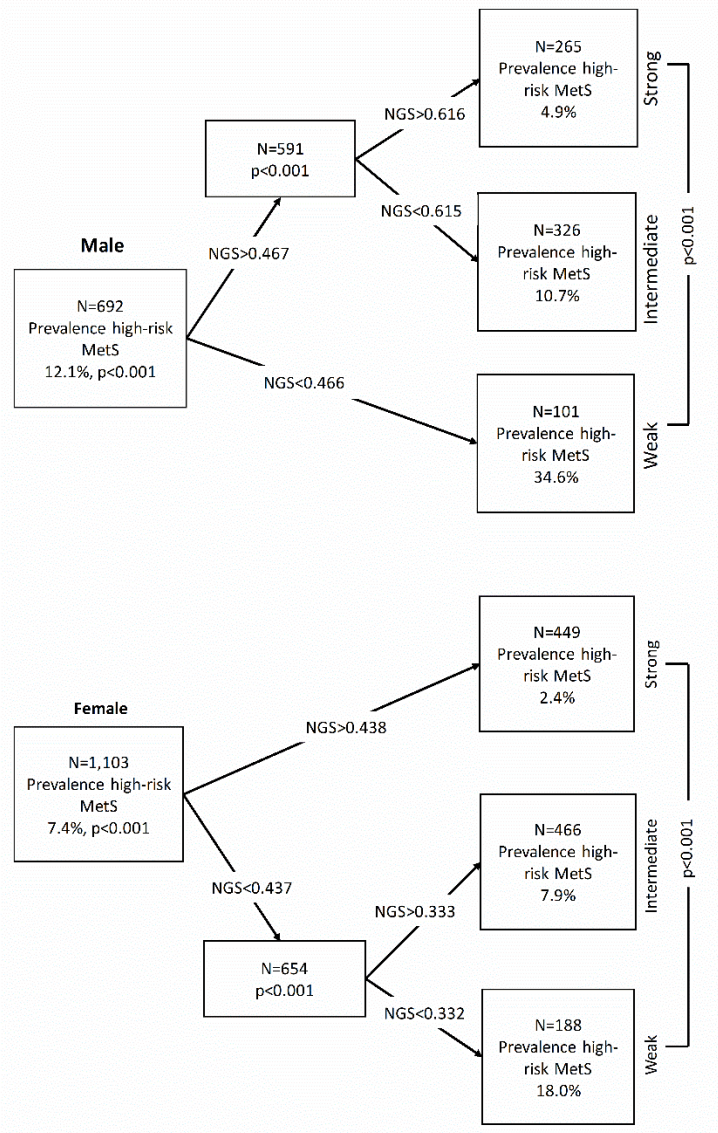

Figure 12. Conditional inference trees for NGS, as predictors in identifying risk of MetS according to the IDF criteria in males and females.

NGS is measured as grip strength (kg/body mass (kg). IDF= International Diabetes Federation, MetS= metabolic syndrome, NGS= normalized grip strength.

Figure 4 provides plots of the association between NGS and MetS score for males and females, inspection of the locally weighted scatterplot smoothing curves provides evidence of a well-defined threshold effect of low strength on the MetS score as continuous outcome.

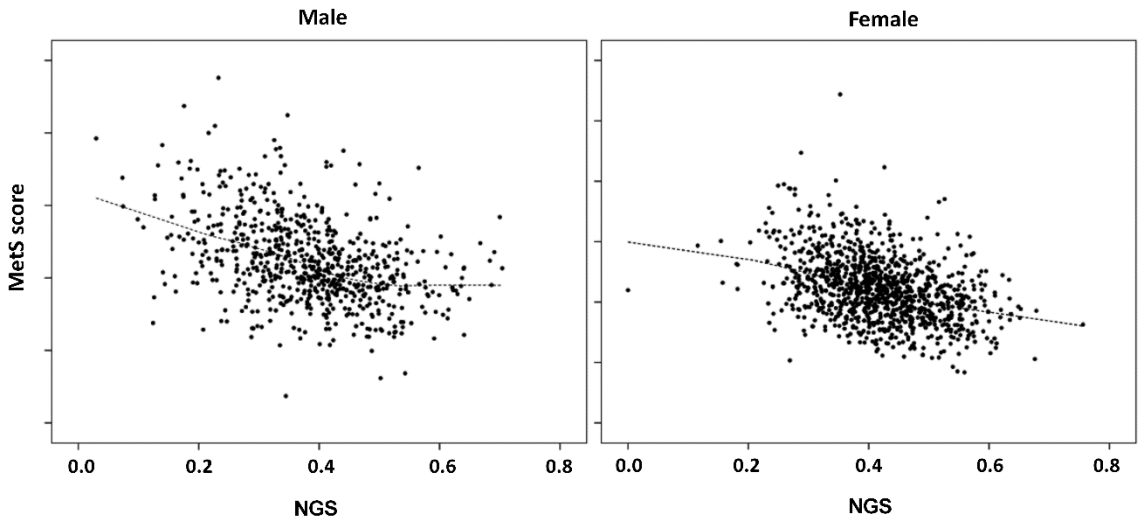

Figure 13. Scatterplots with overlaid locally weighted scatterplot smoothing curves to depict the shape of the association between the NGS and MetS score by sex.
NGS is measured as grip strength (kg)/body mass (kg). MetS= metabolic syndrome; NGS= normalized grip strength.

4. Discussion

This is one of the first studies to identify sex-specific cut-off for NGS to detect a high-risk cardiometabolic phenotype among a large population of college students. The role of muscular strength has been increasingly recognized in the prevention of chronic disease in adult population. [1-3] Evidence suggests that muscle mass and strength decrease progressively after the age of 20 years, [24] whereas in old age, some grip strength and hip strength declines by an average of 1.10 kg per year and 1.31 kg per year, respectively. [25] Therefore, young adulthood seems to be crucial time frame for monitoring and intervening to reduce the risk of weakness and cardiometabolic disease.

Few studies have proposed cut-offs for low muscular strength among adults for screening cardiometabolic risk; however, this has yet to receive adequate attention in young adult populations, and information is scarce. Most studies have analyzed the older adult population. For example, Lee et al. [26] demonstrated that cardiometabolic risk was 54% lower for individuals with relative handgrip strength (absolute handgrip strength divided by BMI) in the 75th percentile compared with the 25th percentile. In addition, Duchowny et al. [27] established cut-off points for muscle weakness assessed as handgrip strength in a nationally representative sample by race and sex among older American adults. Senechal et al. [11] determined low muscle strength cut-off points for the prediction MetS using a composite score of normalized strength from the chest press and leg press. Among middle-aged adults, Strand et al. [28] revealed an association between handgrip strength and all-cause mortality and cardiovascular mortality, confirming the role of handgrip strength as a mortality predictor [29]. Finally, among young adults, Wilkerson et al. [30] investigated 62 collegiate football players (mean age 19.9 years) and found that low leg muscle strength was associated with an increased likelihood of MetS.

In line with studies mentioned earlier, our study revealed cut-offs for NGS by sex and identified 3 cardiometabolic risk categories ("high", "intermediate", and "low"). The ROC curves generated for this study showed acceptable AUCs and 95%CI limits, suggesting that the resultant cut-offs were not owing to chance (both AUC ≥ 0.72). Specifically, among males in the highest strength category, only 4.9% had the MetS phenotype, as compared with 10.7% among males with intermediate strength and 34.6% among males with low strength. Among the females in the highest category, only 2.4% had the MetS phenotype, as compared with 7.9% among females with intermediate strength and 18% among those with low strength. The identification of the 3 categories of cardiometabolic risk coincides with the findings of Peterson et al. [31] who determined by sex the distribution of high cardiometabolic risk according to the cut-off points: weak, intermediate, and strong. These cut-off points were obtained from a similar size sample but not related to the age range. The cut-off points are lower than those identified in our study.

However, the AUCs observed for this threshold were 0.72-0.74 for males and 0.72 for females, whereas in the study performed by Senechal et al. [11] the AUCs were 0.65 for males and 0.81 for females. The lower sensitivity and specificity reported in our study might be related to differences in age (20-50 years *vs.* 18-30 years), sample size of the populations studied (1795 *vs* 5685), and the methods used to assess muscle strength (handgrip *vs.* leg and bench press), as well as the use of a composite measure of MetS. Thus, our findings reinforce the concept that muscle strength may be an important modifiable lifestyle factor for CVD risk assessment in the same way that physical inactivity, body composition, and healthy dietary patterns are important.

Our findings therefore support previous results demonstrating that low muscle strength is associated with MetS. These findings coincide with Sasaki et al. [32] in which for each 5 kg increase grip strength, the number of deaths caused by heart disease and stroke diminishes significantly. A plausible explanation for the role of muscle strength in MetS prevalence may be through the metabolic and structural changes that improve muscle insulin sensitivity and glycemic control [33]. As demonstrated by Wu et al. [34] in a recent meta-analysis, there is a 63% higher risk of premature mortality owing to CVD among adults with low handgrip muscle strength.

The strengths of this study include the large sample size and a commonly used and feasible test for assessing muscle strength. However, there are some limitations that need to be highlighted. First, owing to the cross-sectional nature of the study design, we were unable to draw causal relationships. Thus, we were unable to deduce whether low NGS leads to increased risk of MetS, or conversely whether poor cardiometabolic profiles lead to declines in muscle strength. Future longitudinal studies are needed to better understand how declines in muscle strength contribute to health risks in college-aged adults. Second, the ROC curve analysis does not enable adjustments for potential confounders within the model, and data were not adjusted prior the ROC curve analysis. Finally, we only analyzed relatively healthy individuals; therefore, the generalization of our results is limited to healthy younger adults. Our study suggests that NGS could be used as a complementary tool that may help clinicians and practitioners screen for high cardiometabolic risk.

5. Conclusion

In summary, our sex-specific NGS cut-offs could be incorporated into a clinical setting for identifying college students at high cardiometabolic disease risk and used as a target for strength training programs designed to reduce the risk of MetS. Longitudinal studies are necessary to determine of increasing handgrip strength reduces the likelihood of MetS.

Financial support
The FUPRECOL Adults Study were design and funded by Ramirez-Velez Robinson (IP). Additionally, FUPRECOL has been partially supported by the Universidad del Rosario (Code N° FIUR DN-BG001), Institución Universitaria Antonio José Camacho (Code N° 111-02.01.48/16). Universidad Santo Tomás (Code N°2013004), Universidad Manuela Beltrán (Code N° FT201204), and Universidad de Boyacá (Code N° RECT60). The funder had no role in the study design, data collection, data analysis and interpretation, preparation of the manuscript, or decision to publish.

6. References

[1] Jurca R, Lamonte MJ, Church TS, Earnest CP, Fitzgerald SJ, Barlow CE, et al. Associations of muscle strength and fitness with metabolic syndrome in men. *Med Sci Sports Exerc* 2004;36:1301-7.

[2] Zheng Y, Manson JE, Yuan C, Liang MH, Grodstein F, Stampfer MJ, et al. Associations of weight gain from early to middle adulthood with major health outcomes later in life. *JAMA* 2017;318:255-69.

[3] López-Martínez S, Sánchez-López M, Solera-Martínez M, Arias-Palencia N, Fuentes-Chacón RM, Martínez-Vizcaíno V. Physical activity, fitness, and metabolic syndrome in Young adults. *Int J Sport Nut Exerc Metab* 2013;23:312-21.

[4] Fraser BJ, Huynh QL, Schmidt MD, Dwyer T, Venn AJ, Magnussen CG. Childhood muscular fitness phenotypes and adult metabolic syndrome. *Med Sci Sports Exerc* 2016;48:1715-22.

[5] Ramírez-Vélez R, Meneses-Echavez JF, González-Ruíz K, Correa JE. Muscular fitness and cardiometabolic risk factors among Colombian Young adults. *Nutr Hosp* 2014;30:769-75. [in Spanish].

[6] Ramírez-Vélez R, Peña-Ibagon JC, Martínez-Torres J, Tordecilla-Sanders A, Correa-Bautista JE, Lobelo F, et al. Handgrip strength cutoff for cardiometabolic risk index among Colombian children and adolescents: the FUPRECOL study. *Sci Rep* 2017;7:42622. Doi:10.1038/srep42622.

[7] McGrath R, Vincent BM, Al Snih S, Markides KS, Peterson MD. The association between muscle weakness and incident diabetes in older Mexican Americans. *J Am Med Dir Assoc* 2017;18:452:e7-452, 12.

[8] Peterson MD, Dichowny K, Meng Q, Wang Y, Chen X, Zhao Y. Low normalized grip strength is a biomarker for cardiometabolic disease and physical disabilities among U.S. and Chinese adults. *J Gerontol A Biol Sci Med Sci* 2017;72:1525-31.

[9] García-Hermoso A, Carrillo HA, González-Ruíz K, Vivas A, Triana-Reina HG, Martínez-Torres J, et al. Fatness mediates the influence of muscular fitness on metabolic syndrome in Colombian collegiate students. *PLoS One* 2017;12: e0173932. Doi:10.1371/journal. Pone.0173932.

[10] Alley DE, Shardell MD, Peters KW, McLean RR, Dam T, Kenny AM, et al. Grip strength cut points for the identification of clinically relevant weakness. *J Gerontol A Biol Sci Med Sci* 2014;69:559-66.

[11] Senechal M, McGavock JM, Church TS, Lee DC, Earnest CP, Sui X, et al. Cut points of muscle strength associated with metabolic syndrome in men. *Med Sci Sports Exerc* 2014;46:1475-81.

[12] Eckman M, Gigliotti C, Sutermaster S, Butler PJ, Mehta K. Using handgrip strength to screen for diabetes in developing countries. *J Med Eng Technol* 2016;40:8-14.

[13] Leong DP, Teo KK, Rangarajan S, Kutty VR, Lanas F, Hui C, et al. Reference ranges of handgrip strength from 125.462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. *J Cachexia Sarcopenia Muscle* 2016;7:535-46.

[14] Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum Jr A, Prlandini A, et al. Prognostic value of grip strength: findings form the Prospective Urban Rural Epidemiology (PURE) study. *The Lancet* 2015;386:266-71.

[15] World Health Organization. *Obesity: preventing and managing the global epidemic.* Geneva: World Health Organization;2000.

[16] Pietrobelli A, Rubiano F, St-Pnge MP, Heymsfield SB. New bioimpedance analysis system: improved phenotyping with whole-body analysis. *Eur J Clin Nutr* 2004;58:1479-84.

[17] Kelly J, Metcalfe J. Validity and reliability of body composition analysis using the Tanita BC418-MA. *J Exerc Physiol Online* 2012;15:74-83.

[18] Ramírez-Vélez R, Correa-Bautista JE, González-Ruíz K, Vivas A, Triana-Reina HR, Martínez-Torres J, et al. Body adiposity index performance in estimating body fat percentage in Colombian college students: findings from the FUPRECOL-Adults study. *Nutrients* 2017;9:40. Doi:10.2290/nu9010040.

[19] Liu P, Ma F, Lou H, Liu Y. The utility of fat mass index vs body mass index and percentage of body fat in the screening of metabolic syndrome. *BMC Public Health* 2014;13:629. Doi: 10.1186/1471-2458-13-629.

[20] Vivas-Díaz JA, Ramírez-Vélez R, Correa-Bautista JE, Izquierdo M. Hand-grip strength of Colombian university students. *Nutr Hosp* 2016;33:113. Doi:10.20960/nh.113. [in Spanish]

[21] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung and Blood Institute; American Heart association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-5.

[22] Ramírez-Vélez R, Triana-Reina HR, Carrillo HA, Ramos-Sepúlveda JA, Rubio F, Poches-Franco L., et al. A cross-sectional study of Colombian university students´self-perceived lifestyle. *SpringerPlus* 2015;4:289. Doi:10.1186/s40064-015-1043-2.

[23] Peterson MD, McGrath R, Zhang P, Markides KS, Al Snih S, Wong R. Muscle weakness is associated with diabetes in older Mexican: the Mexican Health and Aging study. *J Am Med Dir Assoc* 2016;17:933-8.

[24] Gallagher D, Visser M, De Meersman RE, Sepúlveda D, Baumgartner RN, Pierson RN, et al. Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. *J Appl Physiol* 1997;83:229-39.

[25] Xue QL, Beamer BA, Chaves PH, Guralnik JM, Fied LP. Heterogeneity in rate of decline in grip, hip and knee strength and the risk of all-cause mortality: The Women´s Health and Aging Study II. *J Am Geriatr Soc* 2010;58:2076-84.

[26] Lee WJ, Peng LN, Chiou ST, Chen LK. Relative handgrip strength is a simple indicator of cardiometabolic risk among middle-aged and older people: a nationwide population-based study in Taiwan. *PLoS One* 2016;11:e0160876. Doi:10.1371/journal.pone.0160876.

[27] Duchoway KA, Peterson MD, Clarke PJ. Cut points for clinical muscle weakness among older Americans. *Am J Prev Med* 2017;53:63-9.

[28] Strand BH, Cooper R, Bergland A, Jorgensen L, Schirmer H, Skirbek V, et al. The association of grip strength from midlife onwards with all-cause and cause-specific mortality over 17 years of follow-up in the Tromso study. *J Epidemiol Community Health* 2016;70:1214-21.

[29] García-Hermoso A, Cavero-Redondo I, Ramírez Vélez R, Ruíz J, Ortega FB, Lee DC, et al. Muscular strength as a predictor of all-cause mortality in apparently healthy population: a systematic review and meta-analysis of data from approximately 2 million men and women. *Arch Phys Med Rehabil.* 2018;99:2100-13.

[30] Wilkerson GB, Bullard JT, Bartal DW. Identification of cardiometabolic risk among collegiate football players. *J Athl Train* 2010;45:67-74.

[31] Peterson M, Zhang P, Saltarelli WA, Visich PS, Gordon PM. Low muscle strength thresholds for the detection of cardiometabolic risk in adolescents. *Am J Prev Med* 2016; 50: 593-9.

[32] Sasaki H, Kasagi F, Yamada M, Fujita S. Grip strenth predicts cause-specific mortality in middle-aged and elderly persons. *Am J Med* 2007;120:337-42.

[33] DiPrieto L, Dziura J, Yeckel CW, Neufer PD. Exercise and improved insulin sensitivity in older women: evidence of the enduring benefits of higher intensity training. *J Appl Physiol (1985)* 2006;100:142-9.

[34] Wu Y, Wang W, Liu T, Zhang D. Association of grip strength with risk of all-cause mortality, cardiovascular diseases, and cancer in community-dwelling populations: a meta-analysis of prospective cohort studies. *J Am Med Dir Assoc* 2017;18:551. Doi:10.1016/j.jamda.2017.03.011.

Chapter 4: Ideal Cardiovascular Health, handgrip strength, and muscle mass among college students: The FUPRECOL Adults Study

1. Introduction

With the rising rates of noncommunicable diseases over the past 30 years, a growing number of adults are exhibiting cardiometabolic risk factors, including hypertension, dyslipidemia, and dysglycemia [25]. Decreased physical activity (PA) and sedentary behavior-combined with poor dietary habits have been implicated as potential contributing factors in the noncommunicable disease crisis [27]. In Colombia, the number of patients with cardiovascular risk factors has increased rapidly because of longer lifespan, the aging of the population, and lifestyle changes. During the period from 1998 to 2011, 21-25% of total deaths were due to cardiovascular disease (CVD) [5]. The crude mortality rate varied from 93.5 to 108.8 per 100,000 habitants, whereas the age adjusted mortality rate varied from 108.6 to 95.5 deaths per 100,000 [23].

Assessments of CVD risk in college students aged 18-24 years show an alarmingly high prevalence of abnormal risk facto profiles [6]. Approximately 33% of young adults are overweight [4], and this excess weight leads to dyslipemia and increases the risk of metabolic syndrome [22] and CVD [24]. Early detection and intervention are critical because 80% of CVD events are preventable through diet and life-style [36]. In response to the increasing burden of noncommunicable diseases, including CVD, the American Heart Association (AHA) established the 2020 strategic Impact Goals to define the concept of Ideal Cardiovascular Health (CVH) and the metrics needed to monitor it across populations [17]. The 7 metrics for ideal CVH in adults (age ≥ 20 years) comprise 4 health behaviors (current smoking, body mass index [BMI], physical activity and healthy diet score] and 3 physiological health factors (total cholesterol, blood pressure, and fasting plasma glucose levels). The few studies that have analyzed this ideal CVH in young adults suggest a direct association with markers related to future cardiovascular events [30], such a carotid intima media thickness [26] of left ventricular structure and function later in life [7].

Although there is scientific evidence regarding the role of muscle strength preservation in preventing cardiometabolic risk and mortality in several populations [9], to the best of our knowledge, only one study has analyzed the relationship between ideal CVH and muscle strength in children and adolescents from Colombia, and it showed a positive association between the two [31]. Poor diet, obesity and physical inactivity have been shown to be the leading CVD risk factors in Colombian adults and another Latin American countries [34], raising concerns about whether an increased risk of these conditions also affects cardiometabolic status. These changes, in addition to the adoption of a Western lifestyle and diet, have led to an increase in the prevalence of overweight and obesity among Colombians, particularly among university students [8].

In addition, the prevalence of ideal CVH has not been examined in college students in any Latin American population. It is very important to identify the risk factors and to take steps to control noncommunicable diseases in Colombia. Therefore, the objective of this study was to investigate the relationship between handgrip strength, muscle mass, and Ideal CVH among college students. It was hypothesized that higher scores on 7 metrics for ideal CVH, indicating better CVH, are associated with higher levels of handgrip strength and muscle mass in Colombian college students.

2. Methods

2.1 Experimental approach to the problem

This was a secondary analysis of cross-sectional of data from the Association of the Prehensile Force with Early Manifestations of Cardiovascular Risk in Young Colombian Adults (FUPRECOL). Adults study, which investigated the association between muscular strength and metabolic risk factors in Colombian collegiate students.

2.2 Subjects

The students were enrolled in public or private universities from 3 district areas of Colombia: the capital district of Bogotá (Cundinamarca), Tunja (Boyacá) and Santiago de Cali (Valle del Cauca). We recently published a complete description of the FUPRECOL Adults study´s design and methods and the primary outcomes for our current cohort [29]. The original sample consisted of adults (male: n=707; female: n=1,131). Of this group, 1,835 collegiate students (61,4% of women) had valid data for body composition and all the components of the cardiometabolic variables. There were no differences in the study´s key characteristics (ie., age, sex distribution, BMI, and ideal CVH components) between the current study sample and the original FUPRECOL Adults sample (n=1,838, all p >0.100).

