RESEARCH ARTICLE

Anthropometric measures in predicting myocardial infarction risk. Do we know what we are measuring? Bias in research occurred worldwide when the true unhealthy body composition was not well compared

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Abstract

Obesity is a major risk factor for myocardial infarction (MI). However, how to measure whole-risk with simple baseline characteristics? Anthropometrically, association for metrics does not equate causation on incident MI. Besides, association may present effects of bias rather than the true putative risk may be responsible for all or much of the epidemiological causality, and a different body composition between groups with similar baseline confounding variables may provide false-positives in outcomes. Thus, in evaluating whole-risk by anthropometry all metrics are not enterely valid at all times, and the lack of balance between measurements will be particularly prone to the generation of false-positive results. The purpose of this article is to critically review key findings for association biases from different studies. From the INTERHEART, waist-to-hip ratio (WHR) has been deemed as an excellent MI risk predictor, and other results have conferred to WHR a greater excess risk in women than in men. Nevertheless, a novel insight have revealed that WHR-associated risk would appear biased if metrics to compare had no balance and equivalence relation. Baseline characteristics of thousands of MI cases are well known, but anthropometry, mathematics and epidemiology have taught us something, and comment on it below. To date, no method was used to address biases for balancing the distribution of measurements between groups to be compared. Thus, WHR and waist circumference as being mathematical fraction and unit of whole-length, repectivelly, presented association biases when true unhealthy body composition was not well compared by group and by sex. It occurred for unbalancing both measurements and unhealthy body composition when comparing strength of association for metrics. Only waist-to-height ratio as being measure directly associated to a volume of risk yields no biases and should be the metric used to compare the body composition of risk, either by age or by sex.

Keywords: Myocardial infarction, risk prediction, obesity, anthropometric indicator, body composition, bias.

1. Introduction

Body mass index (BMI) as anthropometric measure of general obesity is a major risk factor for cardiovascular diseases (CVD_S), mainly heart disease and stroke as the leading cause of death[1, 2]. However, how to measure the true unhealthy body composition (BC) with simple baseline characteristics? In epidemiology, as in real life, not everything that is attractive at the first look is its true nature. In research also occur false appearances and bias that valuable conclusions may turn out to be worthless. Thus, a thorough understanding of bias is essential because association of obesity-related anthropometrics (OA_S) does not always equate causation on incident myocardial infarction (MI). Interestingly, association for OA may present effects of bias rather than the true putative risk may be responsible for all or much of the epidemiological causality, and in non-randomised study designs, baseline differences on the unhealthy BC between groups to be compared may introduce systematic bias in results. Similarly, a different BC between groups with similar baseline confounding variables may provide bias if the true-risk assignment does not account for the covariates that predict receiving true-risk. Thus, all OA are not valid for the whole-risk assessment at all times. In this sense, technological methods for assessing BC of risk such as dual-energy X-ray absorptiometry (DEXA), computed tomography and magnetic resonance imaging can support the criterion of a more accurate evaluation, but in anthropometry, critical scrutiny covering all potential mechanisms of bias, is indispensable to avoid wrong conclusions and a message clinically consequential. Hence, a high strength of association is not the same as causality when predicting MI risk.

Conceptually, each OA provides its own biological meaning depending on the part of the BC that is capable of discriminating while the notion of equality in the estimate of whole-risk may be respected. If not, the lack of balanced distribution between measurements on a dataset will be particularly prone to the generation of false-positive results. On this issue, the equivalence relation (R) is a key mathematical concept for specifying whether two OA are the same with respect to a given whole-risk. Thus, any OA will be comparable to other or not depending on the whole-risk measured. Therefore, a strong association would lead us to infer or not a whole-risk given that the true nature of risk should come from the selective unhealthy BC instead the mere results of association. At once, a rigorous anthropometric assessment should be independent on the epidemiological burden of other factors such as plasma lipids level, blood pressure, smoking, plasma glucose level, physical activity, diet, age or even sex-specific hormones level that influence CVD risk.

2. Association of obesity-related anthropometrics and MI risk

The diagnosis of BMI-defined obesity is the failure to considerer the impact of adiposity on metabolic processes that result in increased MI risk. Hence, accurate estimation of the BC as well as body fat distribution is highly relevant from a public health perspective[3]. Previous studies have showed association of BMI and MI, although showing a lower strength than abdominal obesity measures[4-9]. Despite this, BMI has the importance of being OA proposed to define the ideal cardiovascular health and to predict CVD risk[10, 11]. However, as unit of mass/m^2 it is only a surrogate measure of general body fatness without providing accurate information about the unhealthy BC as waist circumference (WC) measured. In fact, evidence is accumulating in support

of WC as OA linked to visceral adipose tissue, and the only one among single measurements that predict MI and cardiometabolic risk [4, 7, 9, 12-16]. However, from the INTERHEART study waist-to-hip ratio (WHR) has been deemed as an excellent MI risk predictor above BMI and WC[4, 17, 18, 19], and besides, being chosen as optimal index in a CVD risk score[20]. In addition, results from the UK Biobank have conferred to WHR a greater excess risk of MI in women than in men[21].