Exclusion criteria included the following: medical or clinical diagnosis of a major systemic disease, including malignant conditions such as cancer, type 1 or 2 diabetes, high blood pressure, hypothyroidism, or hyperthyroidism; regular use of multivitamins; chronic inflammatory conditions, including rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis, and infectious conditions. The volunteers received no compensation for their participation. All participants provided written consent, and each study was approved by the University of Rosario Review Board (Bogotá UMB Code N° 01-1802-2013, UR code N° CEI-ABN026-000010; Cali UNIAJC Code N° 111-02.01.48/16; Tunja Code N° RECT 60) and complied with the Declaration of Helsinki (World Medial Association for Human Subjects)

2.3 Procedures

Clinical Examination. Clinical examinations were performed between January 25, 2015, and March 30, 2017, by trained personnel and followed standardized routines described in detail elsewhere [29]. Briefly, body mass and muscle mass were measured using tetrapolar whole body impedance (Tanita Model Tanita BC 420 MA® and SC-331S®; Tanita, Tokyo, Japan). A detailed description of the bioelectrical impedance analysis (BIA) technique can be found in a previous study [32]. Muscle mass was normalized as muscle mass per body mass, i.e., muscle mass in kg/body mass in kg. In a study to validate 2 portable BIA devices for body composition assessment, multiple regression analyses showed clinically acceptable agreement between the Tanita BC 420 MA® and SC-331S® device and magnetic resonance imaging for visceral adipose tissue and fat mass measurements (R^2>0.70, r>0.84) [38]. The corresponding intraobserver technical error (% reliability) of the measurements was 95%. Before testing, participants were required to adhere to these BIA manufacturer´s instructions, including not to (http://www.tanita.com/es/bc-418/): (a) eat or drink within 4 hours of the test; (b) consume caffeine or alcohol within 12 hours of the test; (c) take diuretics within 7 days of the test; (d) do physical exercise within 12 hours of the test; and (e) urinate within 30 minutes of the test.

Waist circumference (WC) (cm) was measured at the uppermost border of the iliac crest around the abdomen. When this point was not evident, WC was measured at the midpoint between the last rib and the iliac crest using a metal tape measure (Lufkin W606PM®, Allers Parsippany, NJ, USA) in accordance with the International Society for the Advancement of Kinanthropometry guidelines [21]. The evaluation process was performed by a team of professionals (4 physical therapy professors) with

extensive experience in anthropometric measurement. Two percent of the sample was measured twice to ensure the quality of the measurements. The technical error of measurement values were less than 2% for all anthropometric variables.

We used a handgrip strength test (T.K.K. 5401-5001, Grip-A; Takei Scientific Instrument, Tokio, Japan), adjusted for each participant by sex and hand size as PA "proxy". The participants were instructed to stand with their arms completely extended, squeezing and to gradually and continuously squeeze the handgrip as hard as they could for at least 2 seconds. The test was performed twice, alternating hands between tests. A 90-second rest period was provided between trials. The best score for each hand was recorded in kilograms [32]. The handgrip score (kg) was calculated as the average of the left and right hands and then expressed per kilogram of body mass. The reproducibility of our data was *R*=0.96. Intrarater reliability was assessed by determining the intraclass correlation coefficient (0.98, confidence interval [CI] 95% 0.97-0.99, *n*=20, median age= 22.8 ± 1.4 years, 66,2 ± 5.4 kg, 1.67 ± 0.1 m, 24.9 ± 3.1 kg/m2). As there is substantial covariance between strength capacity and body mass and the link between strength and both physical function and chronic health is directly mediated by the proportion of strength relative to body mass, handgrip strength was normalized as grip strength (NGS) per body mass, i.e., handgrip strength in kg/body mass in kg[1]. In male, unfit and fit NGS values at these points were <0.47 and >0.48, respectively [10]. These cutoff points have been associated with the detection of metabolic syndrome in Colombian collegiate students.

Ideal Cardiovascular Health Behaviors. A standardized survey, the "FANTASTIC" lifestyle questionnaire (family, PA, nutrition, tobacco toxins, alcohol, sleep/stress, personality type, insight, and career), was used to collect comprehensive information about substance use through personal interviews with the participants [28]. The physically active category was defined as ≥ 150 minutes of moderated activity per week [11]. Data on smoking were collected through self-reported FANTASTIC questionnaire (number of cigarettes smoked per day). Ideal smoking status was determined as nonsmoker or quit smoking >12 months ago. The accuracy of the information about lifestyle covariables obtained from the FANTASTIC questionnaire has been validated with different cross-sectional studies and is described in detail elsewhere [28].

Body mass index was calculated as (body mass/height2) and was classified using the World Health Organization (WHO) criteria (normal: 18.5-24.9 kg/m2; overweight: 25.0-29.9 kg/m2; and obese: ≥30kg/m2) [40]

Dietary intake was measured using the test of Adherence to Mediterranean Died (KIDMED) [35]. This scale comprises 16 items with an affirmative or negative response; for example: "consumes fish regularly (at least 2-3 times per week)", which are related to patterns associated with the Mediterranean diet. Twelve of these items have positive connotations (+1) while the other four have negative values (-1). The final score ranges from -4 to +12. The total score ranges from -4 to +12. The total score was divided into two categories of Mediterranean diet quality: ≤ 7 points= poor diet quality and ≥ 8 points= good diet quality (optimal Mediterranean diet style). Participants who had ≥ 8 points were categorized as having an ideal healthy diet, whereas those with 7 point or less were classified as having a non-ideal diet. This instrument has a reliability of *Cronbach´s alpha*=0.86.

Cardiovascular Health Risk Factors. For blood measurements the participants were asked to arrive in a fasting state; abstain from exercise training, caffeine, nicotine, and alcohol 12 hours before the clinical examination; and continue their regular medication routines. Capillary blood samples (40 µL) were collected for determining serum biochemical parameters, including fasting glucose and total cholesterol, using portable Cardiocheck equipment (Mexglobal SA, Parsippany, NJ, USA).

Blood pressure was measured with an automatic monitor (Omrom HEM 705 CP; Health-care Co, Kyoto, Japan) following the recommendations of the European Heart Society (Each participant sat quietly with legs uncrossed for 5-10 minutes before blood pressure measurement with the arm supported at the level of the heart).

American Heart Association Criteria. The AHA guidelines [17] were used to determine the CVH profile based on the 7 metrics using the cutoff points for adults, with the participants receiving 1 point for the presence of each ideal metric. The ideal behaviors defined by the AHA are as follows: BMI <25kg/m2, physically active status (≥150 minutes of moderate activity per week), nonsmoking status (either never having smoked or having quit smoking >12 months ago), and a dietary pattern that promotes ideal CVH (≥8 points= good diet quality optimal Mediterranean diet style). The factors were classified as an untreated systolic blood pressure <120 mmHg and diastolic blood pressure <80 mm Hg, untreated total cholesterol ≤200mg/dL, and untreated fasting blood glucose <100 mg/dL.

2.4 Statistical Analyses

Descriptive statistics were computed and summarized; continuous variables are reported using mean values and SDs, and categorical variables are reported using proportions (%). The *t*-test was used to compare unadjusted means, and the chi-square test (x2) was used to explore sex group differences. The associations among NGS, adjusted muscle mass, and ideal CVH metrics and between ideal CVH behaviors and each factor separately were assessed using analysis of covariance. Analyses were conducted for men and women separately and adjusted by age, university center, and alcohol use. Alcohol use was defined as the consumption of any alcoholic beverage 1 to 9 times per week for at least 6 months. Finally using a logistic regression, ideal CVH metrics were examined as a continuous variable, considering the odds ratio (OR) per 1-metric increase in the overall profile to compare the prevalence of low NGS and low medium adjusted muscle mass. The data were analyzed using SPSS-IBM (software, v.22.0, SPSS, Inc., Chicago, IL, USA) and a value of $p \leq 0.05$ was considered statistically significant.

3. Results

The 1,835 participants included 1,128 females (61.4%), and the mean age was 20.56 (2.03) years. Male had lower body mass, height, muscle mass, muscle mass adjusted, blood pressure, handgrip, and NGS levels than female ($p<0.001$), and female had higher glucose and total cholesterol than male ($p<0.001$; Table 1)

Table 8. Characteristics of Colombian collegiate students (mean ± SD or frequencies), by sex

	Female (*n*=1,128)	**Male (*n*= 707)**	***p Value****
Age (y)	20.59 ± 2.09	20.51 ± 20.1	0.624
Body mass (kg)	58.79 ± 10.36	68.91 ± 12.23	<0.001
Height (cm)	159.10 ± 5.86	172.30 ± 6.66	<0.001
Body mass index (kg/m2)	23.21 ± 3.78	23.17 ± 3.60	0.810
Muscle mass (kg)	40.14 ± 3.38	55.08 ± 6.57	<0.001
Muscle mass/body mass	0.69 ± 0.07	0.80 ± 0.08	<0.001
Systolic blood pressure (mmHg)	111.29 ± 11.16	120.28 ± 12.97	<0.001
Diastolic blood pressure (mmHg)	71.74 ± 9.35	74.20 ± 11.45	<0.001
Glucose (mg/dL)	86.05 ± 11.58	84.81 ± 11.99	0.030
Total cholesterol (mg/dL)	146.39 ± 33.34	132.75 ± 30.24	<0.001
Alcohol (≥ 1 times per week), *n* (%)	404 (47.7)	317 (45.2)	0.318
Muscular strength			
Handgrip strength (kg)	24.16 ± 4.75	39.42 ± 7.15	<0.001

Normalized grip strength (NGS)	0.41 ± 0.09	0.58 ± 0.11	<0.001
Goal/ metric			
Not currently smoking, *n* (%)	596 (73.4)	485 (70.5)	0.212
Body mass index <25kg/m2, *n (%)*	827 (73.4)	526 (74.5)	0.616
Physically active, *n* (%)	231 (27.2)	251 (35.9)	<0.001
Healthy diet, *n* (%)	64 (7.5)	45 (6.4)	0.398
Total cholesterol <200 mg/dL, *n* (%)	1,056 (94.5)	676 (97.0)	0.012
Fasting glucose <100 mg/ dL, *n* (%)	1,022 (91.6)	633 (90.9)	0.644
Optimal blood pressure, *n* (%)	937 (83.4)	416 (59.0)	<0.001

**t-test or X^2 test was applied to compare unadjusted means by sex (p<0.001)*

Higher NGS and adjusted muscle mass levels were associated with a higher number of ideal CVH metrics in both sexes (*p* for trend <0.001; Figure 5)

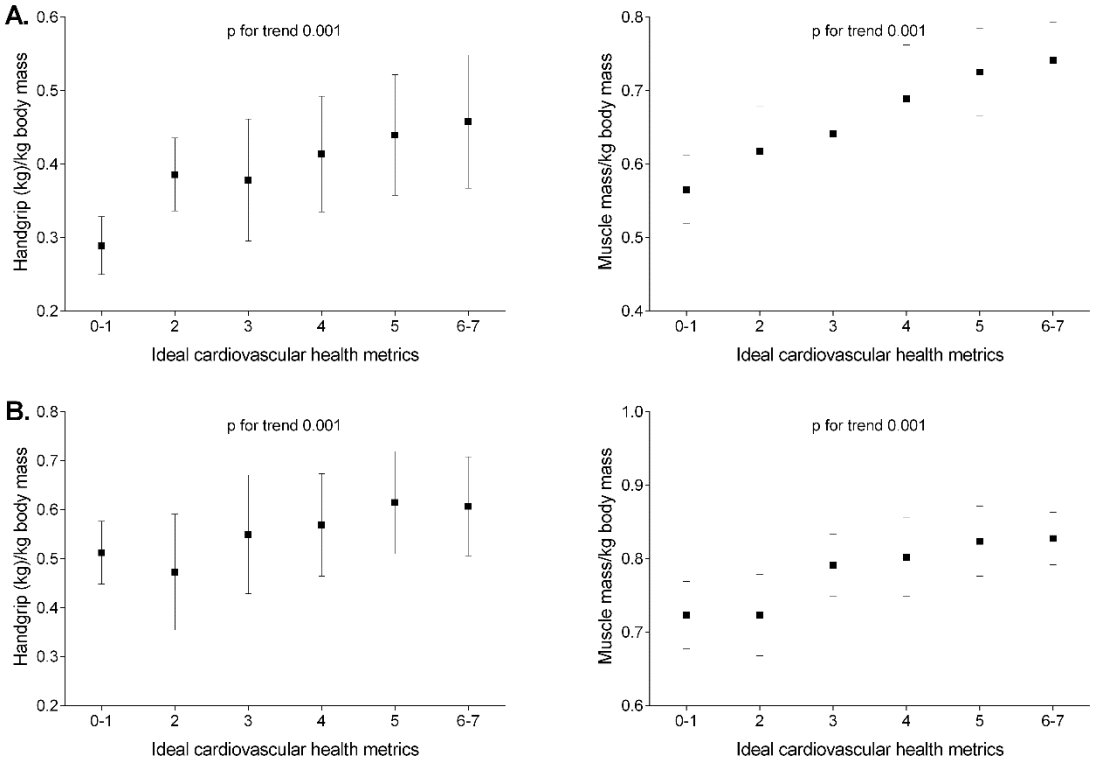

Figure 14. Association between normalized grip strength in college students.

(A) Female and (B) male. We collapsed 0 with 1 and 6 with 7 ideal metrics due to relatively few youths who had 0 (0.1% of total cohort), 1 (0.4% of total cohort), or 6 (12% of total cohort) and 7 (1% of total cohort) ideal CVH metrics. Normalized grip strength (measured as grip strength in kg/body mass). CVH= cardiovascular health.

In addition, higher NGS and adjusted muscle mass levels were associated with a higher number of ideal health behaviors (*p* for trend <0.001 in both male and female) and with a higher number of ideal health factors (*p* for trend <0.001 in both male and female; Figures 6 and 7).

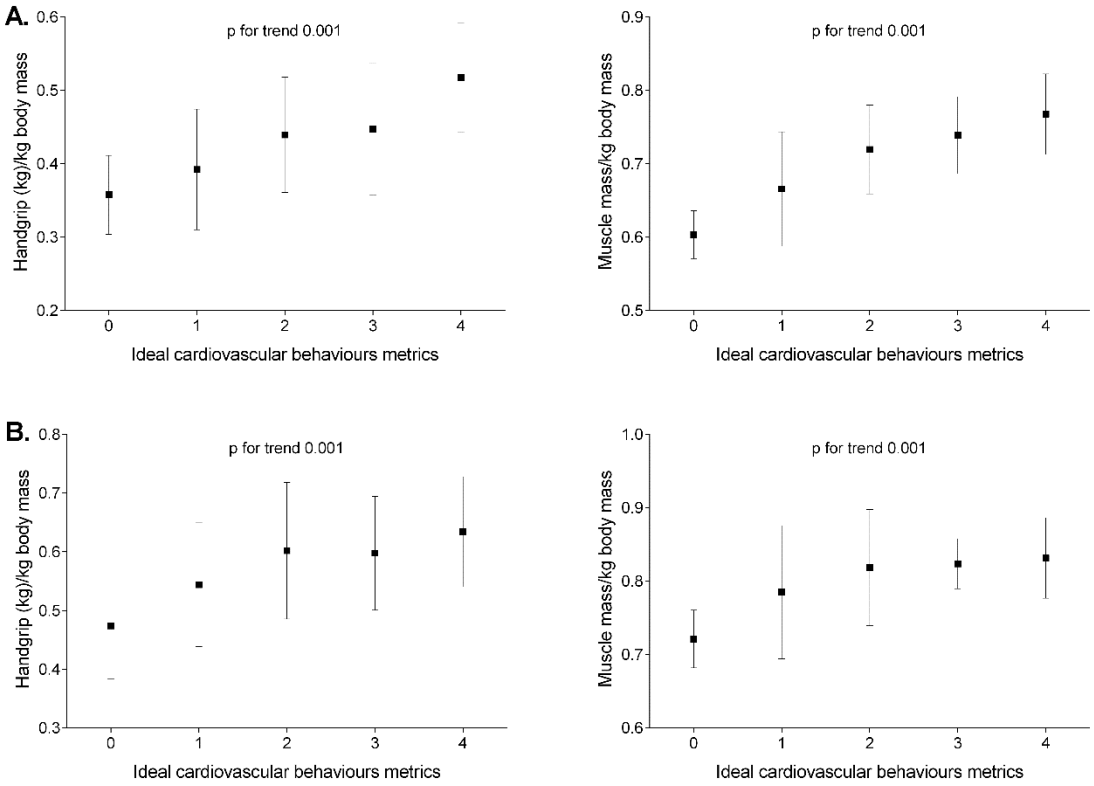

Figure 15. Association between normalized grip strength and adjusted muscle mass across ideal CVH behaviors in college students.

(A) Female and (B) male. Normalized grip strength (measured as grip strength in kg/body mass in kg). Adjusted muscle mass (muscle mass in kg/body mass in kg). Ideal CVH behaviors (smoking, body mass index, physical activity and Mediterranean diet adherence). CVH= cardiovascular health.

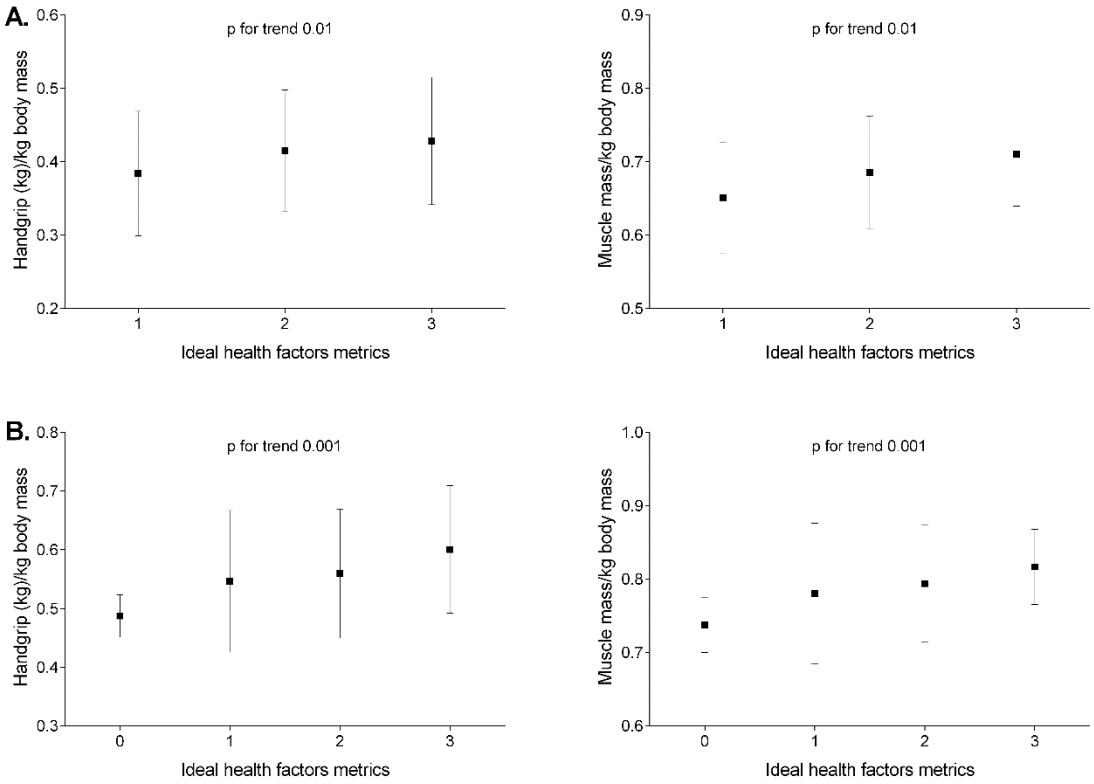

Figure 16. Association between normalized grip strength and adjusted muscle mass across ideal CVH factors in college students.

A) Female and B) male. Normalized grip strength (measured as grip strength in kg/body mass in kg). Adjusted muscle mass (muscle mass in kg/body mass in kg). Ideal CVH factors (total cholesterol, blood pressure, and plasma glucose). CVH= cardiovascular health.

Finally, for the total ideal CVH metrics on a continuous scale from 0 (all 7 poor) to 7 (all 7 ideal), a 1-metric increase was associated with reduced odds of weak NGS (male, OR=0.667 95% CI, 0.544-0.819, female, OR= 0.639 95% CI, 0.522-0.782) and low-medium muscle mass (male, OR=0.719 95% CI, 0.588-0.879, female, OR= 0.656 95% CI, 0.540-0796) (all $p<0.001$).

4. Discussion and conclusion

The findings of this study indicate that in Colombian college students, both handgrip strength and muscle mass are positively associated with the ideal CVH metrics determined by the AHA. These results are insightful considering the large reduction in overall fitness and PA levels observed in Latin American populations in recent decades [13,15]. However, similar to larger studies, we found that handgrip strength may be an underappreciated, modifiable determinant of cardiometabolic risk factors in adults [3].

Although there are very few studies on this topic, Ramírez-Vélez et al. [31] showed that greater handgrip strength was associated with a higher number of ideal CVH metrics in a young population, which, together with our results, seems to suggest that muscular strength should be considered a hallmark for meeting ideal CVH metrics. Along this line, previous studies have shown the relationship between the individual components of ideal CVH and handgrip strength in young adults. Regarding the ideal CVH factors that were analyzed, previous studies provide evidence that muscular strength

is protective against cardiometabolic risk factors [10]. For example, Magnussen et al. [19] reported that the negative association between muscle strength and cardiometabolic risk factors is independent of cardiorespiratory fitness or adiposity level. In addition, López-Martínez et al. [18] demonstrated that in college students, muscle strength is negatively associated with metabolic risk and its individual components. Also, the PURE study suggests that muscle strength is a risk factor for incident CVD and can predict the risk of death in people who develop either CVD or non-CVD in people of diverse economic and sociocultural backgrounds, including Latin American population [15].

A recent prospective study of 7,418 adults (46±9.5 years old) suggested that engaging in resistance exercise, even for less than 1 hour per week, is associated with a lower risk of developing metabolic syndrome, independent of whether the participant engages in aerobic exercise [2]. These results seem to suggest the need to promote increased muscle strength in adults to better manage cardiometabolic risk factors. In this sense, muscle strength training should be considered in the management of cardiometabolic risk factors because studies show that exercise training that aims to increase muscle strength in adults is associated with significantly improved cardiometabolic health [16] and muscle mass [39].

Regarding health behaviors, there is a well-established link between PA, healthy diet, muscular strength [14], and muscle mass [37]. Regular PA is a cornerstone strategy for managing cardiometabolic risk factors. As a consequence, agencies such as the American College of Sports Medicine recommend that adults aged between 18 and 64 years perform activities that increase bone and muscle strength, which includes resistance training, 2-3 days per week [11]. Another recent study of university student shows that the Mediterranean diet and PA are related to healthy body composition parameters in young adults [37]. In addition, a longitudinal study indicates that smoking is inversely related to muscle strength in healthy adults [12]. This may be because circulating cigarette smoke constituents seem to play an important role in the underlying molecular mechanisms of muscle damage, such as reduced oxygen delivery and impaired mitochondrial function [33].

The findings of this study are limited by the cross-sectional design; therefore, the direction of causality cannot be determined. In addition, ideal health behaviors were measured using a self-administered questionnaire, and so, some of the questions may have been misinterpreted deliberately or unintentionally by some of the college students. Finally, the categorization of the ideal CVH metrics relies on the use of binary variables and on the assumption that all risk factors and behaviors contained in this concept contribute equally to the final score.

5. Practical applications

This study shows for the first time the benefit of higher ideal CVH metrics for muscular strength and muscle mass in Colombian collegiate students. Therefore, to reduce the possible future public health burden of muscular weakness, physical educators, researchers, trainers, fitness professionals, physical therapists, and coaches need to encourage the public to optimize lifestyle-related risk factors during the young adult stage.

Financial support

The FUPRECOL Adults Study were design and funded by Ramirez-Velez Robinson (IP). Additionally, FUPRECOL has been partially supported by the Universidad del Rosario (Code N° FIUR DN-BG001), Institución Universitaria Antonio José Camacho (Code N° 111-02.01.48/16). Universidad Santo Tomás (Code N°2013004), Universidad Manuela Beltrán (Code N° FT201204), and Universidad de Boyacá (Code N° RECT60). The funder had no role in the study design, data collection, data analysis and interpretation, preparation of the manuscript, or decision to publish.

6. Reference

[1] Artero EG, Lee De, Lavie CJ, España-Romero V, Sui X, Church TS, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev* 2012;32:351.

[2] Bakker EA, Lee DC, Sui X, Artero EG, Ruiz JR, Eijsvogels TMH, et al. Association of resistance exercise, independent of and combined with aerobic exercise, with the incidence of metabolic syndrome. *Mayo Clin Proc* 2017;92:1214-1222.

[3] Bohannon RV. Muscle strengtrh: Clinical and prognostic value of hand-grip dynamometry. *Curr Opin Clin Nutr Metab Care* 20155;18:465-470.

[4] Burke JD, Reilly RA, Morrell JS, Lofgren IE. The University of New Hampshire´s young adult health risk screening initiative. *J Am Diet Assoc* 2009;109:1751-1758.

[5] Chaparro-Narváez P, Castañeda-Orjuela C, León-Quevedo W, De la Hoz-Restrepo F. Cardiovascular disease mortality among under 75 years old population: An analysis in Colombia of 1998-2011 period. *Int J Health Sci Res* 2015;5:325-338.

[6] Collins KM, Dantico M, Shearer NB and Mossman KL. Heart disease awareness among college students. *J Community Health* 2004;29:405-420.

[7] Desai CS, Ning H, Liu K, Reis JP, Gidding SS, Armstrong A, et al. Cardiovascular health in young adulthood and association with left ventricular structure and function later in life: The coronary artery risk development in young adults study. *J Am Soc Echocardiogr* 2015;28:1452-1461.

[8] Fonseca-Camacho D, Hernández-Fonseca J, Gonzalez-Ruíz K, Tordecilla-Sanders A, Ramírez-Vélez R. A better self-perception of physical fitness is associated with lower prevalence of metabolic syndrome and its components among university students. *Nutr Hosp* 2015;31:1254-1263.

[9] García-Hermoso A, Cavero-Redondo I, Ramírez-Vélez R, Ruíz J, Ortega FB, Lee DC, et al. Muscular strength as a predictor of all-cause mortality in apparently healthy population: A systematic review and meta-analysis of data from approximately 2 million men and women. *Arch Phys Med Rehabil* 2018;99:2100-2113.

[10] García-Hermoso A. Tordecilla-Sanders A, Correa-Bautista JE, Peterson MD, Izquierdo M, Quino-Ávila AC, et al. Muscle strength cut-off for the detection of metabolic syndrome in a non-representative sample of collegiate students from Colombia. *J Sport Health Sci. 2018.* E pub ahead of print.

[11] Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;116:1081-1093.

[12] Kok MO, Hoekstra T, and Twisk JW. The longitudinal relation between smoking and muscle strength in healthy adults. *Eur Addict Res* 2012;18: 70–75

[13] Lear SA, Hu W, Rangarajan S, Gasevic D, Leong D, Iqbal R, et al. The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: The PURE study. *Lancet* 2017;390: 2643–2654.

[14] Lee KS, Lee JK, and Yeun, YR. Effects of a 10-day intensive health promotion program combining diet and physical activity on body composition, physical fitness, and blood factors of young adults: A randomized pilot study. *Med Sci Monit* 2017;23: 1759–1767.

[15] Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A, Orlandini A, et al. Prognostic value of grip strength: Findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet* 2015;386: 266–273

[16] Lin X, Zhang X, Guo J, Roberts CK, McKenzie S, Wu WC, et al. Effects of exercise training on cardiorespiratory fitness and biomarkers of cardiometabolic health: A systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2015;4: e002014

[17] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction. *Circulation* 2010; 121: 586–613

[18] López-Martínez S, Sánchez-López M, Solera-Martinez M, Arias Palencia N, Fuentes-Chacón RM, and Martínez-Vizcaíno V. Physical activity, fitness, and metabolic syndrome in young adults. *Int J Sport Nutr Exerc Metab* 2013;23: 312–321.

[19] Magnussen CG, Schmidt MD, Dwyer T, and Venn A. Muscular fitness and clustered cardiovascular disease risk in Australian youth. *Eur J Appl Physiol* 2012;112: 3167–3171

[20] Mancia G, Fagard R, Narkiewicz K, Redán J, Zanchetti A, Böhm M, et al. 2013 practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of Arterial Hypertension. *J Hypertens* 2013;31: 1925– 1938.

[21] Marfell-Jones MJ, Stewart A, and De Ridder J. International Standards for Anthropometric Assessment. Potchefstroom, South Africa: ISAK, 2006. pp. 1–37.

[22] Martínez-Torres J, Correa-Bautista JE, González-Ruíz, K, Vivas, A, Triana-Reina, HR, Prieto-Benavidez, DH, et al. A cross-sectional study of the prevalence of metabolic syndrome and associated factors in Colombian collegiate students: The FUPRECOL-adults study. *Int J Environ Res Public Health* 2017;14: 233, 2017.

[23] Mathers CD and Loncar D. Updated Projections of Global Mortality and Burden of Disease, 2002–2030: Data Sources, Methods and Results. Geneva, Switzerland: World Health Organization, 2005. https:// www.who.int/healthinfo/statistics/bod_projections2030_paper.pdf. Accessed June 1, 2013.

[24] Morrell JS, Lofgren IE, Burke JD, and Reilly RA. Metabolic syndrome, obesity, and related risk factors among college men and women. *J Am Coll Health* 2012;60: 82–89.

[25] Naghavi M, Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016. *Lancet* 2017;390: 1151–1210.

[26] Oikonen M, Laitinen TT, Magnussen CG, Steinberger J, Sinaiko AR, Dwyer T, et al. Ideal cardiovascular health in young adult populations from the United States, Finland, and Australia and its association with cIMT: the International Childhood Cardiovascular Cohort Consortium. *J Am Heart Assoc* 2013;2: e000244.

[27] Parto P and Lavie CJ. Obesity and cardiovascular diseases. *Curr Probl Cardiol* 2017;42: 376–394.

[28] Ramírez-Vélez R and Agredo RA. The Fantastic instrument's validity and reliability for measuring Colombian adults' life-style [in Spanish]. *Rev Salud Publica (Bogota)* 2012;14: 226–237.

[29] Ramírez-Vélez R, Correa-Bautista JE, Sanders-Tordecilla A, Ojeda Pardo ML, Cobo-Mejía EA, Castellanos-Vega R P, et al. Percentage of body fat and fat mass index as a screening tool for metabolic syndrome prediction in Colombian university students. *Nutrients* 2017;9: e1009.

[30] Ramírez-Vélez R, Saavedra JM, Lobelo F, Celis-Morales CA, del Pozo-Cruz B, and García-Hermoso, A. Ideal cardiovascular health and incident cardiovascular disease among adults: A systematic review and meta-analysis. *Mayo Clin Proc* 20128;93: 1589–1599.

[31] Ramírez-Vélez R, Tordecilla-Sanders A, Correa-Bautista JE, Peterson MD, and Garcia-Hermoso, A. Handgrip strength and ideal cardiovascular health among colombian children and adolescents. *J Pediatr* 2016; 179: 82–89.e81.

[32] Rodríguez-Rodríguez F, Cristi-Montero C, González-Ruíz K, Correa-Bautista JE, and Ramírez-Vélez R. Bioelectrical impedance vector analysis and muscular fitness in healthy men. *Nutrients* 2016; 8: 407.

[33] Rom O, Kaisari S, Aizenbud D, and Reznick AZ. Identification of possible cigarette smoke constituents responsible for muscle catabolism. *J Muscle Res Cell Motil* 2012;33: 199–208.

[34] Seron P, Irazola V, Rubinstein A, Calandrelli M, Ponzo J, Olivera H, et al. Ideal cardiovascular health in the southern cone of Latin America. *Public Health* 2018;156: 132–139.

[35] Serra-Majem L, Ribas L, Ngo J, Ortega RM, Garcia A, Pérez RC, Aranceta J. Food, youth and the Mediterranean diet in Spain. Development of KIDMED, Mediterranean diet quality index in children and adolescents. *Public Health Nutr* 2004;7: 931–935.

[36] Stampfer MJ, Hu FB, Manson JE, Rimm EB, and Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000;343: 16–22.

[37] Stefan L, ˇCule M, Milinovi´c I, Juranko D, and Spori ˇs G. The relationship between lifestyle factors and body composition in young adults. *Int J Environ Res Public Health* 2017;14: e893.

[38] TANITA Institute. Technology for measuring the VAT accumulation risk through bioelectrical impedance analysis (BIA) in comparison with image analysis applied to magnetic resonance imaging (MRI). Abstracts of the NAASO (North American Association for the Study of Obesity) Annual Meeting. November 14-18, 2004, Las Vegas, Nevada, USA. *Obes Res*. 2004;12 Suppl: A1-246.

[39] Terzis G, Georgiadis G, Stratakos G, Vogiatzis I, Kavouras S, Manta P, et al. Resistance exercise-induced increase in muscle mass correlates with p70S6 kinase phosphorylation in human subjects. *Eur J Appl Physiol* 2008; 102: 145–152.

[40] World Health Organization. Obesity: Preventing and Managing the Global Epidemic: World Health Organization, 2000. https://www. who.int/nutrition/publications/obesity/WHO_TRS_894/en/. Accessed June 1, 2013.

Chapter 5: General Discussion

Detection of Metabolic Syndrome by body composition and muscular strength screening tools (Study I-II)

MetS is defined as a cluster of interconnected factors (central obesity, elevated blood pressure, impaired glucose tolerance and atherogenic dyslipidaemia) that increase the risk of coronary heart disease, stroke and type 2 diabetes; it has been related to insulin resistance, obesity and muscular weakness, independent of age and body size [1-5]. These are considered the result of behavioural factors like physical inactivity and excess food fat intake [1,3]. In this sense, there is growing evidence that highlights different measures of central body obesity (such as waist circumference-WC, waist-hip ratio-WHR, body mass index-BMI) and muscular strength (MS- such as normalised handgrip strength- NGS) as being strongly related to MetS risk [4,6-8].

In clinical practice, the bioelectrical impedance analysis (BIA) is the most frequently used method to assess body composition and calculate BF%, due to its simplicity, low cost and highest correlation with gold standards such as dual-energy X-ray absorptiometry (DXA) or computed tomography (CT) [9]. According to this context, one of the studies that composes this thesis, proposed body fat percentage (BF%) and fat mass index (FMI), based on BIA, as screening tools which can estimate the fat mass and body adiposity dysfunction associated with MetS. This is because of the strongest relation with the components of MetS (mean arterial pressure, glucose, HDL-C, triglycerides, total cholesterol and waist circumference, $p<0.05$ for all). The results are similar to those presented by Knowles et al. [10], who found correlations between WC, BMI, WHR, Waist height ratio, and Visceral adiposity index (VAI) with MetS components ($p<0.001$).

In this sense, it was found that BF% and FMI had a moderate discriminatory power in the identification of MetS for both sexes in Colombian young adults, according to the Receiver Operating Characteristic (ROC) analysis (BF%: Area Under the Curve - AUC=0.835, % sensitivity=96.1, % specificity= 57.5 for men; AUC= 0.887, % sensitivity=97.4, % specificity= 55.9 for women, both $p<0.001$*;* FMI: AUC=0.838, % sensitivity=95.8, % specificity= 56.2 for men; AUC= 0.889, % sensitivity= 97.6, % specificity=56.9 for women, both $p<0.001$). When these results are compared with similar studies carried out among adults, some discrepancies were found for BF%, which showed limited effectiveness for predicting MetS compared to other body composition indexes; this could be explained by the heterogeneity of the populations. [11,12]. Besides, other researchers such Peltz et al. [13] determined the accuracy of FMI as a convenient tool for assessing obesity compared with BF%, using BIA as the reference method; they found a correlation coefficient of 0.976 in men and 0.992 in women (both *$p<0.001$).* On the other hand, the results of our study about the FMI cut-offs (≥ 6.9 kg/m^2 in men and ≥ 11.8 kg/m^2 in women), was similar to those presented by Schutz et al. [14], who defined the overfat status when FMI is greater than 8.2 kg/m^2 in men and 11.8 kg/m^2, which contribute to the development of a set of recommended ranges to predict MetS.

As an approximate physiological mechanism explanation of our results, the determination of BF% and FMI as measures of the distribution of fatty adipose tissue are highlighted, which is considered one of the predominant underlying risk factors of the appearance of MetS, as a result of behavioural factors like physical inactivity and excess food fat intake, which generate excess energy that is stored as subcutaneous or visceral fat [1,3]. The visceral adipose tissue, specifically constituted by white adipose tissue, is metabolically active and secretes dozens of hormones, free fatty acids (FFA), adipocytokines and inflammatory factors (TNF-α, interleukin 6, angiotensinogen, PAI-1, and resistin) [15,16,17,]. In this sense, the of fat accumulation generates a destructive effect on glucose

metabolism, like insulin resistance and pancreatic beta cell dysfunction; this is defined as lipotoxicity, and is characterised by impaired glucose oxidation and glycogen synthesis and decreased glucose transport-phosphorylation as a result of the fat accumulation of intracellular toxic metabolites of FFA as triacylglycerol (TAG) [1,18,19].

Other measures related to MetS risk include MS from the HGS, which is recognised as a simple inexpensive measure of overall MS and useful prognostic indicator of mortality; when corrected for body mass, it is associated with a higher prevalence of MetS in adults, independent of age and body size, and is considered to reflect muscle mass as an important health indicator [4, 5]. In this sense, the second study that composes this thesis proposed NGS cut-off for the detection of MetS in a collegiate student population from Colombia, taking into account that this is one of the first studies to identify sex specific cut-offs in this population.

This study proposes three cardiometabolic risk categories for NGS by sex, catalogued as weak (<0.466 for men and <0.332 for women, p<0.001 for both), intermediate (0.466-0.615 for men and 0.0332-0.437 for women, p<0.001 for both) and strong (>0.615 for men and >0.437 for women); the AUC was shown to be acceptable (>0.72, % sensitivity > 84.0, % specificity > 56.0, p<0.001) for men and women. Therefore, when comparing the MetS phenotype by cut-off for NGS, it was found that, among males in the highest strength category, 4.9% had MetS, in the intermediate strength category 10.7% and in the low strength category 34.6% had MetS. In women in the highest category, only 2.4% had the MetS phenotype, compared with 7.9% and 18% among females with intermediate and low strength, respectively.

Different studies showed similar results, like that of Senechal et al. [20], whose objective was to identify a threshold of muscle strength (using normalised strength from the chest press and leg press) associated with MetS in 5685 men aged <50 years and 1541 men aged >50 years; low MS was established as the lowest age-specific 20th percentile and high MS was above 20th percentile. The study found that in men aged <50 years, the threshold of MS associated with MetS was 2.57 kg, with the odds of MetS in the first group being 2.20 (95%CI: 1.89-2.54) higher in those with low MS, independent of age, smoking, and alcohol intake. Likewise, Lee et al. [21] demonstrated that individuals with relative handgrip strength (absolute hand-grip strength divided by BMI), in the 75th percentile compared with the 25th percentile, had a 54% lower cardiometabolic risk.

In this sense, Peterson, et al. [22] established the importance of MS measured as NHS due its association with cardiometabolic disease and physical disabilities in middle-age to older men and women; for the loss of every 0.05 kg of MS, the odds of diabetes in American adults increased by 49%, the odds of hyperglycaemia by 46%, the odds of hypertriglyceridemia by 15%, the odds of low HDL-cholesterol by 22%, the odds of hypertension by 19%, and the odds of disability status by 36% (all p<0.01). Similar works were presented by Ramírez-Vélez et al. [23], who determined the association between the new ratio of NHS and increased visceral fat level mass (MVF), and the prevalence of MetS and Ideal CVH; they found that subjects with lower MVF ratio (Q1) showed worse CVH metrics (accomplishment 0-2 metrics) and a higher prevalence of MetS (32.2%, p<0.0001*)* in young Colombian adults.

Therefore, these findings allowed different strategies to be determined, like resistance training, as part of the physical activity recommendations for the primary and secondary prevention of MetS and associated chronic diseases in adults; this was due to the role of skeletal muscle in the metabolism of glucose and triglycerides [24,25]. Several studies have elucidated the health impact of physical activity and exercise to increase mitochondrial oxidative capacity and skeletal muscle capillarisation

and generate anti-inflammatory effects which contribute to improved insulin signalling, glucose uptake and metabolic flexibility [26]. The interventional study by Tomeleri et al. [27] has shown that 12 weeks of resistance training reduces MetS components (glucose: -20.4%, waist circumference: -1.5% and systolic blood pressure: -6.2%, all $p<0.05$) and inflammatory biomarkers (CRP: -28.6%, TNF-α: -21.6%, all *$p<0.05$*), and generates different body composition and physical fitness levels, like reduced body fat (-6.0%, $p<0.01$), increased skeletal muscle mass (+6.1 kg, $p<0.01$) and MS (+14.0, $p<0.001$) in older women.

However, due to the cross-sectional nature of the study design, it was not possible to determine causal relationships, suggesting that future longitudinal studies are needed to better understand the physiological mechanism that explains how body fat contributes to health risks in college-aged adults.

Cardiovascular Health and muscular strength (Study III)

With the rising rates of deaths from CVD, which is considered the number one cause of death globally [28, 29], Cardiovascular health (CVH) has been considered the highest strategic impact goal, with focus on reducing cardiac heart disease and stroke death rates and the prevalence of risk factors by 20%, through the adoption of seven metrics comprise four healthy behaviours (abstinence from smoking, ideal body mass index [BMI], physical activity at goal and consumption of a healthy diet that promotes CVH) and three physiological health factors (untreated total cholesterol <200mg/dL, untreated blood pressure <120/<80 mm Hg, and absence of T2DM) [30].

In this sense, several studies have established that young adults who reach middle age with some health behaviours and factors (cholesterol, blood pressure and no cigarette consumption), have a lower risk of developing CVD and greater longevity; this highlights the importance of identifying and treating CVD risk factors at an early age [31-33]. The results may be supported by the systematic review and meta-analysis by Ramirez-Vélez et al. [34], which established that the incidence of CVD was lower (*HR=0.28, 95%CI: 0.23-0.33, p<0.001, I2=72.0%)* in individuals who had an ideal CVH profile (achieve 5-7 metrics) compared with individuals with a poor ideal CVH profile (meeting only 1-2 metrics).

On the other hand, the role of physical fitness as one of the strongest predictors of individual future health status is well established, and is characterised by the ability to perform daily activities with vigour. These daily activities can be performed through capacities that are associated with a low risk of the development of chronic diseases and premature death, especially cardiorespiratory fitness and MS, and specifically, as mentioned above, because MS is considered as an indicator for preventing cardiometabolic risk and mortality in several populations, thus highlighting its importance [24, 35,36].

In this sense, the third study that composed this thesis had the purpose of investigating the relationship between MS (determined as handgrip strength), muscle mass, and ideal CVH among Colombian College students, taking into account that only one study has analysed this relationship in the Colombian population, specifically in children and adolescents [37]

The findings of this study indicate that, in Colombian college students, MS and muscle mass are positively associated with ideal CVH metrics, which are similar to the results presented by Ramirez-Vélez et al. [37]. In the same line, different studies such the PURE study, suggest that MS is a risk factor for incident CVD and is catalogued as a predictive tool to identify the risk of death in people who develop CVD [35]. In this sense, the protective effect of muscle strength training on improved health parameters such as cardiometabolic health and muscle mass is well established, and can be

explained by the role of muscle as an endocrine organ [38-40]. The muscle has anti-inflammatory properties for the release of cytokines such IL-6, IL-1ra and IL-10, which together help with the reduction of FFA, suppress TNF-α expression, down-regulate TLR 4 expression and reduce the activation of NF-kB signalling and cytokine production; consequently, this improves glucose homeostasis and lipolysis during exercise [27, 41-44].

Besides, the link between physical activity, a healthy diet, and muscular strength on CVH is well-established, due the beneficial effect on vascular function; this implicates the increase in shear stress on the vascular lumen, generating the activation of acetylcholine (Ach) signalling and phospholipase activity in endothelial cells, due to an increase in intracellularly released Ca_2, prostaglandin I2 (PGI2), and the relaxation of smooth muscle cells by the cyclic adenosine monophosphate (cAMP) action. Also, phosphoinositide 3-kinase (PI3K) is activated for the vascular endothelial growth factor receptor 2 (VEGFR2) activity, which induces phosphorylated protein kinase B (AKT)-mediated nitric oxide synthase endothelium (eNOS) phosphorylation, leading to the increased production of NO [45].

However, the findings of this study are limited by the cross-sectional nature of the study design, which means that the causality direction cannot be determined.

Reference

[1] Samson SL, Garber AJ. Metabolic Syndrome. *Endocrinol Metab Clin North Am.* 2014;43(1):1-23. Doi: 10.1016/j.ecl.2013.09.009.

[2] Alshehri AM. Metabolic Syndrome and cardiovascular risk. *J Family Community Med.* 2010;17(2):73-78.

[3] O´Neill S, O´Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev.* 2015;16(1):1-12. Doi: 10.1111/obr.12229.

[4] Jurca R, Lamonte MJ, Barlow CE, Kampert JB, Church TS, Blair SN. Association of muscular strength with incidence of metabolic syndrome in men. *Med Sci Sports Exerc.* 2005;37(11):1849-55. Doi: 10.1249/01.mss.0000175865.17614.74

[5] Byeon JY, Lee MK, Yu MS, Kang MJ, Lee DH, Kim KC, et al. Lower Relative Handgrip Strength is Significantly Associated with a higher prevalence of the Metabolic Syndrome in Adults. *Metab Syndr Relat Disord.* 2019;17(5):280-288. Doi: 10.1089/met.2018.0111.

[6] González-Muniesa P, Martínez-González MA, Hu EB, Després JP, Matsuzawa Y, Loos RJF, Moreno LA, Bray GA, Martínez JA. Obesity. *Nat Rev Dis Prim* 2017;3:17034

[7] Bener A, Yousafzai MT, Darwish S, Al-HAmaq AO, Nasralla EA, Abdul-Ghani M. Obesity index that better predict metabolic syndrome: Body mass index, waist circumference, waist hip ratio, or waist height ratio. *J Obes* 2013;2013:269038

[8] López-Martínez S, Sánchez-López M, Solera-Martínez M, Arias-Palencia N, Fuentes-Chacón RM, Martínez-Vizcaíno V. Physical activity, fitness, and metabolic syndrome in Young adults. *Int J Sport Nut Exerc Metab* 2013;23:312-21.

[9] Xu L, Cheng X Wang J, Cao Q, Sato T, Wang M, Zhao X, Liang W. Comparisons of body-composition prediction accuracy: a study of 2 biolectric impedance consumer devices in healthy Chinese persons using DXA and MRI as criteria methods. *J Clin Densitom* 2011;14:458-464.

[10] Knowles KM, Paiva LL, Sanchez SE, Revilla L, Lopez T, Yasuda MB, Yanez ND, Gelaye B, Williams MA. Waist circumference, body mass index, and other measures of adiposity in predicting cardiovascular disease risk factors among Peruvian adults. *Int J Hypertens* 2011;2011:1-10.