On the other hand, complex metrics such as waist-to-height ratio (WHtR), whole-body fat percentage (%BF), conicity index, and adiposity measured by technological methods could be better indicators than WC alone to predict cardiovascular events and mortality, even with sex differences[5, 14, 20, 22-27]. Additionally, WHtR and %BF have showed the highest discriminative abilities in relationship with a unhealthy BC, and WHtR has been more strongly correlated with %BF and adiposity variables in men than it is with WC[24, 27]. In this line, WHtR and %BF as being anthropometrically valid for the biological risk assessment appear to be strengthened for the estimate of whole-risk. Thereby, WC and height, and skinfolds to a lesser extent, in keeping a relationship with abdominal and relative adiposity would be the basic simple measurements for evaluating cardiometabolic and MI risk, including cardiovascular mortality[12-16, 20, 22-40]. Complementary, study in South African women has showed that DEXA-derived visceral adiposity and WC had the same overall performance in discriminating the presence of any 2 metabolic syndrome components, and endomorphy and subscapular skinfold have been significantly associated to MI in men[24, 27, 41, 42]. Further, patients of both sexes assessed by computed tomography have presented better MI risk prediction as visceral adiposity increases and abdominal subcutaneous area decreases[16, 22]. On these bases, the whole-risk compared between different OA and by sex would be not necessarily the same and false-positive inferences would occur from the mere strength of association of each one.

3. What is new about anthropometrics associated with MI?

While overweight/obesity, enlarged WC, WHR risk cutoff of <1, and WHtR cutoff of ≥0.5 have been verified baseline characteristics in MI subjects worldwide, most of the OA showed associated risk, but with strength and sex differences [4-9, 12, 13, 15-19, 21-24]. Mathematical observations in novel studies have explained selection bias for WHR respect to WC and WHtR in MI men, and therefore, revealing that whole-risk comparison between cases and controls was not the same [23, 24, 27]. Since anthropometrically-estimated %BF and mesomorphy presented high magnitude of association, something does not add up between association for BMI and WHR and its relationships with the true-risk. Conceptually, the true unhealthy BC derives from %BF, fundamentally the part linked to intra-abdominal fat depots functioning as a neuroendocrine organ[43]. On the other hand, mesomorphy represents relative muscularity, but association with MI is artificial and does not equate causation[24, 44]. Thus, BMI and WHR as being anthropometrically linked to musculoskeletal component, and more weakly correlated with %BF than other metrics, they have presented information bias and associated spurious risk[23, 24, 27]. Indeed, an important question lies in the discrepancy observed between the strongest association for WHR, and their worst correlations with measures of general and central adiposity in both sexes [4, 17-19, 21, 23, 27]. That way, discrepancy between strength of association for WHR

and a lower anthropometric coherence for the true-risk should give birth to the idea that something was wrong on the risk association. Consequently, a systematic error would be committed on the true-risk assignment for WHR and BMI if their data were slanted in an artificial direction for partially capturing a dimension of spurious-risk. Additionally, from the SWEDEHEART registry WC has been associated to recurrent CVD events after MI, regardless of other risk factors, included BMI, but with different results between sexes[45]. In contrast, WHtR-%BF-associated risk have showed anthropometric coherence that justify risk excess per se, and it could help explain the abundance of MI among individuals with raised visceral fat, irrespective of BMI, HC or mesomorphy rating[23, 24, 27, 44].

4. Lessons from anthropometry, mathematics and epidemiology: Another insight when measuring the true-risk

Arithmetic value and true-risk measured from each anthropometric depends on formula, unit of measure and measurements derived from structural bodily components. At once, standard human body characteristics and mathematical equivalence between measurements and OA to be compared should be taken into account for epidemiological inferences (Figure 1). The rationale behind our consideration is as follows:

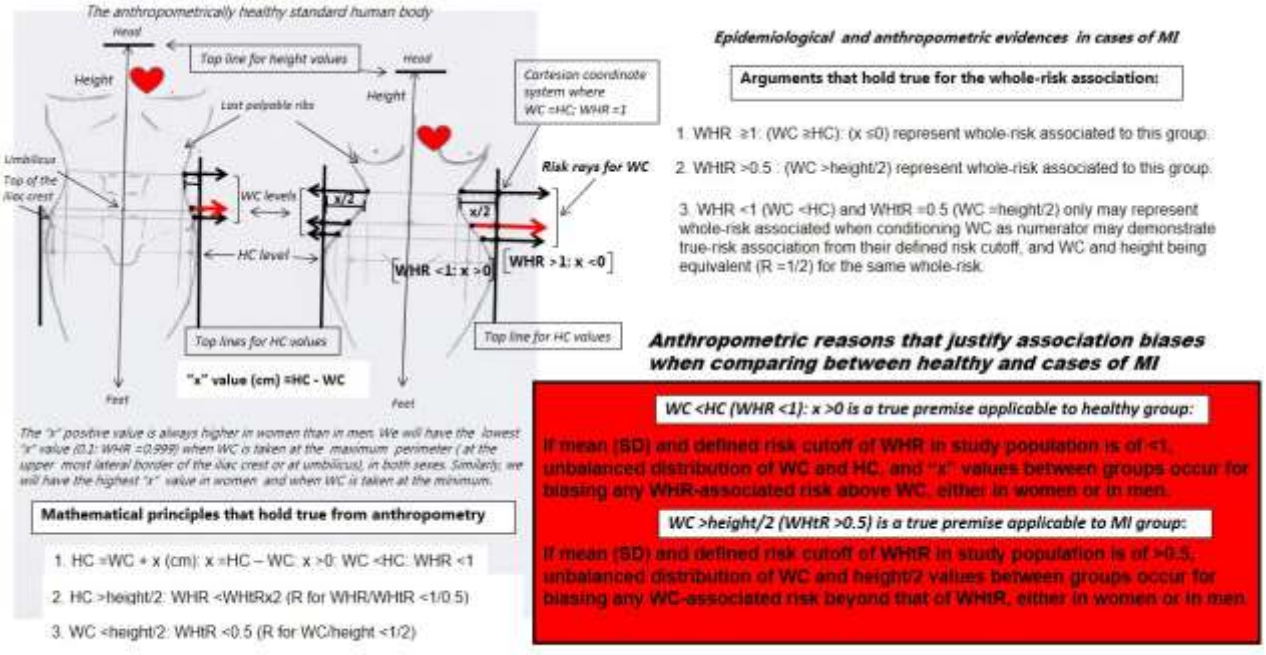

Figure 1. Models of standard human body and anthropometric measurements. Geometric lines drawn in a Cartesian plane for understanding metrics and rays of risk. Mathematical principles as well as epidemiological and anthropometric arguments that hold true in both healthy and MI subjects.
Anthropometric reasons that justify association biases when comparing between groups are explained. Measurements at baseline would represent mean values per standard deviation for WC, HC, WHR, and "x" distance being actually valid for any anthropometrically healthy population and ethnicity. On the respective rays of risk for WC would lie points of increased abdominal obesity representing mean values of cases of MI as well as biological changes pointing towards greater excess

risk as WC increases. HC denotes hip circumference; MI, myocardial infarction; R, equivalence relation; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; X, subtracting HC by WC. Footnote: Original drawings built by the author. Dimensions are not to scale.

4.1. Muscle, bone, fat and residual mass as being different biological components present not differentiation by body weight (unit of mass), and therefore, a higher BMI does not always involve greater body fat excess, at least in normal or overweight people[2, 24, 27]. Besides, weight and height differences between sexes is not respected by BMI formula, which involves that both sexes may present the same BMI, but different BC to be compared. In this sense, error of estimate for the true unhealthy BC may occur in comparing BMI with other OA, and either by age or by sex.

4.2. Height measurement depends on bone structure of the adult. In this sense, height never correlates with adiposity, and therefore, it does not account for the true-risk per se[20, 23, 27, 44]. However, height as being a volume factor would exert a modulator effect for conditioning the storage and distribution of the body fat as well as relative volume that it occupies in a three-dimensional space[24, 27]. Thereby, a significant height difference between groups and sexes conditions the whole-risk estimated by each concerned OA. Mathematically, WC and WHtR would be equivalent for the same whole-risk if and only if WC = height/2 (WC/height =0.5), and therefore, WHtR being the entity of whole-risk conditioned on WC, but height/2 taking the same value as WC (e.g., 80/160, 84/168, 85/170 etc.). If not, error of estimate for the true unhealthy BC may occur in comparing WC alone with WHtR. Thus, if WC >height/2: WHtR >0.5 (e.g., 80.3/158, 82.6/162, 82.8/162.4 etc.,) protective underestimation occurs for height respect to WC whether WC alone receives the whole-risk. It is clear, if baseline characteristic shows mean (SD) of WC higher than it is height/2, WHtR turn out to be the entity of whole-risk when comparing, but not WC per se. This is because whole-risk is conditioned on both WC and height as volume factors (Figure 2).