[11] Mohammadreza B, Farzad H, Davoud K, Fereidoun AF. Prognostic significance of the complex "Visceral Adiposity Index" vs. simple anthropometric measures: Tehran lipid and glucose study. *Cardiovasc Diabetol* 2012;11:20.

[12] Mousa U, Kut A, Bozkus Y, Cicek Demir C, Anil C, Bascil Tutuncu N. Performance of abdominal bioelectrical impedance analysis and comparison with other known parameters in predicting the metabolic syndrome. *Exp Clin Endocrinol Diabetes* 2013, 121, 391-396.

[13] Peltz G, Aguirre MT, Sanderson M, Fadden MK. The role of fat mass index in determining obesity. *Am J Hum Biol* 2010; 22: 639-647.

[14] Schutz Y, Kyle U, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasions aged 18-98 years. *Int J Obes* 2002;26:953-960.

[15] Saklayen MG. The Global Epidemic of the Metabolic Syndrome. *Curr Hypertens Rep.* 2018;20(2):12. Doi: 10.1007/s11906-018-0812-z.

[16] Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab.* 2004;89(6):2548-56. Doi: 10.1210/jc.2004-0395.

[17] Carobbio S, Pellegrinelli V, Vidal-Puig A. Adipose tissue function and expandability as determinants of lipotoxicity and the Metabolic Syndrome. *Adv Exp Med Biol.* 2017;960:161-196. Doi: 10.1007/978-3-319-48382-5_7.

[18] Yazici D, Sezer H. Insuline resistance, Obesity and Lipotoxicity. *Adv Exp Med Biol.*2017;960:277-304. Doi: 10.1007/978-3-319-48382-5_12.

[19] Van Pelt DW, Newsom SA, Schenk S, Horowitz JF. Relatively low endogenous fatty acid mobilization and uptake helps preserve insulin sensitivity in obese women. *Int J Obes. (Lond).* 2015;39(1):149-55. Doi: 10.1038/ijo.2014.70.

[20] Senechal M, McGavock JM, Church TS, Lee DC, Earnest CP, Sui X, et al. Cut points of muscle strength associated with metabolic syndrome in men. *Med Sci Sports Exerc* 2014;46:1475-81.

[21] Lee WJ, Peng LN, Chiou ST, Chen LK. Relative handgrip strength is a simple indicator of cardiometabolic risk among middle-aged and older people: a nationwide population-based study in Taiwan. *PLoS One* 2016;11:e0160876. Doi:10.1371/journal.pone.0160876.

[22] Peterson MD, Duchowny K, Meng Q, Wang Y, Chen X, Zhao Y. Low Normalized Grip Strength is a Biomarker for Cardiometabolic Disease and Physical Disabilities Among U.S. and Chinese Adults. *J Gerontol A Biol Sci Med Sci.* 2017;72(11):1525-1531. Doi:10.1093/Gerona/glx031.

[23] Ramírez-Vélez R, Correa-Rodríguez M, Izquierdo M, Schmidt-RioValle J, González-Jiménez E. Muscle fitness to visceral fat ratio, metabolic syndrome and ideal cardiovascular health metrics. *Nutrients.* 2018;11(1). Pii.E24. Dooi: 10.3390/nu11010024.

[24] Artero EG, Lee DC, Lavie CJ, España-Romero V, Sui X, Chruch TS, Blair SN. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev.* 2012;32(6):351-8. Doi: 10.1097/HCR.0013e3182642688.

[25] Stump CS, Henriksen EJ, Wei Y, Sowers JR. The metabolic syndrome: a role of skeletal muscle metabolism. *Ann Med*. 2006;38(6):389-402. Doi: 10.1080/07853890600888413.

[26] Wijndaele K, Duvigneaud N, Matton L, Duquet W, Thomis M, Beunen G, et al. Muscular strength, aerobic fitness, and metabolic syndrome risk in Flemish adults. *Med Sci Sports Exerc.* 2007:39(2):233-40. Doi: 10.1249/01.mss.0000247003.32589.ag

[27] Tomeleri CM, Souza MF, Burini RC, Cavaglieri CR, Ribeiro AS, Antunes M, et al. Resistance training reduces metabolic syndrome and inflammatory markers in older women: A randomized controlled trial. *J Diabetes.* 2018;10(4):328-337. Doi: 10.1111/1753-0407.12614.

[28] World Health Organization. Cardiovascular disease. [internet]. 2017 [cited 2019 Jun]. Available from: https://www.who.int/cardiovascular_diseases/about_cvd/en/

[29] Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, et al. Reducing the Global Burden of Cardiovascular Disease, Part 1: The Epidemiology and Risk Factors. *Circ Res.* 2017; 121:677-694. DOI: 10.1161/CIRCRESAHA.117.308903.

[30] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association´s strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121(4):586-613. Doi:10.1161/CIRCULATIONAHA.109.192703.

[31] Stamler J, Stamler R, Neaton JD, Wentworth D, Daviglus ML, Garside D, et al. Low Risk-Factor Profile and Long-term Cardiovascular and Noncardiovascular Mortality and Life Expectancy: Findings for 5 Large Cohorts of Young Adult and Middle-Aged Men and Women. *JAMA* 1999;282(21):2012-8.

[32] Casagrande SS, Menke A, Cowie CC. Cardiovascular Risk Factors of Adults Age 20-49 Years in the United States, 1971-2012: A series of Cross-Sectional Studies. *PloS One.*2016;11(8): e0161770. Doi: 10.1371/journal.pone.0161770.

[33] Bucholz EM, Gooding HC, de Ferranti SD. Awareness of Cardiovascular Risk Factors in U.S. Young Adults Aged 18-39 Years. Am J Prev Med. 2018;54(4):e67-77.

[34] Ramírez-Vélez R, Saavedra JM, Lobelo F, Celis-Morales CA, Pozo-Cruz BD, García-Hermoso A. Ideal Cardiovascular Health and Incident Cardiovascular Disease Among Adults: A Systematic Review and Meta-analysis. *Mayo Clin Proc.* 2018;93(11):1589-1599. Doi: 10.1016/j.mayocp.2018.05.035.

[35] Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*. 2015;386(9990):266-73. Doi: 10.1016/S014-6736(14)62000-6.

[36] García-Hermoso A, Cavero-Redondo I, Ramírez-Vélez R, Ruiz JR, Ortega FB, Lee D-C, et al. Muscular Strength as a Predictor of All-Cause Mortality in an Apparently Healthy Population: A Systematic Review and Meta-Analysis of Data from Approximately 2 Million Men and Women. Arch Phys Med Rehabil. octubre de 2018;99(10):2100-2113.e5.

[37] Ramírez-Vélez R, Tordecilla-Sanders A, Correa-Bautista JE, Peterson MD, and Garcia-Hermoso, A. Handgrip strength and ideal cardiovascular health among Colombian children and adolescents. *J Pediatr* 2016; 179: 82–89.e81.

[38] Phillips SA, Mahmoud AM, Brown MD, Haus JM. Exercise interventions and peripheral arterial function: implications for cardiometabolic disease. *Prog Cardiovasc Dis.* 2015;57(5):521-34. Doi: 10.1016/j.pcad.2014.12.005.

[39] Lin X, Zhang X, Guo J, Roberts CK, McKenzie S, Wu WC, et al. Effects of Exercise Training on Cardiorespiratory Fitness and Biomarkers of Cardiometabolic Health: A systematic Review and Meta- Analysis of Randomized Controlled Trials. *J Am Heart Assoc.* 2015;4(7). Pii: e002014. Doi: 10.1161/JAHA.115.002014.

[40] Terzis G, Georgiadis G, Stratakos G, Vogiatzis I, Kavouras S, Manta P, et al. Resistance exercise-induced increase in muscle mass correlates with p70S6 kinase phosphorylation in human subjects. *Eur J Appl Physiol* 2008; 102: 145–152.

[41] Rada I, Deldioque L, Francaux M, Zbinden-Foncea H. Toll like receptor expresión induced by exercise in obesity and metabolic syndrome: a systemic review. *Exerc Immunol Rev.* 2018;24:60-71.

[42] Pedersen BK. Exercise-induced myokines and their role in chronic diseases. *Brain Behav Immun.* 2011;25(5):811-6. Doi: 10.1016/j.bbi.2011.02.010.

[43] Pedersen BK, Fischer CP. Physiological roles of muscle-derived interleukin-6 in response to exercise. *Curr OPin Clin Nutr Metab Care.* 2007;10(3):265-71. Doi: 10.1097/MCO.0b013e3280ebb5b3.

[44] Pedersen BK, Febbraio MA. Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiol Rev.* 2008;88(4):1379-406. Doi: 10.1152/physrev.90100.2007.

[45] Fernandes T, Gomes-Gatto CV, Pereira NP, Alayafi YR, das Neves VJ, Oliveira EM. NO signaling in the Cardiovascular System and Exercise. *Adv Exp Med Biol.*2017;1000:211-245. Doi: 10.1007/978-981-10-4304-8_13.

Chapter 6: Conclusions, practical applications and future perspectives

Study 1 (chapter 2)

Conclusion 1: In the first study, it can be conclude that BF% and FMI had a moderate discriminatory power in the identification of MetS in Colombian university students and is demonstrated that a BF% ≥ 38.9% in women and ≥25.5% in men, and an FMI ≥11.8 kg/m^2 in women and ≥ 6.9 kg/m^2 in men, are thresholds that could be used to predict Colombian young adults at high risk of MetS. This study reports the first cutoff points for identification of MetS by BF% and FMI in Colombian young adults.

Practical application 1: This study demonstrates the discriminatory capability of the BF% and FMI in the detection of MetS in University students, which highlight the important implications for evaluating CVD and MetS risks factors.

Future perspective 1: Longitudinal studies are required to elucidate the mechanisms responsable that explain how body fat contribute to health risks in college-aged adults.

Study 2 (chapter 3)

Conclusion 2: In summary, the sex-specific NGS cut-offs could be incorporated into a clinical setting for identifying college students at high cardiometabolic disease risk and used as a target for strength training programs designed to reduce the risk of MetS. Longitudinal studies are necessary to determine of increasing handgrip strength reduces the likelihood of MetS.

Practical application 2: This study demonstrates the discriminatory capability of the NGS in the detection of MetS in University students, which highlight the important implications for evaluating CVD and MetS risks factors.

Future perspective 2: Longitudinal studies are required to elucidate the mechanisms responsible that explain how Muscular strength contribute to the detection of MetS in college-aged adults.

Study 3 (chapter 4)

Conclusion 3: The findings of this study indicate that NGS and muscular strength are positively associated with ideal CVH metrics in Colombian collegiate students. The categorization of the ideal CVH metrics relies on the assumption that all risk factors and behaviors contained in this concept contribute equally to the final score.

Practical application 3: This study suggest the importance to generate preventive strategies to reduce the future public health burden associated to muscular weakness, and should be focused on the lifestyle-related risk factors during the young adult stage.

Future perspective 3: Longitudinal studies are required to elucidate the mechanisms responsible that explain how Muscular strength is associated to the lifestyle-related health factors in college-aged adults.

Conclusiones generales

Estudio 1 (Capítulo 2)

Conclusión 1: En este primer estudio, se puede concluir que el porcentaje de tejido graso (BF%- *Siglas en inglés Body fat percentage)* y el índice de masa grasa (FMI- *Siglas en inglés Fat mass index)* tuvo moderado poder discriminatorio en la identificación de Síndrome metabólico (MetS- *Siglas en inglés Metabolic Syndrome)* en estudiantes universitarios de Colombia y se demuestra que un BF% ≥ 38.9% en mujeres y ≥25.5% en hombres, y un FMI ≥11.8 kg/m^2 en mujeres y ≥ 6.9 kg/m^2 en hombres, son umbrales que podrían usarse para predecir adultos jóvenes Colombianos con alto riesgo de síndrome metabólico. Este estudio reporta los primeros puntos de corte para identificar el síndrome metabólico a través del BF% y FMI en adultos jóvenes Colombianos.

Aplicaciones prácticas 1: Este estudio demuestra la capacidad discriminatoria del BF% y el FMI en la detección de MetS en estudiantes universitarios, lo que destaca las importantes implicaciones para evaluar los factores de riesgo de las Enfermedades cardiovasculares (CVD-*Siglas en inglés Cardiovascular Disease)* y el síndrome metabólico.

Perspectivas futuras 1: Se requieren de estudios longitudinales que diluciden los mecanismos responsables de explicar cómo la masa grasa contribuye al riesgo en la salud de adultos universitarios.

Estudio 2 (Capítulo 3)

Conclusión 2: En resumen, los puntos de corte de fuerza prensil ajustada (NGS- *siglas en inglés Normalized handgrip strength*) específicos por sexo, podrían incorporarse en un entorno clínico para identificar a estudiantes universitarios con alto riesgo de enfermedad cardiometabólica y utilizarse como objetivo para programas de entrenamiento de fuerza diseñados para reducir el riesgo de síndrome metabólico. Estudios longitudinales son necesarios para determinar como el aumento de la fuerza prensil reduce la probabilidad de aparición de síndrome metabólico.

Aplicaciones prácticas 2: Este estudio demuestra la capacidad discriminatoria de la NGS en la detección de síndrome metabólico en estudiantes universitarios, lo que destaca las importantes aplicaciones para evaluar los factores de riesgo de las Enfermedades cardiovasculares y el síndrome metabólico.

Perspectivas futuras 2: Se requieren de estudios longitudinales que diluciden los mecanismos responsables de explicar cómo la fuerza muscular contribuye en la detección de Síndrome metabólico en adultos universitarios.

Estudio 3 (Capítulo 4)

Conclusión 3: Los hallazgos de este estudio indican que la NGS y la fuerza muscular se asocian positivamente con las métricas ideales de salud cardiovascular en estudiantes universitarios de Colombia. La categorización de las métricas ideales de salud cardiovascular se basa en el supuesto de que todos los factores de riesgo y comportamiento que componen este concepto, contribuyen equitativamente a la puntuación final.

Aplicaciones prácticas 3: Este estudio sugiere la importancia de generar estrategias preventivas para reducir futura carga de salud pública asociada con la debilidad muscular se debe centrar en los factores de riesgo relacionados con el estilo de vida durante la edad adulta.

Perspectivas futuras 3: Se requieren de estudios longitudinales que diluciden los mecanismos responsables de explicar cómo la fuerza muscular se asocia con factores de salud relacionados con el estilo de vida en adultos universitarios.

Chapter 7: Relevant Papers

nutrients

MDPI

Article

Percentage of Body Fat and Fat Mass Index as a Screening Tool for Metabolic Syndrome Prediction in Colombian University Students

Robinson Ramírez-Vélez [1,*], Jorge Enrique Correa-Bautista [1], Alejandra Sanders-Tordecilla [1], Mónica Liliana Ojeda-Pardo [2], Elisa Andrea Cobo-Mejía [2], Rocío del Pilar Castellanos-Vega [2], Antonio García-Hermoso [3], Emilio González-Jiménez [4,5], Jacqueline Schmidt-RioValle [4,5] and Katherine González-Ruíz [6]

1 Centro de Estudios para la Medición de la Actividad Física CEMA, Escuela de Medicina y Ciencias de la Salud, Universidad del Rosario, Bogotá DC 111221, Colombia; jorge.correa@urosario.edu.co (J.E.C.-B.); alesanders_0615@hotmail.com (A.S.-T.)

2 Grupo CORPS, Universidad de Boyacá, Facultad de Ciencias de la Salud, Boyacá 150003, Colombia; mlojeda@uniboyaca.edu.co (M.L.O.-P.); eacobo@uniboyaca.edu.co (E.A.C.-M.); dpcastellanos@uniboyaca.edu.co (R.d.P.C.-V.)

3 Laboratorio de Ciencias de la Actividad Física, el Deporte y la Salud, Facultad de Ciencias Médicas, Universidad de Santiago de Chile, USACH, Santiago 7500618, Chile; antonio.garcia.h@usach.cl

4 Departamento de Enfermería, Facultad de Ciencias de la Salud, Avda. De la Ilustración, 60, University of Granada, 18016 Granada, Spain; emigoji@ugr.es (E.G.-J.); jschmidt@ugr.es (J.S.-R.)

5 Grupo CTS-436, Adscrito al Centro de Investigación Mente, Cerebro y Comportamiento (CIMCYC), University of Granada, 18071 Granada, Spain

6 Grupo de Ejercicio Físico y Deportes, Vicerrectoría de Investigaciones, Universidad Manuela Beltrán, Bogotá DC 110231, Colombia; katherine.gonzalez@docentes.umb.edu.co

* Correspondence: robin640@hotmail.com or robinson.ramirez@urosario.edu.co; Tel.: +57-1-297-0200 (ext. 3428)

Received: 26 June 2017; Accepted: 11 September 2017; Published: 13 September 2017

Abstract: High body fat is related to metabolic syndrome (MetS) in all ethnic groups. Based on the International Diabetes Federation (IDF) definition of MetS, the aim of this study was to explore thresholds of body fat percentage (BF%) and fat mass index (FMI) for the prediction of MetS among Colombian University students. A cross-sectional study was conducted on 1687 volunteers (63.4% women, mean age = 20.6 years). Weight, waist circumference, serum lipids indices, blood pressure, and fasting plasma glucose were measured. Body composition was measured by bioelectrical impedance analysis (BIA) and FMI was calculated. MetS was defined as including more than or equal to three of the metabolic abnormalities according to the IDF definition. Receiver operating curve (ROC) analysis was used to determine optimal cut-off points for BF% and FMI in relation to the area under the curve (AUC), sensitivity, and specificity in both sexes. The overall prevalence of MetS was found to be 7.7%, higher in men than women (11.1% vs. 5.3%; $p < 0.001$). BF% and FMI were positively correlated to MetS components ($p < 0.05$). ROC analysis indicated that BF% and FMI can be used with moderate accuracy to identify MetS in university-aged students. BF% and FMI thresholds of 25.55% and 6.97 kg/m^2 in men, and 38.95% and 11.86 kg/m^2 in women, were found to be indicative of high MetS risk. Based on the IDF criteria, both indexes' thresholds seem to be good tools to identify university students with unfavorable metabolic profiles.

Keywords: obesity; adiposity; fat mass; metabolic syndrome

1. Introduction

With increasing prevalence worldwide, obesity has become a significant public health issue [1]. Obesity has been linked to a number of cardiovascular disease (CVD) risk factors including metabolic syndrome (MetS) [2]. In Colombia, it is estimated that over 50% of adults are overweight or obese and the obesity epidemic has been associated with obesogenic factors, such as an intake of energy-dense diets, a sedentary lifestyle, and low levels of physical activity [3,4] .

In this context, there is growing evidence that suggests that the way in which fat is distributed contributes different effects on the cardiometabolic risk associated with obesity [3–5]. In addition, measures of central body obesity, such as waist circumference and waist–hip ratio, have been suggested as being more strongly related to MetS risk compared to body mass index (BMI) [4,5]. Aside from age or sex, excess body fat is the strongest determinant of an individual's risk of developing MetS [6], and several epidemiological studies have found an association between fat distribution and metabolic risk factors, including high blood pressure, dysglycemia, dyslipidemia, and subsequent risk of MetS [4,5].

Although BMI is the most frequently used method to assess the level of obesity [7], BMI does not differentiate between body lean mass and body fat mass; that is, a person can have a high BMI but still have a low fat mass and vice versa [8,9]. In addition, the ongoing uncertainty as to which measure of body fat is most important at gauging an individual's risk [6], particularly with respect to MetS, may also contribute to the lack of their use and monitoring in clinical practice.

In this sense, Computed Tomography (CT) or dual-energy X-ray absorptiometry (DXA), continue to be the gold standard for evaluating the distribution of body fat [10]. Nevertheless, the high cost and low availability have made it difficult to use in large population studies. Evidently, this factor limits the possible screening of MetS in high-risk populations, especially in developing countries such as Colombia [2,11]. Recently, more research has examined the potential role of body composition measurements in health monitoring [12,13]. Bioelectrical impedance analysis (BIA) is the method that is most frequently used to assess body composition and calculate BF% in clinical practice, given its accuracy, simplicity, low cost, and excellent correlation with DXA, CT, or magnetic resonance imaging (MRI) [14,15].

Alternative simple and inexpensive approaches for assessing body adiposity have been suggested. A recent study highlighted the usefulness of the fat mass index (FMI), measured as kg/m^2, as an indicator of the function of adipose tissue as a surrogate marker of cardiovascular risk in young adults [16]. However, BF% and FFM are known to change with height, weight, sex, and age. Along this line, VanItallie et al. [16] proposed an FMI that considers an individual's height. FMI, like BMI except that it uses a two-compartment model, merits reappraisal and appears to be of interest in the classification of overweight, obese, and underweight patients [17]. Previous research has evaluated the applicability of FMI in the prediction of MetS and has highlighted its close relation with the components of MetS [17]. However, only a few studies have focused on the differential impacts adiposity levels [18–24] in young adults when examining the link between fat and the risk of MetS.

Understanding the specific fat distribution associated with MetS risk is important to improve the interventions that are currently more focused on overall weight loss [5,6]. Our study proposes a gender-specific fat index based on BIA as a way of estimating the fat mass and body adiposity dysfunction associated with MetS. Apart from the study of Liu et al. [17], this is the first study in Colombian young adults (university students) to investigate the association between fat mass by BIA and MetS components. Based on the IDF definition of MetS [2], the aim of the study was to explore thresholds of BF% and FMI for the prediction of MetS among Colombian university students.

2. Methods

2.1. Study Design and Sample Population

During the 2014–2017 academic years, we reviewed a cross-sectional component of the FUPRECOL study that investigated the association between muscular strength and metabolic risk factors in Colombian collegiate students. The FUPRECOL study aimed to establish the general prevalence of cardiovascular risk factors, including anthropometric and metabolic markers, in the study population and to examine the relationships between physical fitness levels, body composition, and cardiometabolic risk factors. We recently published a complete description of the FUPRECOL study design, methods, and primary outcomes for our current cohort [2]. The sample consisted of adults (men: n = 707; women: n = 1128). We removed cases due to missing (n = 37, 2.0%) or erroneous data entry (n = 83, 4.5%) and those which had neither age nor a valid date of birth recorded (n = 28, 1.5%), limiting the analytical sample to 1687 volunteers, which was 63.4% women and a mean age of 20.6 years. The subjects, whose ages ranged from 18 to 35 years, were all of low to middle socioeconomic status (SISBEN levels: 1–4 on a scale of 1–6 as defined by "The System of Identifying Potential Beneficiaries of Social Programs", called SISBEN). The system takes into account sociodemographic characteristics including family composition, employment status, family income, and educational level; living conditions, including construction type and materials; and access to public utilities, which involves sewers, electricity, potable water, and garbage collection. They were enrolled in public or private universities in the capital district of Bogota, Boyacá, and Cali, Colombia.

Exclusion criteria included the following: medical or clinical diagnosis of a major systemic disease including malignant conditions such as cancer, type 1 or 2 diabetes, high blood pressure, hypothyroidism or hyperthyroidism; a history of drug or alcohol abuse; regular use of multivitamins; chronic inflammatory conditions including rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis; infectious conditions; and a BMI $\geq$ 35 kg/m^2. Volunteers received no compensation for their participation.