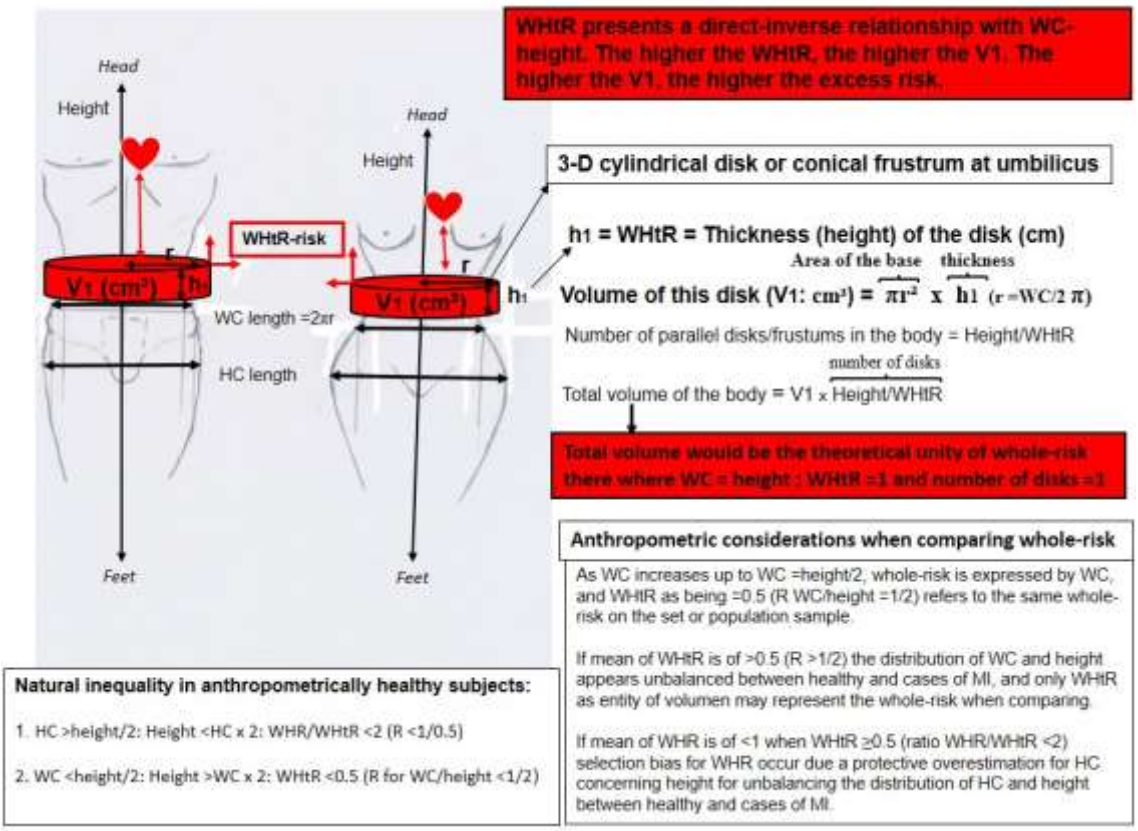

Figure 2. Anthropometric measurements in the standard body human and considerations for determining measure of volume on a three-dimensional abdominal disk. Natural inequality between measurements in any anthropometrically healthy population is mathematically expressed. Formulas as geometrically appropriate. Measurements at baseline would represent mean values per standard deviation for WC, HC, height, WHR and WHtR being actually valid for any study population and ethnicity. The model of disk for representing volume at all times may be applied for both case-control and cohort studies from the respective baseline values. Anthropometric considerations are explained for understanding volume of whole-risk as WHtR increases. h1 denotes height of the disk; HC, hip circumference; MI, myocardial infarction; R, equivalence relation; r, radio of the base; V1, volume of the disk; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio. Footnote: Original drawings built by the author. Dimensions are not to scale.

4.3. HC measurement depends on breadth between both trochanters, gluteal mass and gluteal-femoral fat for determining a geometrical area of defined bodily components, but HC neither discriminates between them nor captures cardiometabolic risk. Conceptually, HC could be modified towards a higher or lower length by physical activity or aging process, respectively, but not justifying a direct impact on MI risk per se, at least while WC, unhealthy BC and %BF are not secondarily affected[24, 27, 44].

On the other hand, HC at baseline is always higher than WC without posing any putative risk or protective effect (Figure 1). Mathematically, HC >WC (WHR <1) is a natural inequality, which responds to a linear equation: HC = WC + x, where subtracting HC by WC we calculate "x" as unit of length (cm), and being their standard value higher in women than in men, but higher than zero in both. Besides, WHR <1 tell us the equal parts of WC that we have in HC, but never showing anthropometric consistency or

true-risk beyond that of WC. In addition, WC and HC represent absolute values without expressing equality for the same whole-risk as mathematical object, and both only may coincide on the same estimate of risk when WC takes the same value as HC (WHR =1; x =0). In this sense, WC and WHR would mathematically be equivalent for the same estimate of whole-risk if and only if HC = WC, and therefore, WHR =1 being the entity of whole-risk conditioned on both WC and HC =WC. If not, error of estimate for the true unhealthy BC may occur in comparing WHR and WC by separated. It is clear, WHR <1 is simply a way of representing size (part/whole) that is not whole number, unlike of WC. Besides, WHR <1 as being a proper fraction will never represent the entity of whole-risk, and any risk-code selected for WHR between their risk cutoff <1 and 0.99 value will be biased if WC receives no risk-code. Only there would be a true-risk for WHR when WC predicts receiving true-risk. If not, WHR may select true negative values as false-positive ones when they merely represent protective overestimation for HC concerning WC. Obviously, only when WHR is ≥1 (x ≤ zero or negative value) can this metric be used in order to draw a valid conclusion for an estimate of whole-risk. Thereby, if baseline characteristic shows mean (SD) of HC higher than it is WC, the true-risk assignment depends on WC receiving whole-risk, which turn out to be the entity of risk to be compared, but never WHR alone.

Mathematically, between any WHR cutoff <1 (e.g., 0.95) and 0.99 we could find different individuals and infinite number of fractions receiving risk-code, but not necessarily referring to the same unhealthy BC as measured from WC [24]. As an example, 93.1/98 vs. 93.9/98 vs. 95/100, etc., =0.95 (0.950-0.959): "x" between 5 and 4.1, 93.8/93.9 vs. 94.2/95 vs. 99/100 etc., =0.99 (0.990-0.999): "x" between 1 and 0.1. Broadly, there would be five values for WHR between 0.95 and 0.99, and infinite fractions for values of "x" between 5 and 0.1; HC >WC in all, and being WC risk cutoff ≥94.4 in each set. Similarly, other values for WHR <1 (e.g., between 0.82 and 0.99: "x" between 18 and 0.1) may be transferred from other populations where mean values for WC and HC were higher or lower than in the example. This is because equal fractions refer not the same whole-risk, and besides, the sensitivity of WHR (hundredths) is not the same as "x" (tenths). It is clear, between two consecutive values of WHR <1 we have 10 of "x" (e.g., between 0.95 and 0.96 we count for 10 of "x" from 5 up to 4.1, what misclassifies whole-risk for 0.95). In any situation, WC depending on their own risk cutoff would show different risk-codes into each fraction while WHR would support a unique value for the risk, but any value of WHR <1 precludes the same estimate of risk for WC and HC making anthropometrically impossible the validity of WHR beyond that of WC alone. These findings may help explain a higher bias for WHR in predicting MI risk in women or middle-age people because their "x" positive value is always higher than in men or elderly, respectively. In fact, WHR <1 at baseline entails unbalance between HC and WC, and the higher "x" value, the higher the bias may occur by selecting a higher number of false-positives there where HC only presents protective overestimation respect to WC.

4.4. WC measurement depends on specific biological components determining a geometrical area (cm^2), which is linked to visceral adiposity and unhealthy BC as a solid estimate of whole-risk[12, 13, 16, 43, 44]. On the other hand, in a healthy human body WC is also lower than height/2

(WHtR <0.5) (Figures 1 and 2). Only when WC and height/2 are mathematically equivalent (R =1) there is notion of equality for the same whole-risk from WC and WHtR. However, evidence supports that WHtR >0.5 is strongly associated to cases of MI [15, 18, 21, 23, 27]. Obviously, when mean (SD) of WHtR is of >0.5 there is not equality between WC and height/2, and only WHtR may be used in order to draw a valid conclusion for the whole-risk (Figure 3). Thus, if WC is of >height/2 WC by separated will present risk overestimation in tallest and underestimation in shortest. Mathematically, WHtR as being of <1 also represents a proper fraction (part/whole) whose decimal value tell us the equal parts of WC that we have in height, but never WC referring to the entity of whole-risk. Quite the opposite is the case, the higher the WHtR, the higher the risk overestimation for WC as compared to WHtR. Similarly, the higher the WHtR, the higher the probability of bias for WC, and if WHtR receives no true-risk WC might capture false risk beyond that real of WHtR. It is clear, if baseline characteristic shows a mean (SD) and defined risk cutoff of WHtR >0.5, this metric predicts receiving whole-risk, but never WC alone.