2.2. Data Collection

Subjects were screened for inclusion in the study via personal interviews. Interview questions collected consisted of health status, medical history, CVD risk factors, and lifestyle. After completing another general information questionnaire, participants were instructed to wear shorts and a T-shirt to the physical exam. They were also required to remove all worn jewelry and metal objects. Once the subjects were barefoot and in their underwear, their body weight (kg) was measured using an electric scale (Model Tanita® BC-418®, Tokyo, Japan) with a range of 0–200 kg and with an accuracy of within 100 g. Height was measured with a portable stadiometer with a precision of 0.1 cm and a range of 0–2.5 m (Seca® 274, Hamburg, Germany). BMI was calculated by using the formula proposed by Quetelet where BMI = body mass (kg)/height (m^2). Body mass index status was evaluated according to the World Health Organization (WHO) criteria [24]. The waist circumference (WC) (cm) was measured as the narrowest point between the lower costal border and the iliac crest. When this point was not evident, it was measured at the midpoint between the last rib and the iliac crest, using a metal tape measure (Lufkin W606PM®, Parsippany, NJ, USA), in accordance with the International Society for the Advancement of Kinanthropometry guidelines [25]. The evaluation process was carried out by a team of professionals (four physical therapy professors) with extensive experience in anthropometric measurement. Two percent of the sample was measured twice in order to ensure quality of measures. The technical error of measurement (TEM) values was less than 2% for all anthropometric variables.

BF% and FMI were determined for BIA by a tetrapolar whole body impedance (Tanita Model BC-418®, Tokyo, Japan). A detailed description of the BIA technique can be found in a previous study [2]. For the calculation of intra–inter observer TEM, at least 50 subjects needed to be measured (30 men, 20 women, aged 22.3 $\pm$ 2.1 years). The corresponding intra-observer technical error (% reliability) of the measurements was 95%. FMI was then calculated by dividing each subject's fat

mass (kg) by the square of his or her height (m), as previously described [17]. In a sub-sample (48 adults, 54% women, range mean age = 20 to 40 years old), we verified the validity of BIA for predicting BF% in Colombian adults using DXA as a reference. Our analysis showed a strong agreement between the two methods, as reflected in the range of BF% (Lin's concordance correlation coefficient = 0.943 (95% CI = 0.775 to 0.950, p = 0.041) and bias −0.6 (SD 2.2; 95% CI = −5.0 to 3.7). In line with our findings, a previously study has shown a high correlation between fat mass determined by BIA and that obtained by a CT scan and DXA [14,15,26]. Thus, these results show that BIA and DXA are comparable methods for measuring body composition with lower/higher body fat percentages.

2.3. Metabolic Syndrome Diagnosis

After the subjects had fasted for 10–12 h, blood samples were obtained from capillary sampling between 6:00 a.m. and 9:00 a.m. Participants were asked not to engage in prolonged exercise in the 24 h prior to testing. The biochemical profile included the following: (i) high-density lipoprotein cholesterol (HDL-C); (ii) triglycerides; (iii) low-density lipoprotein cholesterol (LDL-C); (iv) total cholesterol; (v) glucose fasting by enzymatic colorimetric methods (CardioChek PA®, Polymer Technology Systems, PTS, Indianapolis, IN, USA). The inter-assay reproducibility (coefficient of variation) was determined from 16 replicate analyses of 8 capillary blood pools over a period of 15 days. The percentages obtained were 2.6% for triglycerides, 2.0% for total cholesterol, 3.2% for HDL-C, 3.6% for LDL-C, and 1.5% for fasting glucose.

Blood pressure was taken on the left arm at the heart level with an automatic device Omron M6 Comfort (Omron® Healthcare Europe B.V., Hoofddorp, The Netherlands) while the participants were sitting still. The blood pressure monitor cuff was placed two to three finger-widths above the bend of the arm and a two-minute pause was allowed between the first and second measurements with a standard cuff for an arm circumference of 22–32 cm.

MetS was defined in accordance with the updated harmonized criteria of the IDF [2]. Participants were considered to have MetS if they showed three or more of the following: (1) abdominal obesity for individuals (WC $\geq$ 80 cm in women and $\geq$ 90 cm in men) [27]; (2) hypertriglyceridemia ($\geq$150 g/dL); (3) low HDL-C (<50 mg/dL in women and <40 mg/dL in men); (4) high blood pressure (systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 85 mmHg); (5) high fasting glucose ($\geq$100 mg/dL).

2.4. Lifestyle Co-Variables

A standardized questionnaire, FANTASTIC lifestyle, was used to collect comprehensive information about substance use via a personal interview with participants [28]. Alcohol consumption and smoking status were defined as subjects who had consumed any alcoholic beverage $\geq$1 times per week, and those who had smoked $\geq$10 cigarettes per week, for at least six months, as previously described by Ramírez-Vélez et al. [28]. Participants who exercised three or more times a week for >30 min were categorized as physically active (PA), and those who exercised less than three times a week were considered insufficiently physically active. The accuracy of information about lifestyle co-variables obtained from the FANTASTIC questionnaire has been validated by different cross-sectional studies and described in detail elsewhere [28,29].

2.5. Ethics Statement

Informed consent was obtained from each participant. The protocol was based on the Helsinki Declaration Accord (World Medical Association for Human Subjects). Moreover, ethical approval was obtained from the Universidad Manuela Beltrán (UMB N° 01-1802-2013).

2.6. Statistical Analysis

Participants' characteristics obtained were given as mean values and standard deviation (SD). Histograms and Q–Q plots were used to verify the normality of the selected variables. Independent two-tailed t-tests for continuous variables, and chi-square (χ^2) tests for categorical variables, were used

to examine sex differences or MetS grouping. The relationships between BF%, FMI, and MetS components were tested by means of partial correlation coefficients. This analysis was adjusted by age, sex, tobacco, and alcohol consumption, and PA levels. To predict MetS with BF% and FMI, we used area under the curve (AUC), ranging between 0 and 1 (a worthless and a perfect test, respectively), which is a global indicator of diagnostic performance, and represents the ability of the test to correctly classify participants with high risk MetS by p-values < 0.01 and an AUC > 0.80. The positive likelihood ratio LR (+) and the negative likelihood ratio LR (−) were also determined. Cutoff points were chosen based on the highest Youden index, i.e., the point on the receiver operating characteristic curve (ROC) that is farthest from the line of equality [30]. Data analysis was performed using the Statistical Package for the Social Sciences for Windows SPSS, version 21.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

3. Results

3.1. Descriptive Characteristics

Descriptive characteristics of the participants are presented in Table 1. The final sample had a mean age of 20.6 years (SD 3.0; range 19–24 years), with 63.4% of participants being women. Women were found to have significantly lower height, WC, blood pressure, triglycerides, and PA than men ($p < 0.05$). The prevalence of MetS was higher in men than in women at 11.2% vs. 5.3% ($p < 0.001$).

Table 1. Characteristics among a sample of college students from Colombia (mean (SD) or frequency (%)).

Characteristic	Men (n = 617)	Women (n = 1070)	p-Value
Anthropometric			
Age (years)	20.6 (2.2)	20.6 (2.0)	0.843
Weight (kg)	58.9 (10.0)	69.9 (12.4)	<0.001
Height (cm)	159.8 (6.1)	172.5 (6.7)	<0.001
WC (cm)	78.4 (9.5)	71.5 (7.9)	<0.001
BMI (kg/m^2)	23.2 (3.7)	23.2 (3.7)	0.356
Body fat (%)	15.7 (6.7)	27.0 (7.2)	0.028
FMI	3.9 (2.3)	6.5 (2.7)	<0.001
Body mass index status n (%) *			
Underweight	34 (5.5)	71 (6.7)	<0.001
Normal weight	425 (68.8)	725 (57.8)	
Overweight	128 (20.8)	220 (20.5)	
Obese	31 (5.0)	54 (5.0)	
Blood pressure			
Systolic blood pressure (mmHg)	120.83 (13.0)	111.28 (11.1)	<0.001
Diastolic blood pressure (mmHg)	74.83 (11.4)	71.78 (9.3)	<0.001
Mean arterial pressure (mmHg)	97.83 (10.8)	91.53 (8.9)	<0.001
Metabolic biomarkers			
Total cholesterol (mg/dL)	132.26 (30.8)	146.27 (33.3)	0.212
Triglycerides (mg/dL)	93.01 (48.7)	88.10 (43.7)	0.011
LDL-C (mg/dL)	38.92 (10.4)	43.98 (12.8)	<0.001
HDL-C (mg/dL)	81.89 (26.5)	87.85 (26.2)	0.589
Glucose (mg/dL)	84.36 (12.2)	85.99 (11.6)	0.002
Metabolic Syndrome n (%) *			
Yes	73 (11.2)	59 (5.3)	0.001
Life-style n (%) *			
Tobacco (≥10 cigarettes per week)	183 (29.7)	213 (19.9)	0.289
Alcohol (≥1 times per week)	294 (47.6)	381 (35.6)	0.358
PA (three or more times a week for >30 min)	213 (34.5)	228 (21.3)	0.011

Continuous variables are reported as mean values (standard deviations) and categorical variables are reported as numbers and percentages in brackets. Significant between-sex differences (t-tests or * chi-square test χ^2). WC: waist circumference; BMI: body mass index; FMI: fat mass index; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; PA: physical activity.

At least one MetS component was found in 818 participants (48.5%), two MetS components were present in 341 participants (20.2%), three MetS components were found in 126 participants (7.7%), and four or more components of MetS were present in 80 participants (4.7%) (Figure 1).

Nutrients **2017**, *9*, 1009 6 of 13

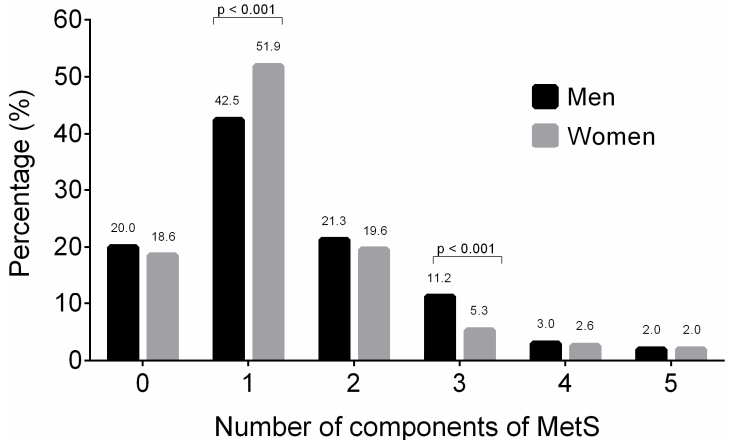

Figure 1. Distribution of the prevalence of metabolic syndrome components according to sex.

Figure 1. Distribution of the prevalence of metabolic syndrome components according to sex.

3.2. Clinical Characteristics and Distribution by MetS Status

3.2. Clinical Characteristics and Distribution by MetS Status

Independent of sex, participants with MetS had significantly higher weight, body mass index, WC, BF%, FMI, and total cholesterol and triglyceride levels ($p < 0.01$) (Table 2). Furthermore, participants without MetS were more active (34.5% vs. 17.8% for men, and 21.1% vs. 6.8% for women, $p < 0.01$).

Independent of sex, participants with MetS had significantly higher weight, body mass index, WC, BF%, FMI, and total cholesterol and triglyceride levels ($p < 0.01$) (Table 2). Furthermore, participants without MetS were more active (34.5% vs. 17.8% for men, and 21.1% vs. 6.8% for women, $p < 0.01$).

Table 2. The descriptive characteristics of participants with and without MetS in both sexes.

Table 2. The descriptive characteristics of participants with and without MetS in both sexes.

Variable	Men (n = 617)			Women (n = 1070)		
	MetS (n = 73)	Non-MetS (n = 544)	p Value	MetS (n = 59)	Non-MetS (n = 1011)	p Value
Anthropometric						
Age (years)	21.7 (3.4)	20.4 (3.1)	0.229	22.3 (3.8)	20.5 (2.8)	<0.001
Weight (kg)	80.8 (15.8)	67.3 (10.7)	<0.001	76.4 (13.8)	57.4 (8.8)	<0.001
Height (cm)	172.7 (7.5)	172.1 (6.6)	0.129	161.1 (5.6)	158.9 (5.8)	0.902
WC (cm)	89.5 (11.6)	76.7 (8.0)	<0.001	84.9 (8.8)	70.5 (7.1)	0.145
BMI (kg/m^2)	27.0 (4.7)	22.6 (3.1)	<0.001	29.3 (4.7)	22.7 (3.3)	<0.001
Body fat (%)	23.5 (7.5)	14.5 (5.7)	0.005	37.3 (6.0)	26.2 (6.8)	<0.001
FMI (kg/m^2)	6.6 (3.1)	3.4 (1.8)	<0.001	11.2 (3.4)	6.1 (2.4)	<0.001
Body mass index status n (%) *						
Underweight	4 (0.6)	30 (5.0)	0.129	0.0 (0.0)	71 (6.6)	0.145
Normal weight	16 (2.6)	408 (66.1)	<0.001	8 (0.8)	717 (67.0)	<0.001
Overweight	37 (6.0)	91 (14.8)	<0.001	23 (2.1)	197 (18.4)	<0.001
Obese	16 (2.6)	15 (2.4)	<0.001	28 (2.6)	26 (2.4)	<0.001
Blood pressure						
Systolic blood pressure (mmHg)	131.01 (11.96)	119.36 (12.44)	0.461	123.50 (11.03)	110.33 (10.64)	0.809
Diastolic blood pressure (mmHg)	83.60 (10.75)	73.48 (10.07)	0.160	81.61 (13.82)	71.10 (8.60)	0.237
Mean blood pressure (mmHg)	107.30 (10.20)	96.42 (10.07)	0.176	102.55 (9.16)	90.71 (8.36)	0.518
Metabolic biomarkers						
Total cholesterol (mg/dL)	146.01 (39.6)	130.27 (29.1)	<0.001	153.39 (33.7)	145.74 (33.3)	0.955
Triglyceride (mg/dL)	163.03 (75.9)	83.04 (33.7)	<0.001	139.83 (66.6)	84.90 (40.2)	<0.001
HDL-C (mg/dL)	31.27 (5.9)	40.06 (10.5)	<0.001	36.51 (9.0)	44.52 (12.9)	0.002
LDL-C (mg/dL)	86.01 (30.8)	81.31 (26.0)	0.077	89.61 (28.4)	87.57 (26.1)	0.571
Glucose (mg/dL)	92.44 (13.8)	85.14 (11.6)	0.065	92.58 (14.1)	89.49 (11.3)	0.142
Life-style n (%) *						
Tobacco (≥10 cigarettes per week)	19 (26.0)	155 (28.5)	0.769	5 (8.5)	198 (19.6)	0.088
Alcohol (≥1 times per week)	36 (49.3)	294 (54.0)	0.563	22 (37.3)	394 (38.7)	0.378
PA (three or more times a week for >30 min)	13 (17.81)	188 (34.5)	0.005	4 (6.8)	213 (21.0)	0.018

Continuous variables are reported as mean values (standard deviations) and categorical variables are reported as numbers (percentages). Significant between-sex differences (t-tests or * chi-square test χ^2). WC: waist circumference; BMI: body mass index; FMI: fat mass index; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; PA: physical activity. The mean blood pressure was calculated using the following formula: (systolic blood pressure + (2 × diastolic blood pressure))/3.

Table 3 shows the partial correlation between BF%, FMI, and MetS components. Overall, BF% and FMI were weakly positively correlated with all MetS parameters (all $p < 0.05$), except HDL, which was negatively correlated.

Table 3. Results of the partial correlation analysis between body fat percentage (BF%), fat mass index (FMI), and MetS components.

Variable	Glucose (mg/dL)	HDL-C (mg/dL)	Triglycerides (mg/dL)	Total Cholesterol (mg/dL)	MAP (mmHg)	WC (cm)	FMI (kg/m^2)
Body fat (%)	0.188 *	−0.239 **	0.230 **	0.279 **	0.276 **	0.827 **	0.960 **
FMI (kg/m^2)	0.113 **	−0.256 **	0.230 **	0.162 *	0.272 **	0.860 **	1
WC (cm)	0.106 *	−0.219	0.248	0.858 **	0.271 **	1	
Mean blood pressure (mmHg)	0.004	−0.022 **	0.179 **	0.259 **	1		
Total cholesterol (mg/dL)	−0.008	−0.341 **	0.241 **	1			
Triglycerides (mg/dL)	0.125 **	−0.170 **	1				
HDL-C (mg/dL)	−0.158 **	1					
Glucose (mg/dL)	1						

Analysis adjusted by co-variables: age, sex, tobacco, alcohol, and physical activity. * $p < 0.05$; ** $p < 0.01$. WC: waist circumference; FMI: fat mass index; HDL-C: high-density lipoprotein cholesterol; MAP: mean arterial pressure. The mean blood pressure was calculated using the following formula: (systolic blood pressure + (2 × diastolic blood pressure))/3.

3.3. Optimal Cut-Off Value in the Screening of MetS

The ROC analysis showed that BF% and FMI parameters could be used to detect MetS according to the IDF criteria among Colombian university students (Table 4; Figure 2). Since multiple levels of risk were desired, the selection of the resulting cut-off values was based on multiple combinations of sensitivity and specificity. The focus was on higher sensitivity for the BF% and FMI thresholds in an effort to identify the majority of cases of MetS according to the IDF criteria. In men, the cut-off point value of 25.5% for BF% provided a sensitivity of 96.1%, an LR (+) value of 2.3, a specificity of 57.5%, and an LR (−) value of 0.06. For FMI, the cut-off value of 6.9 kg/m^2 provided a sensitivity of 95.8%, an LR (+) value of 2.2, a specificity of 56.2%, and an LR (−) value of 0.07. With respect to BF% among the women in the study population, the cut-off point value of 38.9% provided a sensitivity of 97.4%, an LR (+) value of 2.2, a specificity of 55.9%, and an LR (−) value of 0.04. The ROC curve for FMI was also obtained, using a cut-off value of 11.8 kg/m^2, a sensitivity of 97.6%, an LR (+) of 2.2, a specificity of 56.9%, and an LR (−) of 0.04.

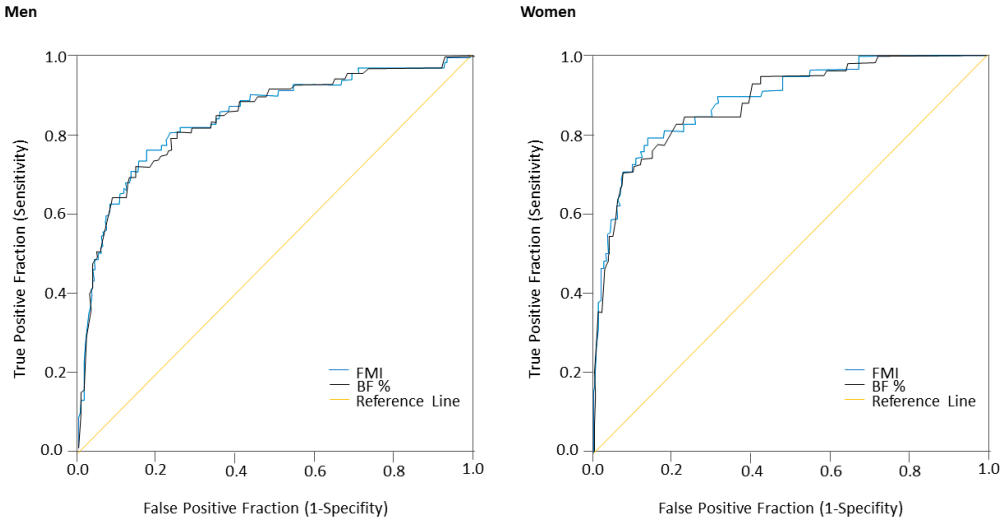

Figure 2. ROC curves for BF% and FMI for prediction of the prevalence of MetS according to IDF criteria in men and women.

Table 4. Parameters of the ROC curves analysis for the diagnostic performance of body fat percentage (BF%) and fat mass index (kg/m^2) in identifying high risk of MetS according to the IDF criteria in men and women.

Parameter			BF%	FMI
High risk of MetS	Men	AUC	0.835	0.838
		95% CI	0.779–0.891	0.779–0.892
		p value	<0.001	<0.001
		Cut-off	25.5	6.9
		Sensitivity (%)	96.1	95.8
		Specificity (%)	57.5	56.2
		LR (+)	2.3	2.2
		LR (−)	0.06	0.07
	Women	AUC	0.887	0.889
		95% CI	0.842–0.932	0.844–0.933
		p value	<0.001	<0.001
		Cut-off	38.9	11.8
		Sensitivity (%)	97.4	97.6
		Specificity (%)	55.9	56.9
		LR (+)	2.2	2.2
		LR (−)	0.04	0.04

AUC: area under the curve; CI: confidence interval; LR (+): positive likelihood ratio; LR (−): negative likelihood ratio.

4. Discussion

In our study, we found that the MetS prevalence was higher in men than in women (11.2% vs. 5.3%; $p < 0.001$), which is an intermediate value compared to those reported in local and international studies, ranging from 2 to 13% [31–33], that BF% and FMI were positively correlated to MetS components ($p < 0.05$), and that the ROC analysis showed that both the BF% and FMI had a moderate discriminatory power in the identification of MetS among Colombian university students.

The higher prevalence of MetS, at 11.2%, seen in male subjects in our results does not coincide with Ruano-Nieto et al. [34] who found that the estimated prevalence of MetS was 8.4% for women and 6.1% for men in a population of Ecuadorian university students. The overall prevalence of MetS in our study, at 7.7%, was also greater than that in other Latin American countries such as Chile at 4.9% and Argentina at 4.1% [35,36]. Clearly, the prevalence of MetS could differ between studies depending on the MetS cluster used, the design method, and the target population. In this study, we used the IDF and AHA/NHLBI [2] joint statement, as it was an international attempt to harmonize the definition of MetS; central obesity is not an obligatory component of this definition and it is ethnic-specific.

Of those components, abdominal obesity, the most prevalent manifestation of MetS, is a marker of dysfunctional adipose tissue, and is of central importance in clinical diagnosis [37–41]. Our results show correlation between BF%, FMI, and all of the cardiometabolic biomarkers analyzed, including mean arterial pressure, glucose, HDL-C, LDL-C, triglycerides, and total cholesterol (<0.05 for all). These findings agree with Knowles et al. [19], who studied a population of young Peruvian adults and found significant correlations between the fat parameters and the above-mentioned cardiometabolic biomarkers. Blood lipid disorders and adipose tissue are the key etiologic defects that define MetS; we found all fat indices used in this study were associated with BF%. In contrast, other researchers such as Schuster et al. [40], who studied a sample of 444 young adults in Brazil, only found correlations between the BF% and glucose, HDL-C, and triglycerides. Our result may be different due to degree and the prevalence varying on the basis of ethnicity, genetic susceptibility, lifestyle, and geographic location. In addition, our results showed lower values of weight, height, and WC in women compared to men. This aligns with Liu et al. [17], who studied a population of 1698 adults in China. In all likelihood, these differences in body composition were due to sexual dimorphism [31] and diet [34]. Sex-specific hormones are another possible explanation. For example, the triglyceride levels and blood pressure were also lower among women in comparison to men. In this context, much of the risk of MetS associated with sex can be explained by the change in steroid hormone levels and the metabolism

of carbohydrates and lipids [39]. An increase in total fat and the distribution of central fat, resulting from alterations in biomarker-disease, such as fasting glucose, triglycerides, and ferritin, which are mediators of MetS, has been reported in female Hispanic/Latino adults [40]. This coincides with previous research, in which this finding was correlated with lower cardiovascular morbidity and dysfunctional adipose tissue in women [39,41]. Furthermore, the observation of ongoing changes in body composition by sex and its relationship with obesity has demonstrated that obesity affects individuals no matter their muscle mass, fat mass, height, and weight [41].