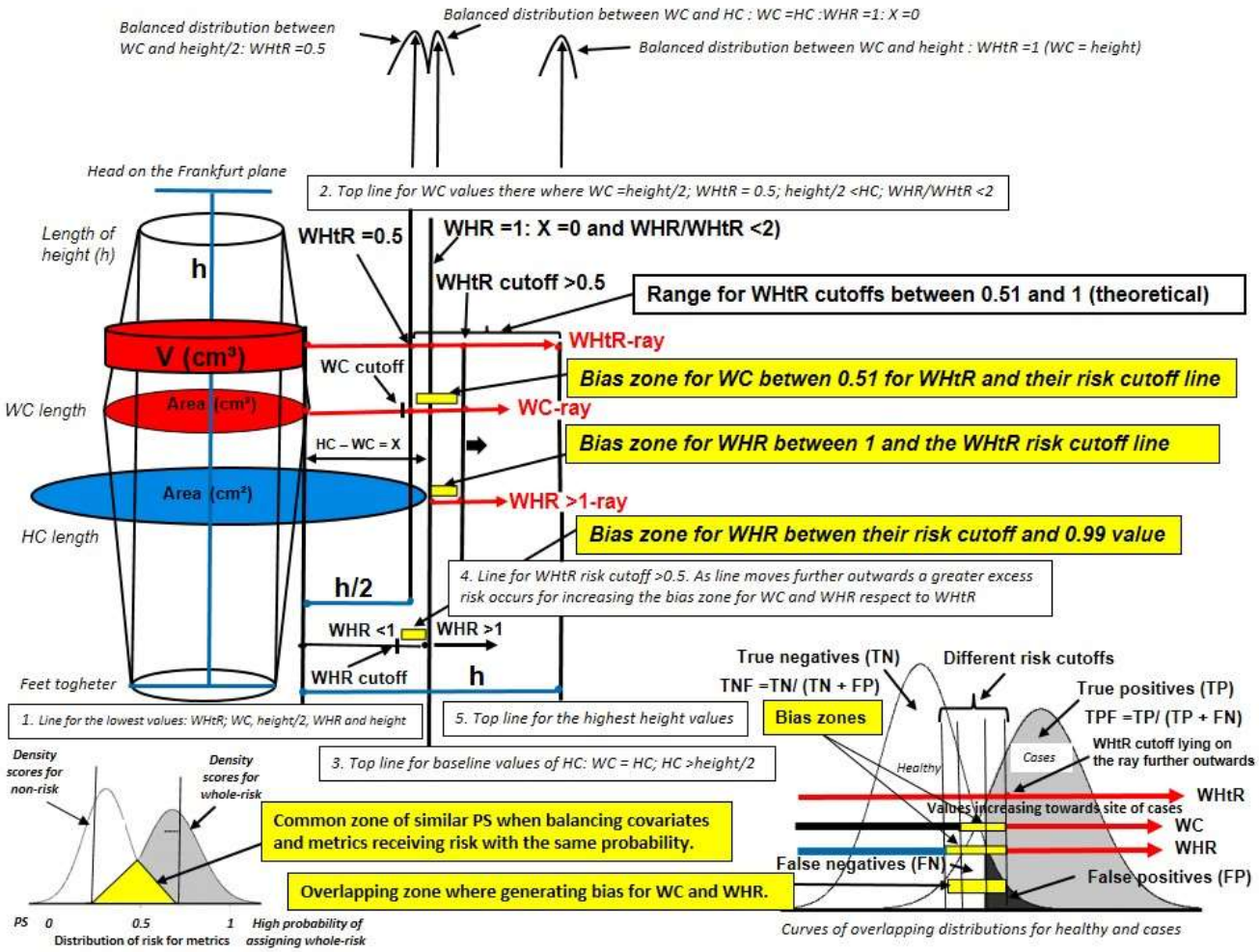

Figure 3. Original assembly of measurements and metrics on a human body simulating a geometric figure. Geometric and number lines in a Cartesian plane for representing mean values in healthy and cases of MI. Subtitled curves of distribution as appropriate. This is transferable to any study population. All reference values may be represented lying on the respective lines drawn. We may find the points with the lowest baseline values (healthy or controls) lying on a respective line in the origin. Similarly, risk cutoffs and cutting lines lying where appropriate. The highest baseline values (unhealthy or cases) would lie on the arrowhead of the rays of risk moving further outwards (right site). Other points would represent mean values per standard deviation for WC, HC, height/2, height, WHR and WHtR being actually valid for any study population and ethnicity. In the respective lines and risk rays drawn would lie points of increased abdominal obesity representing values for thousands of cases of MI as well as biological changes pointing towards greater excess risk as WC increases and HC and height condition the whole-risk. We have pointed the theoretical cutting lines for WHtR and WHR there where would occur a balanced distribution between WC-height/2, WC-HC and WC-height when pooling healthy and cases of MI. Curves of distribution of values between healthy and cases as well as density scores for metrics are represented for a better understanding of bias (right site for cases and higher risk). The model plotted may be applied for both case-control and cohort studies. HC denotes hip circumference; MI, myocardial infarction; PS, propensity score; TNF, true negative fraction; TPF, true positive fraction, V, volume; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; X, subtracting HC by WC.
Footnote: Original drawings built by the author. Dimensions are not to scale.