The AUC values for the MetS ROC analyses, at 0.835 for men and 0.838 for women, indicate that BF% has moderate diagnostic capabilities to identify subjects with MetS ($\geq$3 risk factors). Interestingly, when considering MetS in our study, FMI showed the greatest AUC to predict MetS risk in women compared to men. Results show that metabolic disorders are present in young adult independent of age, smoking, physical activity, or fitness levels [42]. There is a growing interest in suggesting cut-off points for body fat levels for the early detection of CVD risk. Future longitudinal studies should be carried out to understand the role of different levels of adiposity on CVD risk stratification within a college population.

In contrast, another study carried out by Mohammadreza et al. [43] among Iranian adults found that BF% was not as effective a parameter for predicting MetS as other anthropometric indexes such as BMI, waist-to-height ratio, and waist-to-hip ratio. In this same line, Mousa et al. [44] studied a population of young adults and found that the predictive power of BF% and BMI for screening MetS was limited. This discrepancy in results could be explained by the heterogeneity of the sample populations. Consequently, the applicability and usefulness of BF% and FMI in the prediction of MetS require further studies of different populations and ethnic groups. These results are partially consistent with previous studies that showed BF% was positively correlated with single metabolic risk factors, such as BMI and triglycerides, and negatively correlated with HDL cholesterol in men, but not in women [45,46].

To our knowledge, few studies have explored the use of FMI as a proxy of obesity. In a study of 538 Mexican American college students (373 women and 165 men), the validity of FMI and BMI against BF% with BIA as the reference method was evaluated [47]. Correlations between FMI and BF% resulted in correlation coefficients of 0.976 in men ($p < 0.001$) and 0.992 in women ($p < 0.001$). However, similar to our findings, the correlations between FMI and PBF were higher ($r = 0.960$, $p < 0.01$). In a study of 2986 healthy white men and 2649 white women, age 15 to 98 years in Switzerland, the mean FMI in the overall age group was 4.9 (1.8) kg/m^2 in men and 6.6 (2.4) kg/m^2 in women [48], compared to our results, of 6.6 (3.1) kg/m^2 in men and 11.2 (3.4) kg/m^2 in women without MetS. This difference can be explained by the fact that FMI cutoffs in the Swiss group were derived from BMI and not from MetS cutoffs. On the other hand, in the Peltz et al. study [47], the median FMI in the overall age group was 7.3 (interquartile range 4.5) kg/m^2 in men and 9.0 (interquartile range 5.9) kg/m^2 in women. Our FMI means fell within the lower range of the Mexican American normal FMI ranges in both men and women. This was expected, as South Americans have a lower percentage of body fat across all age groups when compared to non-Hispanic whites, Mexican Americans, and non-Hispanic blacks [49]. In a subsequent study from the same group (5635 apparently healthy adults from a mixed non-randomly selected Caucasian population) in Switzerland, obesity was defined as an FMI greater than 8.2 kg/m^2 in men and 11.8 kg/m^2 in women [50], which are similar than our FMI cutoffs of $\geq$6.9 kg/m^2 in men and $\geq$11.8 kg/m^2 in women in our study. These findings, although limited, show an interesting agreement with our results, which collectively contribute to the concept of developing one set of recommended ranges that are not affected by height.

Our results have public health and clinical implications as college populations have been reported as a period in life when several behavioral and metabolic changes occur. These changes, in addition to the adoption of a Western lifestyle and diet, have led to a rise in the prevalence of overweight and obese Colombians, particularly among university students [32,51]. Further studies are needed to

identify clinical characteristics in young adults that could be used in screening tests to predict MetS risk in adulthood.

The principal limitation of this study was the use of cross-sectional data. Furthermore, it is also true that the hydration status of the participants could have modified the results of the BF% measured with BIA. Most BIA prediction equations assume that the fat mass and fat-free mass consist of 73% water [52]. These major limitations of the BIA method remain unresolved. Secondly, the assessment of other biomarkers, such as insulin, adiponectin, and c-reactive protein levels, which could have shown additional information about prognostic assessment, was not performed. These and other questions deserve further investigation by future well-designed longitudinal studies.

The main strength of our study is the fact that our study compared the predictive power of both BF% and FMI while providing cutoff values for the prediction of MetS in university students from Colombia. Considering the wide use of BIA methods and their extension to assess body composition, our study has important implications for evaluating CVD and metabolic risks in high-risk subjects, such as those with MetS.

5. Conclusions

In conclusion, BF% and FMI had a moderate discriminatory power in the identification of MetS in Colombian university students. Apart from the differences between our cut-off points and those reported in other research in geographically different populations, this study reports the first cutoff points for identification of MetS by BF% and FMI in Colombian young adults. We demonstrated that a BF% $\geq$38.9% in women and $\geq$25.5% in men, and an FMI $\geq$11.8 kg/m^2 in women and $\geq$6.9 kg/m^2 in men, are thresholds that could be used to predict Colombian young adults at high risk of MetS.

Acknowledgments: This study was part of the project entitled "Body Adiposity Index and Biomarkers of Endothelial and Cardiovascular Health in Adults", which was funded by Centre for Studies on Measurement of Physical Activity, School of Medicine and Health Sciences, Universidad del Rosario (Code N° FIUR DN-BG001), and Universidad de Boyacá (Code N° RECT 60). The funder had no role in the study design, data collection, data analysis and interpretation, the preparation of the manuscript, or the decision to publish.

Author Contributions: Robinson Ramírez-Vélez, Jorge Enrique Correa-Bautista, Alejandra Sanders-Tordecilla, Mónica Liliana Ojeda-Pardo, Elisa Andrea Cobo-Mejía, and Rocío del Pilar Castellanos-Vega conceived and designed the study; Antonio García-Hermoso, Emilio González-Jiménez, Jacqueline Schmidt-RioValle contributed to the data analysis; Katherine González-Ruíz analyzed the data and wrote the paper. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

BF	body fat
BIA	bioelectrical impedance analysis
BMI	body mass index
CI	confidence interval
CT	computed tomography
CVD	cardiovascular disease
DXA	dual-energy x-ray absorptiometry
FUPRECOL	association between muscular strength and metabolic risk factors in colombia
FMI	fat mass index
HDL-C	high-density lipoprotein cholesterol
IDF	international diabetes federation
LDL-C	low-density lipoprotein cholesterol
MetS	metabolic syndrome
MRI	magnetic resonance imaging

PA	physical activity
SD	standard deviation
WC	waist circumference
WHO	World Health Organization

References

1. Roth, G.A.; Johnson, C.; Abajobir, A.; Abd-Allah, F.; Abera, S.F.; Abyu, G.; Ahmed, M.; Aksut, B.; Alam, T.; Alam, K.; et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *J. Am. Coll. Cardiol.* **2017**, *70*, 1–25. [CrossRef] [PubMed]
2. Alberti, K.G.; Eckel, R.H.; Grundy, S.M.; Zimmet, P.Z.; Cleeman, J.I.; Donato, K.A.; Fruchart, J.C.; James, W.P.; Loria, C.M.; Smith, S.C., Jr.; et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* **2009**, *120*, 1640–1645. [PubMed]
3. Ramírez-Vélez, R.; Correa-Bautista, J.E.; González-Ruíz, K.; Vivas, A.; Triana-Reina, H.R.; Martínez-Torres, J.; Prieto-Benavides, D.H.; Carrillo, H.A.; Ramos-Sepúlveda, J.A.; Villa-González, E.; et al. Body Adiposity Index Performance in Estimating Body Fat Percentage in Colombian College Students: Findings from the FUPRECOL-Adults Study. *Nutrients* **2017**, *9*, 40. [CrossRef] [PubMed]
4. González-Muniesa, P.; Mártinez-González, M.A.; Hu, F.B.; Després, J.P.; Matsuzawa, Y.; Loos, R.J.F.; Moreno, L.A.; Bray, G.A.; Martinez, J.A. Obesity. *Nat. Rev. Dis. Prim.* **2017**, *3*, 17034. [CrossRef] [PubMed]
5. Bener, A.; Yousafzai, M.T.; Darwish, S.; Al-Hamaq, A.O.; Nasralla, E.A.; Abdul-Ghani, M. Obesity index that better predict metabolic syndrome: Body mass index, waist circumference, waist hip ratio, or waist height ratio. *J. Obes.* **2013**, *2013*, 269038. [CrossRef] [PubMed]
6. Fox, C.S.; Massaro, J.M.; Hoffmann, U.; Pou, K.M.; Maurovich-Horvat, P.; Liu, C.Y.; Vasan, R.S.; Murabito, J.M.; Meigs, J.B.; Cupples, L.A.; et al. Abdominal visceral and subcutaneous adipose tissue compartments: Association with metabolic risk factors in the Framingham Heart Study. *Circulation* **2007**, *116*, 39–48. [CrossRef] [PubMed]
7. Wellens, R.I.; Roche, A.F.; Khamis, H.J.; Jackson, A.S.; Pollock, M.L.; Siervogel, R.M. Relationships between the body mass index and body composition. *Obes. Res.* **1996**, *4*, 35–44. [CrossRef] [PubMed]
8. Nuttall, F.Q. Body Mass Index: Obesity, BMI, and Health: A Critical Review. *Nutr. Today* **2015**, *50*, 117–128. [CrossRef] [PubMed]
9. Baumgartner, R.N.; Heymsfield, S.B.; Roche, A.F. Human body composition and the epidemiology of chronic disease. *Obes. Res.* **1995**, *3*, 73–95. [CrossRef] [PubMed]
10. Rollins, K.E.; Javanmard-Emamghissi, H.; Awwad, A.; Macdonald, I.A.; Fearon, K.C.H.; Lobo, D.N. Body composition measurement using computed tomography: Does the phase of the scan matter? *Nutrition* **2017**, *41*, 37–44. [CrossRef] [PubMed]
11. González-Ruíz, K.; Correa-Bautista, J.E.; Ramírez-Vélez, R. Body adiposity and its relationship of metabolic syndrome components in Colombian adults. *Nutr. Hosp.* **2015**, *32*, 1468–1475. [PubMed]
12. De Schutter, A.; Lavie, C.J.; Gonzalez, J.; Milani, R.V. Body composition in coronary heart disease: How does body mass index correlate with body fatness? *Ochsner J.* **2011**, *11*, 220–225. [PubMed]
13. Mazzoccoli, G. Body composition: Where and when. *Eur. J. Radiol.* **2016**, *85*, 1456–1460. [CrossRef] [PubMed]
14. Jeong, D.L.S.; Min, H.; Kim, Y.; Choi, S.; Kim, Y. Measuring performance evaluation of body fat measuring instrument applying body measuring value method. *Korean J. Health Promot. Dis. Prev.* **2006**, *6*, 79–87.
15. Xu, L.; Cheng, X.; Wang, J.; Cao, Q.; Sato, T.; Wang, M.; Zhao, X.; Liang, W. Comparisons of body-composition prediction accuracy: A study of 2 bioelectric impedance consumer devices in healthy Chinese persons using DXA and MRI as criteria methods. *J. Clin. Densitom.* **2011**, *14*, 458–464. [CrossRef] [PubMed]
16. VanItallie, T.B.; Yang, M.U.; Heymsfield, S.B.; Funk, R.C.; Boileau, R.A. Height-normalized indices of the body's fat-free mass and fat mass: Potentially useful indicators of nutritional status. *Am. J. Clin. Nutr.* **1990**, *52*, 953–959. [PubMed]
17. Liu, P.; Ma, F.; Lou, H.; Liu, Y. The utility of fat mass index vs. body mass index and percentage of body fat in the screening of metabolic syndrome. *BMC Public Health* **2014**, *14*, 341. [CrossRef] [PubMed]

18. Amato, M.C.; Giordano, C. Visceral adiposity index: An indicator of adipose tissue dysfunction. *Int. J. Endocrinol.* **2014**, *2014*, 730827. [CrossRef] [PubMed]
19. Knowles, K.M.; Paiva, L.L.; Sanchez, S.E.; Revilla, L.; Lopez, T.; Yasuda, M.B.; Yanez, N.D.; Gelaye, B.; Williams, M.A. Waist circumference, body mass index, and other measures of adiposity in predicting cardiovascular disease risk factors among Peruvian adults. *Int. J. Hypertens.* **2011**, *2011*, 1–10. [CrossRef] [PubMed]
20. Techatraisak, K.; Wongmeerit, K.; Dangrat, C.; Wongwananuruk, T.; Indhavivadhana, S. Measures of body adiposity and visceral adiposity index as predictors of metabolic syndrome among Thai women with PCOS. *Gynecol. Endocrinol.* **2016**, *32*, 276–280. [CrossRef] [PubMed]
21. Li, L.; Wang, C.; Bao, Y.; Peng, L.; Gu, H.; Jia, W. Optimal body fat percentage cut-offs for obesity in Chinese adults. *Clin. Exp. Pharmacol. Physiol.* **2012**, *39*, 393–398. [CrossRef] [PubMed]
22. Cho, Y.G.; Song, H.J.; Kim, J.M.; Park, K.H.; Paek, Y.J.; Cho, J.J.; Caterson, I.; Kang, J.G. The estimation of cardiovascular risk factors by body mass index and body fat percentage in Korean male adults. *Metabolism* **2009**, *58*, 765–771. [CrossRef] [PubMed]
23. Amato, M.C.; Giordano, C.; Galia, M.; Criscimanna, A.; Vitabile, S.; Midiri, M.; Galluzzo, A.; AlkaMeSy Study Group. Visceral Adiposity Index: A reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* **2010**, *33*, 920–922. [CrossRef] [PubMed]
24. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*; Report of a WHO Consultation on Obesity, 3–5 June 1997, WHO/NUT/NCD/98.1 1997; WHO: Geneva, Switzerland, 1997.
25. Marfell-Jones, M.; Olds, T.; Stewart, A. *International Standards for Anthropometric Assessment*; ISAK: Potchefstroom, South Africa, 2006.
26. Yamakage, H.; Ito, R.; Tochiya, M.; Muranaka, K.; Tanaka, M.; Matsuo, Y.; Odori, S.; Kono, S.; Shimatsu, A.; Satoh-Asahara, N. The utility of dual bioelectrical impedance analysis in detecting intra-abdominal fat area in obese patients during weight reduction therapy in comparison with waist circumference and abdominal CT. *Endocr. J.* **2014**, *61*, 807–819. [CrossRef] [PubMed]
27. Cornier, M.A.; Després, J.P.; Davis, N.; Grossniklaus, D.A.; Klein, S.; Lamarche, B.; Lopez-Jimenez, F.; Rao, G.; St-Onge, M.P.; Towfighi, A.; et al. Assessing adiposity: A scientific statement from the American Heart Association. *Circulation* **2011**, *124*, 1996–2019. [CrossRef] [PubMed]
28. Ramírez-Vélez, R.; Agredo, R.A. The Fantastic instrument's validity and reliability for measuring Colombian adults' life-style. *Rev. Salud Publica (Bogota)* **2012**, *14*, 226–237. [CrossRef] [PubMed]
29. Silva, A.M.; Brito Ida, S.; Amado, J.M. Translation, adaptation and validation of the Fantastic Lifestyle Assessment questionnaire with students in higher education. *Cienc. Saude Colet.* **2014**, *19*, 1901–1909. [CrossRef]
30. Fluss, R.; Faraggi, D.; Reiser, B. Estimation of the Youden Index and its associated cutoff point. *Biom. J.* **2005**, *47*, 458–472. [CrossRef] [PubMed]
31. Ruiz, Á.J.; Aschner, P.J.; Puerta, M.F.; Cristancho, R.A. IDEA study (International Day for the Evaluation of Abdominal Obesity): Primary care study of the prevalence of abdominal obesity and associated risk factors in Colombia. *Biomedica* **2012**, *32*, 610–616. [CrossRef] [PubMed]
32. Fonseca-Camacho, D.F.; Hernández-Fonseca, J.M.; González-Ruíz, K.; Tordecilla-Sanders, A.; Ramírez-Vélez, R. A better self-perception of physical fitness is associated with lower prevalence of metabolic syndrome and its components among university students. *Nutr. Hosp.* **2014**, *31*, 1254–1263. [PubMed]
33. Li, C.I.; Kardia, S.L.; Liu, C.S.; Lin, W.Y.; Lin, C.H.; Lee, Y.D.; Sung, F.C.; Li, T.C.; Lin, C.C. Metabolic syndrome is associated with change in subclinical arterial stiffness: A community-based Taichung community health study. *BMC Public Health* **2011**, *11*, 808. [CrossRef] [PubMed]
34. Ruano-Nieto, C.I.; Melo-Pérez, J.D.; Mogrovejo-Freire, L.; De Paula-Morales, K.R.; Espinoza-Romero, C.V. Prevalence of metabolic syndrome and associated risk factors in ecuadorian university students. *Nutr. Hosp.* **2015**, *31*, 1574–1581. [PubMed]
35. Martínez, M.A.; Leiva, A.M.; Sotomayor, C.; Victoriano, T.; Von Chrismar, A.M.; Pineda, S. Factores de riesgo cardiovascular en estudiantes de la Universidad Austral de Chile. *Rev. Med. Chile* **2012**, *140*, 426–435. [CrossRef] [PubMed]
36. Gotthelf, S.J. Prevalencia de síndrome Metabólico según definición de la International Diabetes Federation (IDF) en adolescentes escolarizados de la provincia de Salta, Argentina. *Rev. Fed. Argent. Cardiol.* **2013**, *42*, 119–126.

37. Wang, X.; Strizich, G.; Hua, S.; Sotres-Alvarez, D.; Buelna, C.; Gallo, L.C.; Gellman, M.D.; Mossavar-Rahmani, Y.; O'Brien, M.J.; Stoutenberg, M.; et al. Objectively Measured Sedentary Time and Cardiovascular Risk Factor Control in US Hispanics/Latinos With Diabetes Mellitus: Results From the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *J. Am. Heart Assoc.* **2017**, *6*, e004324. [CrossRef] [PubMed]
38. Macias, N.; Quezada, A.D.; Flores, M.; Valencia, M.E.; Denova-Gutiérrez, E.; Quiterio-Trenado, M.; Gallegos-Carrillo, K.; Barquera, S.; Salmerón, J. Accuracy of body fat percent and adiposity indicators cut off values to detect metabolic risk factors in a sample of Mexican adults. *BMC Public Health* **2014**, *14*, 341. [CrossRef] [PubMed]
39. Murphy, M.O.; Loria, A.S. Sex-specific effects of stress on metabolic and cardiovascular disease: Are women at higher risk? *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **2017**, *313*, R1–R9. [CrossRef] [PubMed]
40. Schuster, J.; Vogel, P.; Eckhardt, C.; Morelo, S.D. Applicability of the visceral adiposity index (VAI) in predicting components of metabolic syndrome in young adults. *Nutr. Hosp.* **2014**, *30*, 806–812. [PubMed]
41. Chumlea, W.C.; Sun, S.S. Bioelectrical Impedance Analysis. In *Human Body Composition*; Heymsfield, S.B., Lohman, T.G., Wang, Z.-M., Going, S.B., Eds.; Human Kinetics: Champaign, IL, USA, 2005; pp. 79–88.
42. Zhu, S.; Wang, Z.; Shen, W.; Heymsfield, S.B.; Heshka, S. Percentage body fat ranges associated with metabolic syndrome risk: Results based on the third National Health and Nutrition Examination Survey (1988–1994). *Am. J. Clin. Nutr.* **2003**, *78*, 228–235. [PubMed]
43. Mohammadreza, B.; Farzad, H.; Davoud, K.; Fereidoun, A.F. Prognostic significance of the complex "Visceral Adiposity Index" vs. simple anthropometric measures: Tehran lipid and glucose study. *Cardiovasc. Diabetol.* **2012**, *11*, 20. [CrossRef] [PubMed]
44. Mousa, U.; Kut, A.; Bozkus, Y.; Cicek Demir, C.; Anil, C.; Bascil Tutuncu, N. Performance of abdominal bioelectrical impedance analysis and comparison with other known parameters in predicting the metabolic syndrome. *Exp. Clin. Endocrinol. Diabetes* **2013**, *121*, 391–396. [CrossRef] [PubMed]
45. Wang, J.; Rennie, K.L.; Gu, W.; Li, H.; Yu, Z.; Lin, X. Independent associations of body-size adjusted fat mass and fat-free mass with the metabolic syndrome in Chinese. *Ann. Hum. Biol.* **2009**, *36*, 110–121. [CrossRef] [PubMed]
46. Kim, J.Y.; Oh, S.; Chang, M.R.; Cho, Y.G.; Park, K.H.; Paek, Y.J.; Yoo, S.H.; Cho, J.J.; Caterson, I.D.; Song, H.J. Comparability and utility of body composition measurement vs. anthropometric measurement for assessing obesity related health risks in Korean men. *Int. J. Clin. Pract.* **2013**, *67*, 73–80. [CrossRef] [PubMed]
47. Peltz, G.; Aguirre, M.T.; Sanderson, M.; Fadden, M.K. The role of fat mass index in determining obesity. *Am. J. Hum. Biol.* **2010**, *22*, 639–647. [CrossRef] [PubMed]
48. Kyle, U.G.; Schutz, Y.; Dupertuis, Y.M.; Pichard, C. Body composition interpretation. Contributions of the fat-free mass index and the body fat mass index. *Nutrition* **2003**, *19*, 597–604. [CrossRef]
49. Johnson Stoklossa, C.A.; Forhan, M.; Padwal, R.S.; Gonzalez, M.C.; Prado, C.M. Practical Considerations for Body Composition Assessment of Adults with Class II/III Obesity Using Bioelectrical Impedance Analysis or Dual-Energy X-ray Absorptiometry. *Curr. Obes. Rep.* **2016**, *5*, 389–396. [CrossRef] [PubMed]
50. Schutz, Y.; Kyle, U.U.G.; Pichard, C. Fat-free mass index and fat mass index percentiles in Caucasions aged 18–98 years. *Int. J. Obes.* **2002**, *26*, 953–960.
51. Martínez-Torres, J.; Correa-Bautista, J.E.; González-Ruíz, K.; Vivas, A.; Triana-Reina, H.R.; Prieto-Benavidez, D.H.; Carrillo, H.A.; Ramos-Sepúlveda, J.A.; Villa-González, E.; García-Hermoso, A.; et al. A Cross-Sectional Study of the Prevalence of Metabolic Syndrome and Associated Factors in Colombian Collegiate Students: The FUPRECOL-Adults Study. *Int. J. Environ. Res. Public Health* **2017**, *14*, 233. [CrossRef] [PubMed]
52. Jaffrin, M.Y.; Morel, H. Body fluid volumes measurements by impedance: A review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. *Med. Eng. Phys.* **2008**, *30*, 1257–1269. [CrossRef] [PubMed]

HOSTED BY

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Journal of Sport and Health Science 00 (2018) 1–8

www.jshs.org.cn

Original article

Muscle strength cut-offs for the detection of metabolic syndrome in a nonrepresentative sample of collegiate students from Colombia

Antonio Garcia-Hermoso [a,*], Alejandra Tordecilla-Sanders [b], Jorge Enrique Correa-Bautista [b], Mark D. Peterson [c], Mikel Izquierdo [d], Aura Cristina Quino-Ávila [e], Carolina Sandoval-Cuellar [e], Katherine González-Ruíz [f], Robinson Ramírez-Vélez [b]

[a] *Physical Activity, Sport and Health Sciences Laboratory, University of Santiago de Chile, Santiago de Chile 7500618, Chile*
[b] *Center of Studies in Physical Activity Measurements, School of Medicine and Health Sciences, Universidad del Rosario, Bogotá 111221, Colombia*
[c] *Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, Michigan 48109, USA*
[d] *Department of Health Sciences, Public University of Navarre, CIBERFES (CB16/10/00315), Navarre 31009, Spain*
[e] *CORPS Group, University of Boyacá, Faculty of Health Sciences, Boyacá 153610, Colombia*
[f] *Physical Exercise and Sports Research Group, Manuela Beltrán University, Bogotá 111221, Colombia*

Received 26 October 2017; revised 7 March 2018; accepted 14 May 2018
Available online xxx

Abstract

Background: Evidence shows an association between grip strength and health; however, grip strength cut-offs for the detection of metabolic syndrome (MetS) in Latin American populations are scarce. The purpose of this study was to determine cut-offs of normalized grip strength (NGS) for the detection of MetS in a large nonrepresentative sample of a collegiate student population from Colombia.