4.5. Anthropometrically, from the lowest baseline up to the highest values we may draw horizontal rays of risk for WC and WHtR. As WC and WHtR increase, respective cutoffs and points with greater excess risk move further outwards lying on their rays (Figure 3). However, WC cutoff only may represent the whole-risk when WC-height/2 and WC-HC appear to be balanced in their data distribution (WHtR =0.5; WHR =1, respectively). By contrary, while on a datasets WHtR may demonstrate a risk cutoff >0.5 (without ignoring it) neither WC nor WHR will represent whole-risk due to overlapping and bias zones there where false-positive points might be selected for both, but not for WHtR. Epidemiologically, neither height nor HC may draw rays of risk per se, and besides, HC never taking the same value as height, and hardly WC reaching the same value as height. Thus, any ray of risk for WHR >1 (whole/part) will always depend directly on WC as whole-area. Nevertheless, WHR <1 draws neither ray nor greater excess risk, at least between their risk cutoff and 0.99 value, in which range a higher-lesser bias occurs as HC increases-decreases and WC not moving in their value. Therefore, only WHtR allows us draw a clear ray of risk up to a value of 1, which theoretically represents the unity of whole-risk and total volume (see figure 3). On this approach, we will always find the point for WHtR =0.5 before the line for WHR =1, and WHtR risk cutoff lying much more outwards that it is WC and WHR. Thereby, curves of data and overlapping distributions would explain us that in capturing whole-risk WHtR present much more real sensitivity (true positive fraction) than it is WC and WHR. This is because true negative values for WHtR are never selected as false-positive ones, unlike WC and WHR. Really, between 0.51 and any WHtR risk cutoff up to 1 (e.g., >0.55) we could find different individuals and infinite number of fractions receiving the same binary code for WHtR (non-risk), but not necessarily referring to the same risk-code from WC cutoff. As an example, 82.8/162.4 vs. 88.6/174 vs. 95.4/187 etc., =0.51, 96.7/178 vs. 92.5/168.2 vs. 98.8/179.6, etc., =0.55. Broadly, there would be no risk-code for WHtR ≤0.55 when WC showing different

risk-codes if their cutoffs were >84 or >95 on each set, and WC >height/2 in all. It is clear, the higher the WHtR, the higher the possibility of selecting false-positive points for WC as compared to those true negatives below WHtR risk cutoff. Similarly, other values for WHtR (e.g., between 0.51 and a cutoff of 0.65) may be transferred from other populations where mean values for WC and height were higher or lower than in the example. In any situation, WC depending on their own risk cutoff would show different risk-codes as numerator into each fraction while WHtR would support a unique continuous value up to their risk cutoff. Thus, WC might present association bias respect to WHtR when the whole-risk for both metrics refers to different unhealthy BC.

4.6. Anatomically, HC also is higher than height/2 and lower than height (Figure 1). Hence, there would be no R between WHR and WHtR for comparing the same whole-risk if the first is lower than the second x 2 (WHR/WHtR <2)[23, 24]. Since the balanced distribution between WC and height/2 on the one hand, and between WC and HC on the other hand only may be found on the lines of WHtR =0.5 and WHR =1, respectively, both indices will never capture the same whole-risk. Therefore, bias will occur for WHR respect to WHtR for unbalancing between HC and height/2 (Figures 1 and 3). It is clear, if baseline characteristic for both ratio of WHR/WHtR and ratio of WHR risk cutoff/WHtR risk cutoff is of <2, WHtR turn out to be the entity of whole-risk to be compared, but never WHR alone.

4.7. Geometrically, the concrete volume of a three-dimensional disk or frustum at the umbilicus level might be quantified by WHtR (Figure 2). Simulating a cylinder or truncated cone, volume of this disk will depend on area of the base$_{(s)}$ (πr^2, where WC =2πr: r =WC/2π) and their geometrical height (thickness of the disk =WHtR cm)[24, 27]. Thereby, the human body as a solid would have a number of disks =height of body/WHtR, and the sum of the volume of all the disks would give us the total volume of the body, which would be the theoretical unity of whole-risk where WC = height: WHtR =1: Number of disks =1. Therefore, WHtR gives us the corresponding relative volume (cm^3) that we have by unit of height or disk in direct-inverse relationship with WC-height, and the higher the WHtR, the higher the volume of the disk. On the other hand, although WC values do not move, disk volume may be modulated by height of the body towards a higher or lesser amount of three-dimensional space that risk components occupy, and therefore, for modifying their cardiometabolic effect.