Methods: A total of 1795 volunteers (61.4% female, age = 20.68 ± 3.10 years, mean ± SD), ranging between 18 and 30 years of age participated in the study. Strength was estimated using a handheld dynamometer and normalized to body mass (handgrip strength (kg)/body mass (kg)). Anthropometrics, serum lipids indices, blood pressure, and fasting plasma glucose were measured. Body composition was measured by bioelectrical impedance analysis. MetS was defined as including ≥3 of the 5 metabolic abnormalities according to the International Diabetes Federation definition. A metabolic risk score was computed from the following components: waist circumference, triglycerides, high-density lipoprotein cholesterol, glucose, and systolic and diastolic blood pressure.

Results: Receiver operating curve analysis showed significant discriminatory accuracy of NGS in identifying the thresholds and risk categories. Lower strength was associated with increased prevalence of MetS. In males, weak, intermediate, and strong NGS values at these points were <0.466, 0.466–0.615, >0.615, respectively. In females, these cut-off points were <0.332, 0.332–0.437, >0.437, respectively.

Conclusion: Our sex-specific cut-offs of NGS could be incorporated into a clinical setting for identifying college students at cardiometabolic disease risk.

Keywords: Cardiometabolic risk; Muscular fitness; Receiver operating characteristic curve; Thresholds

1. Introduction

Muscular weakness, as determined with the use of a handgrip dynamometer, is recognized as a marker of health risk, similar to that observed for conventional risk factors.[1–3] López-Martínez et al.[3] demonstrated that muscle strength is negatively associated with metabolic syndrome (MetS) in young adults. Additionally, in a prospective study (follow-up in young adulthood for 20 years), Fraser et al.[4] showed that those in the lowest third tertile of strength were independently associated with adult MetS. Similarly, our group[5,6] and other investigators[7–9] have shown an independent and inverse association between low strength and cardiometabolic risk clustering among adolescents and adults. The contribution of muscular weakness to the progression of sedentary behavior with aging and/or cardiometabolic risk factors (e.g., obesity, MetS, insulin resistance) is equally unequivocal, and recent

Peer review under responsibility of Shanghai University of Sport.
* Corresponding author.
E-mail address: antonio.garcia.h@usach.cl (A. Garcia-Hermoso).

https://doi.org/10.1016/j.jshs.2018.09.004

national efforts to identify cut-offs or thresholds for clinically relevant weakness among young people[10] will help clinicians screen individuals at greatest risk.[11,12]

Senechal et al.[11] determined low muscle strength cut-offs for the prediction of MetS among middle-aged and older males using a composite score of normalized strength from chest press and leg press from a sample of 5685 men aged <50 years and 1541 men aged ≥ 50 years. However, at this time, thresholds derived from handgrip muscle strength, a clinically relevant strength measure, among Latin-American college students remains to be determined. Moreover, even though there is scientific evidence regarding the role of muscle strength preservation for prevention against cardiometabolic risk in several populations, no studies have established the minimum strength capacity associated with the risk of MetS among Latin-American college students. Clinically relevant handgrip strength cut-offs for detecting MetS have been established for youths,[6] adults,[11] and older adults.[7,8]

However, Leong et al.[13] reported considerable heterogeneity in median handgrip strength among 125,462 healthy adults aged 35−70 years from 21 countries in the Prospective Urban Rural Epidemiology study. This finding is important because it has been reported that handgrip strength is predictive of mortality and cardiovascular disease (CVD) independently of country income.[14] Therefore, from a public health perspective, the inclusion of handgrip strength measures in health surveillance systems is clearly justifiable. For example, moderate weight gain from early to middle adulthood is associated with significantly increased risk of major chronic diseases and mortality.[2] Therefore, young adults may also be a good population for monitoring fitness, identifying risk factors, and offering interventions among those at high cardiometabolic risk. For that, cut-offs to determine young adults at caridiometabolic risk are required and to be used later to promote muscular strength and to lower CVD risk in later life.

Thus, our study aimed to determine cut-offs of grip strength for the detection of MetS in a large collegiate student population from Colombia. Such evidence could serve as proof of a concept for the development of broad normative reference test standards for clinical, academic, and community settings.

2. Methods

2.1. Participants and study design

Data were from a cross-sectional component of the FUPRECOL (in Spanish, Asociación de la Fuerza Prensil con Manifestaciones Tempranas de Riesgo Cardiovascular en Adultos Colombianos) study conducted during the 2014−2017 academic years. We recently published a complete description of the FUPRECOL study design, methods, and primary outcomes for our current cohort.[9] A convenience sample comprised 1795 volunteers (61.4% female, age = 20.68 ± 3.10 years, mean ± SD) between ages 18 and 30 years of low to middle socioeconomic status, which was evaluated in accordance with the following Colombian government classification: stratum 1−2 = low, stratum 3−4 = middle, and stratum 5−6 = high). The sample comprised students enrolled in public or private universities from 3 distinct areas of Colombia: the capital district of Bogota (Cundinamarca), Tunja (Boyacá), and Santiago de Cali (Valle del Cauca).

Exclusion criteria included medical or clinical diagnosis of a major systemic disease, including malignant conditions such as cancer, type 1 or 2 diabetes, high blood pressure, and hypothyroidism or hyperthyroidism; a history of drug or alcohol abuse; regular use of multivitamins; chronic inflammatory conditions including rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis; infectious conditions; or a body mass index (BMI) ≥ 35 kg/m^2. Volunteers were not compensated for their participation. Informed consent was obtained from each participant. All participants provided written consent, and each study was approved by the local authorized institutional review boards (Bogotá UMB Code N° 01-1802-2013, UR Code N°CEI-ABN026-000010; Cali UNIAJC Code N° 111-02.01.48/16; Tunja Code N° RECT 60) and complied with the Declaration of Helsinki (World Medical Association for Human Subjects). The students who agreed to participate and who had signed the informed consent form were given appointments for the procedures described in the following.

2.2. Physical examination

Subjects were screened for inclusion in the study via personal interviews. Interview questions included queries about health status, medical history, CVD risk factors, and lifestyle. After completing another general information questionnaire, participants were instructed to wear shorts and t-shirts to the physical examination. They were also required to remove all jewelry and metal objects. Once the subjects were barefoot and in their underwear, their body weight (kg) was measured using an electric scale (Tanita Model BC-418, Tanita Corp., Tokyo, Japan) with a range of 0−200 kg and with an accuracy within 100 g. Height was measured with a portable stadiometer with a precision of 0.1 mm and a range of 0−2.50 m (Seca 274, Vogel and Halke, Hamburg, Germany). BMI was calculated by using the following formula: body mass (kg)/height (m^2). BMI status was evaluated according to the World Health Organization criteria.[15] The waist circumference (WC) was measured in cm as the narrowest point between the lower costal border and the iliac crest. When this point was not evident, it was measured at the midpoint between the last rib and the iliac crest, using a metal tape measure (Lufkin W606PM; Cooper Tools, Parsippany, NJ, USA). The evaluation process was carried out by a team of professionals (4 physical therapy professors) with extensive experience in anthropometric measurement. Measurements for 2% of the sample was carried out twice to ensure quality of measures. The technical error of measurement (TEM) values were <2% for all anthropometric variables.

Body fat percentage (BF%) and fat mass index (FMI) were determined for bioelectrical impedance analysis (BIA) by a tetrapolar whole-body impedance (Tanita Model BC-418; Tanita Corp.,). For the calculation of intra- and inter-observer

Please cite this article as: Antonio Garcia-Hermoso et al., Muscle strength cut-offs for the detection of metabolic syndrome in a nonrepresentative sample of collegiate students from Colombia, Journal of Sport and Health Science (2018), https://doi.org/10.1016/j.jshs.2018.09.004

TEM, at least 50 subjects needed to be measured (30 males, 20 females, aged 22.3 ± 2.1 years). The Tanita Model BC-418 is a reliable system that has good agreement with laboratory-based methods of assessment (hydrostatic weighing: $r = 0.81$, $p < 0.05$; error of 1.68 BF% or DXA: $r = 0.87$, $p < 0.001$).[16,17] The corresponding intraobserver technical error (% reliability) of the measurements was 95%. A detailed description of the BIA technique can be found elsewhere.[18] Before testing, participants were required to adhere to the BIA manufacturer's instructions (http://www.tanita.com/es/bc-418/), including not to (i) eat or drink within 4 h of the test; (ii) consume caffeine or alcohol within 12 h of the test; (iii) take diuretics within 7 days of the test; (iv) do physical exercise within 12 h of the test, and (v) urinate within 30 min of the test. FMI was calculated by dividing each subject's fat mass (kg) by the square of his or her height $(m)^2$, as described previously.[19]

2.3. Muscular strength

Handgrip strength was assessed using an adjustable digital handgrip dynamometer (T-18 TKK SMEDLY III; Takei Scientific Instruments Co., Ltd., Niigata, Japan). Participants watched a brief demonstration of the technique and were given verbal instructions on how to perform the test. The dynamometer was adjusted according to the subjects' hand size based on a predetermined protocol.[20] The best score for each hand was recorded in kg. The handgrip strength was calculated as the average of the left and right hand. Because there is substantial covariance between strength capacity and body mass, and because the link between strength and both physical function and chronic health is directly mediated by the proportion of strength relative to body mass, handgrip strength was a normalized grip strength (NGS) per body mass—for instance, handgrip strength (kg)/body mass (kg). The reproducibility of our data was $R = 0.96$. Intra-rater reliability was assessed by determining the intra-class correlation coefficient (0.98, 95% confidence interval (CI): 0.97−0.99, $n = 20$, median age = 22.88 ± 1.41 years, 66.2 ± 5.41 kg, 1.75 ± 0.1 m, 24.91 ± 3.12 kg/m^2).

2.4. MetS diagnosis

After the subjects had fasted for 10−12 h, blood samples were obtained from capillary sampling from 6:00−10:00 a.m. Participants were asked not to engage in prolonged exercise in the 24 h prior to testing. The biochemical profile included the following: (i) high-density lipoprotein cholesterol (HDL-C), (ii) triglycerides, (iii) low-density lipoprotein cholesterol (LDL-C), (iv) total cholesterol, and (v) glucose fasting by enzymatic colorimetric methods. Inter-assay reproducibility (coefficient of variation) was determined from 80 replicate analyses of 8 plasma pools over a period of 15 days. The percentages obtained were 2.6% (triglycerides), 2.0% (total cholesterol), 3.2% (HDL-C), 3.6% (LDL-C), and 1.5% (fasting glucose).

Blood pressure was taken on the left arm at the heart level with the automatic device Omron M6 Comfort (Omron Healthcare Europe B.V., Hoofddorp, The Netherlands) while the participants were sitting still. The blood pressure monitor cuff was placed 2−3 finger-widths above the bend of the arm, and a 2-min pause was allowed between the first and the second measurement with a standard cuff for an arm circumference of 22−32 cm. The mean arterial pressure (MAP) was calculated using the following formula: MAP = (systolic blood pressure + (2 × diastolic blood pressure))/3.

Participants were considered to have diagnoses of the MetS if they had ≥3 of the following: (i) abdominal obesity (WC ≥ 80 cm in females and WC ≥ 90 cm in males), (ii)

Table 1
Characteristics among a sample of college students from Colombia (mean ± SD, $n = 1795$).

Characteristics	Male ($n = 692$)	Female ($n = 1103$)	p
Anthropometric			
Age (year)	20.51 ± 3.22	20.59 ± 2.99	0.077
Weight (kg)	68.91 ± 12.22	58.79 ± 10.36	<0.001
Height (cm)	172.30 ± 6.65	159.09 ± 5.86	<0.001
WC (cm)	78.23 ± 9.32	71.53 ± 8.02	<0.001
High WC *n* (%)	75 (10.84)	151 (13.69)	0.069
BMI (kg/m^2)	23.17 ± 3.60	23.21 ± 3.77	0.089
Body fat (%)	15.61 ± 6.54	27.03 ± 7.26	0.002
FMI (kg/m^2)	3.81 ± 2.24	6.50 ± 2.75	<0.001
Body mass index status, *n* (%)			
Underweight	(5.49)	72 (6.52)	<0.001
Normal weight	477 (68.93)	735 (66.64)	<0.001
Overweight	144 (20.81)	235 (21.31)	<0.001
Obese	33 (4.77)	61 (5.53)	<0.001
Blood pressure			
Systolic (mm Hg)	120.28 ± 12.97	111.29 ± 11.15	<0.001
Diastolic (mm Hg)	74.19 ± 11.45	71.74 ± 9.35	<0.001
MAP (mm Hg)	97.23 ± 10.90	91.51 ± 8.92	<0.001
Hypertension, *n* (%)	282 (40.75)	187 (16.95)	<0.001
Cardiometabolic parameters			
Total cholesterol (mg/dL)	132.75 ± 30.23	146.39 ± 33.33	0.081
High total cholesterol, *n* (%)	21 (3.03)	62 (5.62)	0.007
Triglycerides (mg/dL)	93.74 ± 48.54	88.50 ± 45.34	0.017
High triglycerides, *n* (%)	54 (7.80)	127 (11.51)	<0.001
LDL-C (mg/dL)	81.07 ± 26.09	87.92 ± 26.15	0.386
High LDL-C, *n* (%)	272 (39.31)	683 (61.92)	<0.001
HDL-C (mg/dL)	39.55 ± 10.67	43.97 ± 12.80	<0.001
Low HDL-C, *n* (%)	383 (55.35)	798 (72.35)	<0.001
Glucose (mg/dL)	84.81 ± 11.99	86.05 ± 11.57	0.010
High glucose, *n* (%)	61 (8.82)	90 (8.16)	0.629
MetS score	−3.85 ± 2.95	−3.94 ± 2.66	0.008
MetS, *n* (%)	84 (12.14)	82 (7.43)	0.001
Lifestyle, *n* (%)			
Tobacco (≥10 cigarettes per week)	199 (28.76)	210 (19.04)	0.548
Alcohol (≥1 time per week)	378 (54.62)	430 (38.98)	0.451
Physical activity levels (≥150 min per week)	243 (35.12)	222 (20.13)	0.001
Muscular strength			
Handgrip (kg)	39.42 ± 7.14	24.07 ± 4.95	<0.001
NGS[a]	0.58 ± 0.11	0.42 ± 0.09	<0.001

[a] NGS measured as handgrip strength (kg)/body mass (kg).
Notes: values are presented as mean ± SD unless otherwise noted.
Abbrevations: BMI = body mass index; FMI = fat mass index; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; MAP = mean arterial pressure; MetS = metabolic syndrome; NGS = normalized grip strength; WC = waist circumference.

Please cite this article as: Antonio Garcia-Hermoso et al., Muscle strength cut-offs for the detection of metabolic syndrome in a nonrepresentative sample of collegiate students from Colombia, Journal of Sport and Health Science (2018), https://doi.org/10.1016/j.jshs.2018.09.004

hypertriglyceridemia (≥150 g/dL), (iii) low HDL-C (<50 mg/dL in females and <40 mg/dL in males), (iv) high blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg) or MAP ≥100 mmHg, and (v) high fasting glucose (≥100 mg/dL). MetS was defined in accordance with the updated harmonized criteria of the International Diabetes Federation (IDF).[21]

We calculated a composite MetS score that reflects a continuous score of the 5 MetS risk factors. The MetS score was calculated from the individual subjects' data, based on the IDF,[21] and the standard deviations were calculated using data from the entire subject cohort at baseline. The equation used was MetS score = ((HDL-C: male ≤40 mg/dL or female ≤50 mg/dL)/SD: female = 1.04 or male = −0.19) + ((triglycerides (TG): 150 mg/dL)/SD: female = 0.99 or male = 0.97) + ((fasting glucose: 100 mg/dL)/SD: female = 0.98 or male = 1.02) + ((WC: male ≥94 cm or female ≥80 cm)/SD: female = 0.99 or male = 0.94) + ((MAP: 100 mmHg)/SD: female = 0.88 or male = 1.07). The mean of this continuously distributed MetS score was therefore 0 by definition.

2.5. Lifestyle covariates

A standardized questionnaire, the "FANTASTIC" lifestyle (family, physical activity (PA), nutrition, tobacco toxins, alcohol, sleep/stress, personality type, insight, and career), was used to collect comprehensive information about substance use via a personal interview with participants. Alcohol consumption and smoking status were defined as subjects who had consumed any alcoholic beverage ≥1 time per week and those who had smoked ≥10 cigarettes per week for at least 6 months, respectively, as previously described by Ramírez-Vélez et al.[22] Participants who exercised ≥3 times a week for >30 min were categorized as "physically active", and those who exercised <3 times a week were considered "physically inactive".[22]

2.6. Statistical analysis

Descriptive characteristics are provided as means, SDs, and percentages. Histograms and Q-Q plots were used to verify the normality of the selected variables. Independent 2-tailed *t* tests for continuous variables and χ^2 tests for categorical variables were used to examine sex differences or the MetS group. Analysis of covariance adjusted for age, tobacco, alcohol, and PA levels (owing to the relationship with MetS) was used to determine the main effects for NGS (weak, intermediate, and strong) and anthropometrics, blood pressure, metabolic biomarkers, and muscle strength outcomes. We calculated standard indices, including sensitivity, specificity, area under the curve (AUC), and receiver operating characteristic (ROC) curve analysis, to establish weak, intermediate, and strong handgrip cut-off scores for subjects (male and female). Such cut-offs could be used to predict MetS according to the IDF criteria. Sensitivity was defined as the probability of classifying correctly those college students presenting MetS (true positives), whereas specificity was defined as the probability of classifying correctly those participants presenting non-MetS (true negatives). The shortest distance in the ROC curve was calculated using the function $\sqrt{(1-\text{sensitivity}^2) + (1-\text{specificity}^2)}$ by maximizing the Youden index. The positive likelihood ratio (LR(+)) and the negative likelihood ratio (LR(−)) were used to analyze the potential diagnostic accuracy of the NGS to discriminate among weak, intermediate, and strong for MetS. Locally weighted scatterplot smoothing curves were used to illustrate the shape of the relationship between the NGS and MetS score. Conditional inference tree analyses were used as an alternative method for determining weak, intermediate, and strong risk thresholds of normalized strength for detection of the high-risk cardiometabolic phenotype, as described previously.[23] Data were analyzed with SPSS Version 24.0 for Windows (IBM Corp., Armonk, NY, USA,) and freely available statistical software R version 3.2.3 (RStudio Team, Boston, MA, USA). A p value <0.05 denoted statistical significance.

3. Results

The 1795 volunteers included 1103 females (61.4%). Their mean age was 20.68 ± 3.10 years. Overall, males had greater body weight, WC, blood pressure, high triglycerides, and PA levels than females ($p \leq 0.001$), whereas females had lower handgrip and NGS ($p < 0.001$). The prevalence of overweight and obesity was 21.31% and 5.53% in females, respectively

Table 2
Parameters of the ROC curves analysis for the diagnostic performance of NGS inidentifying weak, intermediate, and strong risk of MetS according to the IDF criteria in males and females.

Parameters	AUC	95%CI	*p*	Cut-off	Sensitivity (%)	Specificity (%)	LR (+)	LR (−)	Percentile
Male									
Weak	0.720	0.679–0.802	<0.001	<0.466	89.0	57.8	2.11	0.19	≤14
Intermediate	0.740	0.679–0.802	<0.001	0.466–0.615	86.9	56.8	2.10	0.23	15–62
Strong	—	—	—	>0.615	84.3	58.7	2.04	0.26	≥63
Female									
Weak	0.725	0.670–0.780	<0.001	<0.332	84.9	58.5	2.04	0.25	≤17
Intermediate	0.728	0.660–0.777	<0.001	0.332–0.437	85.0	58.3	2.02	0.24	18–60
Strong	—	—	—	>0.437	86.6	57.9	2.05	0.23	≥61

Notes: NGS is measured as grip strength (kg)/body mass (kg).
Abbreviations: AUC = area under the curve; CI = confidence interval; IDF = International Diabetes Federation; LR(+) = positive likelihood ratio; LR(−) = negative likelihood ratio; MetS = metabolic syndrome; NGS = normalized grip strength; ROC = receiver operating characteristic curve.

($p < 0.001$) (Table 1). In males, the prevalence of overweight and obesity was 20.81% and 4.77%, respectively ($p < 0.001$). It was observed that 40.75% of males had high blood pressure. Total cholesterol, and LDL-C levels were significantly higher in females than in males ($p < 0.05$).

Table 2 depicts ROC curve analysis for the diagnostic performance NGS in identifying weak, intermediate, and strong risk of MetS. Since multiple levels of risk were desired, the selection of the resulting cut-off values was based on multiple combinations of sensitivity and specificity. In males, NGS values for weak, intermediate, and strong were <0.466, 0.466-0.615, and >0.615, respectively. In females, these cut-offs were <0.332, 0.332-0.437, and >0.437, respectively (Table 2).

Mean differences in anthropometrics, cardiometabolic risk, and muscle strength parameters according to NGS categories are shown in Table 3. In males and females, analysis of variance adjusted for age, tobacco, alcohol, and PA levels showed that there were differences in body weight, FMI, and muscle strength (all $p < 0.05$).

Conditional inference trees predicting probability of the high-risk cardiometabolic phenotype (MetS according to the IDF criteria) confirmed different low strength thresholds between males and females. Fig. 1 provides results for the primary definition. The first cut-off point identified in males was based on having NGS <0.466 *vs.* ≥0.466. Within the group of subjects with NGS ≥0.466, a second cut-off point was identified as an NGS <0.615. Among the weakest males (NGS <0.466), 34.6% had MetS, as compared with 10.7% among males with intermediate NGS (0.466-0.615), and only 4.9% among males with the highest NGS (>0.615). Among females, the first identified cut-off was based on having an NGS ≥0.332 *vs.* <0.332. Within the group of subjects with an NGS <0.332, a second cut-off point was identified as an NGS ≥0.332. Among the weakest females (NGS <0.332), 18.0% had MetS, as compared with 7.9% among females with intermediate NGS (0.332-0.437) and only 2.4% among females with the highest NGS (>0.437).

Fig. 2 provides plots of the association between NGS and MetS score for males and females. Inspection of the locally weighted scatterplot smoothing curves provides evidence of a well-defined threshold effect of low strength on the MetS score as a continuous outcome.

4. Discussion

This is one of the first studies to identify sex-specific cut-offs for NGS to detect a high-risk cardiometabolic phenotype among a large population of college students. The role of muscular strength has been increasingly recognized in the prevention of chronic disease in adult populations.[1–3] Evidence suggests that muscle mass and strength decrease progressively after the age of 20 years,[24] whereas in old age, some grip strength and hip strength declines by an average of 1.10 kg per year and 1.31 kg per year, respectively.[25] Therefore, young adulthood seems to be crucial time frame for monitoring and intervening to reduce the risk of weakness and cardiometabolic disease.

Table 3
Sex thresholds for weak, intermediate, and strong NGS with anthropometric, blood pressure, metabolic biomarkers, and muscle strength.

Variables	Male ($n = 692$)						Female ($n = 1103$)					
	Weak ($n = 101$)	Intermediate ($n = 326$)	Strong ($n = 265$)	F	P	η_p^2	Weak ($n = 188$)	Intermediate ($n = 466$)	Strong ($n = 449$)	F	P	η_p^2
Anthropometric												
Weight (kg)	80.0 ± 15.8	70.6 ± 11.2	63.5 ± 8.6	91.53	<0.001	0.241	67.5 ± 13.5	59.6 ± 10.1	52.5 ± 6.3	116.01	<0.001	0.227
WC (cm)	87.6 ± 12.7	79.5 ± 8.6	74.3 ± 6.0	100.45	<0.001	0.231	77.0 ± 9.0	72.1 ± 7.3	67.0 ± 5.5	98.05	<0.001	0.199
Body fat (%)	22.2 ± 7.9	16.6 ± 5.7	12.9 ± 4.5	109.76	<0.001	0.247	32.5 ± 7.2	28.1 ± 6.9	22.5 ± 5.9	112.58	<0.001	0.223
FMI (kg/m^2)	6.3 ± 3.4	4.1 ± 1.9	2.8 ± 1.2	117.16	<0.001	0.259	8.9 ± 3.4	6.8 ± 2.6	4.9 ± 1.8	128.13	<0.001	0.241
Blood pressure (mmHg)												
Systolic	123.9 ± 13.8	122.9 ± 12.3	119.4 ± 11.0	12.66	<0.001	0.136	111.7 ± 10.4	111.4 ± 11.4	110.4 ± 10.7	1.46	0.232	0.004
Diastolic	78.6 ± 10.1	76.4 ± 11.0	72.9 ± 9.6	8.83	<0.001	0.026	73.3 ± 9.3	71.7 ± 10.1	72.2 ± 9.8	1.91	0.147	0.005
MAP	101.3 ± 10.3	99.6 ± 10.3	96.1 ± 9.3	13.98	<0.001	0.040	92.5 ± 8.6	91.5 ± 9.3	91.3 ± 8.7	1.42	0.240	0.004
Cardiometabolic biomarkers												
Total cholesterol (mg/dL)	133.4 ± 27.6	142.3 ± 29.8	140.6 ± 26.1	3.24	0.039	0.010	150.0 ± 32.3	148.5 ± 28.6	148.3 (28.5	0.02	0.978	0.001
Triglycerides (mg/dL)	113.6 ± 54.6	103.9 ± 47.2	95.3 ± 40.8	9.83	<0.001	0.029	98.5 ± 42.9	94.0 ± 37.7	86.8 ± 34.9	6.65	0.001	0.017
HDL-C (mg/dL)	38.1 ± 10.2	39.9 ± 10.6	41.5 ± 9.5	4.84	0.008	0.014	38.0 ± 11.4	41.9 ± 11.7	45.2 ± 12.4	15.63	<0.001	0.039
LDL-C (mg/dL)	74.0 ± 23.0	82.7 ± 27.0	81.5 ± 25.3	4.09	0.017	0.016	93.2 ± 27.6	88.4 ± 25.3	85.9 ± 22.9	1.87	0.155	0.006
Glucose (mg/dL)	87.4 ± 11.5	85.5 ± 11.7	82.8 ± 12.1	5.76	0.003	0.017	89.1 ± 8.6	87.6 ± 11.3	85.2 ± 12.5)	6.09	0.002	0.017
MetS score	−1.742 ± 3.160	−3.252 ± 2.762	−4.684 ± 2.369	51.60	<0.001	0.135	−2.191 ± 2.689	−3.437 ± 2.525	−4.729 ± 2.125	54.01	<0.001	0.125
Muscular strength												
Handgrip (kg)	32.0 ± 6.1	38.4 ± 5.9	43.7 ± 6.4	135.94	<0.001	0.288	19.7 ± 3.8	23.1 ± 3.9	26.5 ± 3.7	161.13	<0.001	0.125
NGS[a]	0.403 ± 0.052[a]	0.546 ± 0.042	0.691 ± 0.069	132.83	<0.001	0.764	0.294 ± 0.032	0.388 ± 0.028	0.507 ± 0.054	109.09	<0.001	0.771

[a] NGS is measured as handgrip strength (kg)/body mass (kg). F values and and partial eta-squared (η_p^2) calculated from analysis of variance adjusted for age, tobacco, alcohol, and physical activity levels.

Notes: Values are presented as mean ± SD unless otherwise noted.

Abbreviations: FMI = fat mass index; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; MAP = mean arterial pressure; MetS = metabolic syndrome; NGS = normalized grip strength; WC = waist circumference.

Few studies have proposed cut-offs for low muscular strength among adults for screening cardiometabolic risk; however, this has yet to receive adequate attention in young adult populations, and information is scarce. Most studies have analyzed the older adult population. For example, Lee et al.[26] demonstrated that cardiometabolic risk was 54% lower for individuals with relative handgrip strength (absolute handgrip strength divided by BMI) in the 75th percentile compared with the 25th percentile. In addition, Duchowny et al.[27] established cut-off points for muscle weakness assessed as handgrip strength in a nationally representative sample by race and sex among older American adults. Senechal et al.[11] determined low muscle strength cut-off points for the prediction MetS using a composite score of normalized strength from the chest press and leg press. Among middle-aged adults, Strand et al.[28] revealed an association between handgrip strength and all-cause mortality and cardiovascular mortality, confirming the role of handgrip strength as a mortality predictor.[29] Finally, among young adults, Wilkerson et al.[30] investigated 62 collegiate football players (mean age 19.9 years) and found that low leg muscle strength was associated with an increased likelihood of MetS.

In line with studies mentioned earlier, our study revealed cut-offs for NGS by sex and identified 3 cardiometabolic risk categories ("high", "intermediate", and "low"). The ROC curves generated for this study showed acceptable AUCs and 95%CI limits, suggesting that the resultant cut-offs were not owing to chance (both AUC $\geq$0.72). Specifically, among males in the highest strength category, only 4.9% had the MetS phenotype, as compared with 10.7% among males with intermediate strength and 34.6% among males with low strength. Among the females in the highest strength category, only 2.4% had the MetS phenotype, as compared with 7.9% among females with intermediate strength and 18% among those with low strength. The identification of the 3 categories of cardiometabolic risk coincides with the findings of Peterson et al.,[31] who determined by sex the distribution of high cardiometabolic risk according to the cut-off points: weak, intermediate, and strong. These cut-off points were obtained from a similar size sample but not related to the age range. The cut-off points are lower than those identified in our study.

However, the AUCs observed for this threshold were 0.72−0.74 for males and 0.72 for females, whereas in the study performed by Senechal et al.,[11] the AUCs were 0.65 for males and 0.81 for females. The lower sensitivity and specificity reported in our study might be related to differences in age (20−50 years *vs.* 18−30 years), sample size of the populations studied (1795 *vs*. 5685), and the methods used to assess muscle strength (handgrip *vs*. leg and bench press), as well as the use of a composite measure of MetS. Thus, our findings reinforce the concept that muscle strength may be an important modifiable lifestyle factor for CVD risk assessment in the same way that physical inactivity, body composition, and healthy dietary patterns are important.

Our findings therefore support previous results demonstrating that low muscle strength is associated with MetS. These findings coincide with Sasaki et al.,[32] in which for each 5 kg increase in grip strength, the number of deaths caused by heart disease and stroke diminishes significantly. A plausible explanation for the role of muscle strength in MetS prevalence may be through the metabolic and structural changes that improve muscle insulin sensitivity and glycemic control.[33] As demonstrated by Wu et al.[34] in a recent meta-analysis, there is a 63% higher risk of premature mortality owing to CVD among adults with low handgrip muscle strength.

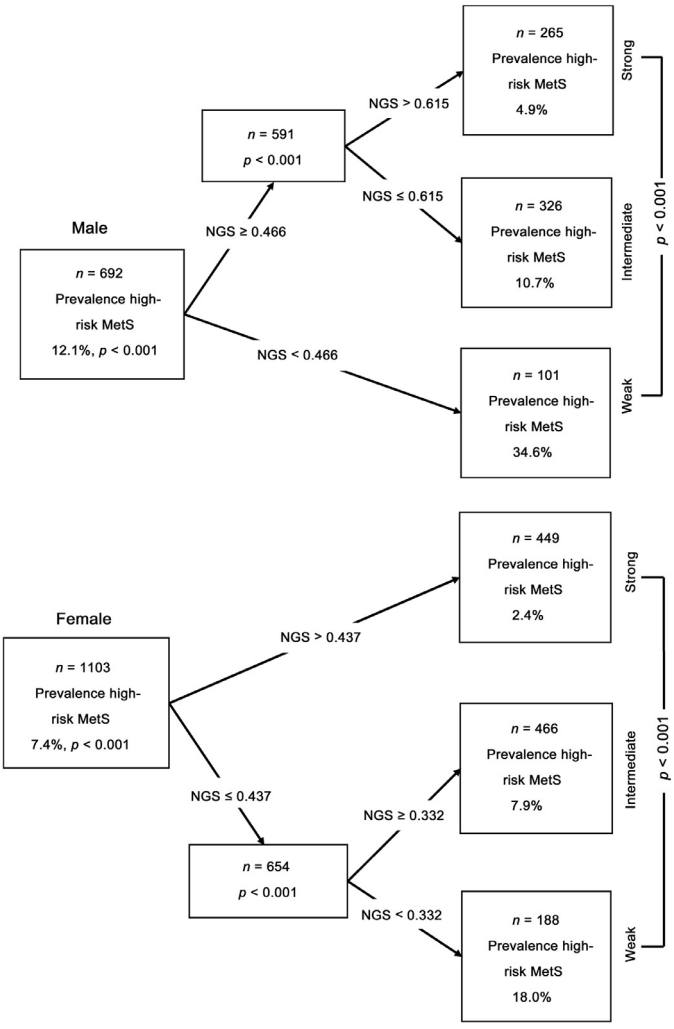

Fig. 1. Conditional inference trees for NGS, as predictors in identifying risk of MetS according to the IDF criteria in males and females. NGS is measured as grip strength (kg)/body mass (kg). IDF = International Diabetes Federation; MetS = metabolic syndrome; NGS = normalized grip strength.

The strengths of this study include the large sample size and a commonly used and feasible test for assessing muscle strength. However, there are some limitations that need to be highlighted. First, owing to the cross-sectional nature of the study design, we were unable to draw causal relationships. Thus, we were unable to deduce whether low NGS leads to increased risk of MetS, or conversely whether poor cardiometabolic profiles lead to declines in muscle strength. Future longitudinal studies are needed to better understand how declines in muscle strength contribute to health risks in college-aged adults. Second, the ROC curve analysis does not enable

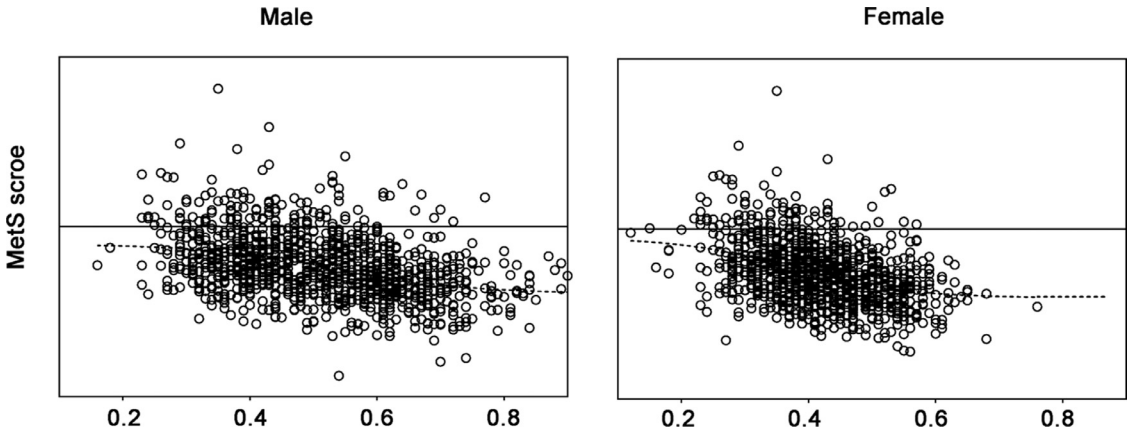

Fig. 2. Scatterplots with overlaid locally weighted scatterplot smoothing curves to depict the shape of the association between the NGS and MetS score by sex. NGS is measured as grip strength (kg)/body mass (kg). MetS = metabolic syndrome; NGS = normalized grip strength.

adjustments for potential confounders within the model, and data were not adjusted prior to ROC curve analysis. Finally, we only analyzed relatively healthy individuals; therefore, the generalization of our results is limited to healthy younger adults. Our study suggests that NGS could be used as a complementary tool that may help clinicians and practitioners screen for high cardiometabolic risk.

5. Conclusion

In summary, our sex-specific NGS cut-offs could be incorporated into a clinical setting for identifying college students at high cardiometabolic disease risk and used as a target for strength training programs designed to reduce the risk of MetS. Longitudinal studies are necessary to determine if increasing handgrip strength reduces the likelihood of MetS.

Acknowledgments

The authors gratefully acknowledge the contributions of Elisa Andrea Cobo, Boyacá University, that assisted the authors in obtaining data. We also acknowledge Monica Ojeda, Boyacá University, for assistance with data analysis. Both of their contributions were without compensation. This study was part of the project entitled Body Adiposity Index and Biomarkers of Endothelial and Cardiovascular Health in Adults, which was funded by the Centre for Studies on Measurement of Physical Activity, School of Medicine and Health Sciences, Universidad del Rosario (Code N°FIUR DN-BG001) and Universidad de Boyacá (Code N° RECT 60). The funder had no role in the study design, data collection, data analysis and interpretation, preparation of the manuscript, or decision to publish.

Authors' contributions

RRV, KGR, and JECB conceived of the study, designed it, and analyzed the data; AGH, ATS, MDP, MI, ACQA, and CSC analyzed the data and wrote the article. All authors approved the final manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

References

1. Jurca R, Lamonte MJ, Church TS, Earnest CP, Fitzgerald SJ, Barlow CE, et al. Associations of muscle strength and fitness with metabolic syndrome in men. *Med Sci Sports Exerc* 2004;**36**:1301–7.
2. Zheng Y, Manson JE, Yuan C, Liang MH, Grodstein F, Stampfer MJ, et al. Associations of weight gain from early to middle adulthood with major health outcomes later in life. *JAMA* 2017;**318**:255–69.
3. López-Martínez S, Sánchez-López M, Solera-Martinez M, Arias-Palencia N, Fuentes-Chacón RM, Martínez-Vizcaíno V. Physical activity, fitness, and metabolic syndrome in young adults. *Int J Sport Nutr Exerc Metab* 2013;**23**:312–21.
4. Fraser BJ, Huynh QL, Schmidt MD, Dwyer T, Venn AJ, Magnussen CG. Childhood muscular fitness phenotypes and adult metabolic syndrome. *Med Sci Sports Exerc* 2016;**48**:1715–22.
5. Ramírez-Vélez R, Meneses-Echavez JF, González-Ruíz K, Correa JE. Muscular fitness and cardiometabolic risk factors among Colombian young adults. *Nutr Hosp* 2014;**30**:769–75. [in Spanish].
6. Ramírez-Vélez R, Peña-Ibagon JC, Martínez-Torres J, Tordecilla-Sanders A, Correa-Bautista JE, Lobelo F, et al. Handgrip strength cutoff for cardiometabolic risk index among Colombian children and adolescents: the FUPRECOL study. *Sci Rep* 2017;**7**:42622. doi:10.1038/srep42622.
7. McGrath R, Vincent BM, Al Snih S, Markides KS, Peterson MD. The association between muscle weakness and incident diabetes in older Mexican Americans. *J Am Med Dir Assoc* 2017;**18**:452:e7–452. 12.
8. Peterson MD, Duchowny K, Meng Q, Wang Y, Chen X, Zhao Y. Low normalized grip strength is a biomarker for cardiometabolic disease and physical disabilities among U.S. and Chinese adults. *J Gerontol A Biol Sci Med Sci* 2017;**72**:1525–31.
9. García-Hermoso A, Carrillo HA, González-Ruíz K, Vivas A, Triana-Reina HR, Martínez-Torres J, et al. Fatness mediates the influence of muscular fitness on metabolic syndrome in Colombian collegiate students. *PLoS One* 2017;**12**: e0173932. doi:10.1371/journal.pone.0173932.
10. Alley DE, Shardell MD, Peters KW, McLean RR, Dam TT, Kenny AM, et al. Grip strength cut points for the identification of clinically relevant weakness. *J Gerontol A Biol Sci Med Sci* 2014;**69**:559–66.
11. Senechal M, McGavock JM, Church TS, Lee DC, Earnest CP, Sui X, et al. Cut points of muscle strength associated with metabolic syndrome in men. *Med Sci Sports Exerc* 2014;**46**:1475–81.

12. Eckman M, Gigliotti C, Sutermaster S, Butler PJ, Mehta K. Using handgrip strength to screen for diabetes in developing countries. *J Med Eng Technol* 2016;**40**:8–14.
13. Leong DP, Teo KK, Rangarajan S, Kutty VR, Lanas F, Hui C, et al. Reference ranges of handgrip strength from 125,462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. *J Cachexia Sarcopenia Muscle* 2016;**7**:535–46.
14. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum Jr A, Orlandini A, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *The Lancet* 2015;**386**:266–73.
15. World Health Organization. *Obesity: preventing and managing the global epidemic*. Geneva: World Health Organization; 2000.
16. Pietrobelli A, Rubiano F, St-Onge MP, Heymsfield SB. New bioimpedance analysis system: improved phenotyping with whole-body analysis. *Eur J Clin Nutr* 2004;**58**:1479–84.
17. Kelly J, Metcalfe J. Validity and reliability of body composition analysis using the tanita BC418-MA. *J Exerc Physiol Online* 2012;**15**:74–83.
18. Ramírez-Vélez R, Correa-Bautista JE, González-Ruíz K, Vivas A, Triana-Reina HR, Martínez-Torres J, et al. Body adiposity index performance in estimating body fat percentage in Colombian college students: findings from the FUPRECOL-Adults study. *Nutrients* 2017;**9**:40. doi:10.3390/nu9010040.
19. Liu P, Ma F, Lou H, Liu Y. The utility of fat mass index vs. body mass index and percentage of body fat in the screening of metabolic syndrome. *BMC Public Health* 2014;**13**:629. doi:10.1186/1471-2458-13-629.
20. Vivas-Díaz JA, Ramírez-Vélez R, Correa-Bautista JE, Izquierdo M. Handgrip strength of Colombian university students. *Nutr Hosp* 2016;**33**:113. doi:10.20960/nh.113. [in Spanish].
21. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;**120**:1640–5.
22. Ramírez-Vélez R, Triana-Reina HR, Carrillo HA, Ramos-Sepúlveda JA, Rubio F, Poches-Franco L, et al. A cross-sectional study of Colombian university students' self-perceived lifestyle. *SpringerPlus* 2015;**4**:289. doi:10.1186/s40064-015-1043-2.
23. Peterson MD, McGrath R, Zhang P, Markides KS, Al Snih S, Wong R. Muscle weakness is associated with diabetes in older Mexicans: the Mexican Health and Aging study. *J Am Med Dir Assoc* 2016;**17**:933–8.
24. Gallagher D, Visser M, De Meersman RE, Sepúlveda D, Baumgartner RN, Pierson RN, et al. Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. *J Appl Physiol* 1997;**83**:229–39.
25. Xue QL, Beamer BA, Chaves PH, Guralnik JM, Fried LP. Heterogeneity in rate of decline in grip, hip, and knee strength and the risk of all-cause mortality: the Women's Health and Aging Study II. *J Am Geriatr Soc* 2010;**58**:2076–84.
26. Lee WJ, Peng LN, Chiou ST, Chen LK. Relative handgrip strength is a simple indicator of cardiometabolic risk among middle-aged and older people: a nationwide population-based study in Taiwan. *PLoS One* 2016;**11**: e0160876. doi:10.1371/journal.pone.0160876.
27. Duchowny KA, Peterson MD, Clarke PJ. Cut points for clinical muscle weakness among older Americans. *Am J Prev Med* 2017;**53**:63–9.
28. Strand BH, Cooper R, Bergland A, Jorgensen L, Schirmer H, Skirbek V, et al. The association of grip strength from midlife onwards with all-cause and cause-specific mortality over 17 years of follow-up in the Tromso study. *J Epidemiol Community Health* 2016;**70**:1214–21.
29. García-Hermoso A, Cavero-Redondo, I, Ramírez-Vélez R, Ruiz J, Ortega FB, Lee DC, et al. Muscular strength as a predictor of all-cause mortality in apparently healthy population: a systematic review and meta-analysis of data from approximately 2 million men and women. *Arch Phys Med Rehabil*. 2018;99:2100−13.
30. Wilkerson GB, Bullard JT, Bartal DW. Identification of cardiometabolic risk among collegiate football players. *J Athl Train* 2010;**45**:67–74.
31. Peterson M, Zhang P, Saltarelli WA, Visich PS, Gordon PM. Low muscle strength thresholds for the detection of cardiometabolic risk in adolescents. *Am J Prev Med* 2016;**50**:593–9.
32. Sasaki H, Kasagi F, Yamada M, Fujita S. Grip strength predicts cause-specific mortality in middle-aged and elderly persons. *Am J Med* 2007;**120**:337–42.
33. DiPietro L, Dziura J, Yeckel CW, Neufer PD. Exercise and improved insulin sensitivity in older women: evidence of the enduring benefits of higher intensity training. *J Appl Physiol (1985)* 2006;**100**:142–9.
34. Wu Y, Wang W, Liu T, Zhang D. Association of grip strength with risk of all-cause mortality, cardiovascular diseases, and cancer in community-dwelling populations: a meta-analysis of prospective cohort studies. *J Am Med Dir Assoc* 2017;**18**:551. doi:10.1016/j.jamda.2017.03.011.

García-Hermoso, A., Correa-Bautista, J. E., Izquierdo, M., Tordecilla-Sanders, A., Prieto-Benavides, D., Sandoval-Cuellar, C., González-Ruíz, K., & Ramírez-Vélez, R. (2019). Ideal cardiovascular health, handgrip strength, and muscle mass among college students: the FUPRECOL adults study. *The Journal of Strength & Conditioning Research*, *33*(3), 747-754. https://doi.org/10.1519/JSC.0000000000003052