Epidemiologically, WHtR would have the importance of capturing whole-risk above WC area, at least when height may have significant differences between groups to be compared and being mean (SD) of WHtR >0.5[23, 24, 27]. On this approach, WC and WHtR would not be comparable. So, if baseline characteristic for both WHtR and WHtR risk cutoff is of >0.5, this metric turn out to be the entity of whole-risk to be compared.

5. Implications for an anthropometrically correct MI risk prediction

Evidence supports that BMI strongly depends on metabolically healthy musculoskeletal component and body fat mass, especially of the subcutaneous, without discriminating the unhealthy intra-abdominal fat[24]. Why to choose BMI to assess MI risk if it captures metabolically contradictory components? The consequence of this chimera is that to describe individuals at risk based on BMI

is unfounded and potentially misleading. Accordingly, the concepts of ideal anthropometric health and BMI-classified obesity should not be considered synonymous or interchangeable; at least that we accept misclassification and paradoxical information for biological risk assessment. It is clear that BMI fails to discriminate between harmful body fat and healthy component being actually an inappropriate formula to assess the association between excess fat mass and MI. Besides, while a part of the musculoskeletal component (mesomorphy) may be associated to MI, as %BF increases, a part of the association for BMI would capture false risk, and therefore, information bias occurring for the true unhealthy BC in both sexes. That way, the excessive body weight in individuals who have a high BMI and normal %BF (e.g. people/athletes with high mesomorphy rating) would indicate a score of spurious-risk, but never performing better than WC[24, 27].

Respect to WHR, it is well known that it has showed the highest predictive abilities[4, 13, 17-20, 23]. Nevertheless, WHR may present bias respect to WC when the risk assignment for both refers no to the same whole-risk, and therefore being not well compared[24, 27].

Moreover, WHR and WHtR contrast different risk if HC and height do not present a relationship of height/HC =2. This ratio would occur if and only if WHR/WHtR = 2 (e.g., 0.90/0.45, 0.95/0.475, 1/0.5 etc.), what also appears anthropologically unlikely as seen above. Thus, selection bias occurred for WHR respect to WHtR due to protective overestimation for HC with regard to height[23, 27].

On the other hand, risk association for WC and WHtR will be equivalent if and only if WHtR is very close to 0.5, but any WHtR value of >0.5 precludes the same estimate of risk for WC and height making anthropometrically impossible the validity of WC beyond that of WHtR.

In another sense, a different cardiometabolic effect among visceral and extra-abdominal fat have been argued when using WC to measure total abdominal adipose tissue. However, evidence supports that the higher the intra-abdominal fat, the higher the WC value, irrespective of subcutaneous extra-abdominal fat. From the Framingham study, visceral fat has been strongly associated with a metabolic risk profile and MI in both sexes, and technological studies have observed that the ratio visceral fat/subcutaneous extra-abdominal fat presented a direct association with MI while subcutaneous area showing inverse[12, 14, 16, 22, 43, 46]. The anthropometric explanation would be because as intra-abdominal fat increases, subcutaneous adipose tissue of the extra-abdominal space suffers a mechanic effect of compression, which makes decrease their relative thickness and volume (tight fat). Moreover, it is noteworthy that %BF measured by DEXA strongly depends on WC and height rather than BMI in adult individuals[47]. Thus, in MI men %BF has more strongly correlated with WHtR than it is with WC (intra-abdominal + subcutaneous area), and therefore, not necessarily referring to WC as whole-risk for an accurate comparison, but taking it into account for a relative volume by unit of height[24, 27] (see figure 2). Thereby, sophisticated volumetric imaging methods have showed differences for the association of visceral and subcutaneous fat with an adverse metabolic risk profile in both sexes[46].

From another insight, in observational studies propensity score methods have been used to address selection biases for balancing the distribution of covariates between groups to be compared[48]. In this

sense, as a result, risk assignment for WHR and WC may be systematically biased if values between WC, HC, height/2 and height show no balanced distribution where appropiate, and therefore, the concerned OA may not be directly comparable (Figure 3). In agreement with stratification method all subjects who have (nearly) similar baseline characteristic, and therefore, similar propensity score would have the same probability (nonzero) to receive risk-code being the risk assignment strongly ignorable[48]. Comparing the similarity of healthy and MI subjects in the same strata should begin with a comparison of the means or medians of the single measurements and the distribution of their categorical counterparts between groups. If after conditioning there remain systematic differences between means or medians, this would be an indication that the propensity score model has not been correctly specified for unbalancing the distribution of the measurements and the whole-risk assignment. In this line, a recent research also has demonstrated association bias for WHR by unbalancing HC respect to WC and height in MI men [49].

6. Discussion

The anthropometric robustness from BMI and WHR to link BC and MI risk is unclear and diffuse. Conceptually, each of them provides its own meaning without a verifiable associated risk beyond that of WC. Nevertheless, only a rigorous interpretation removing bias could avoid confusing or paradoxical information, independently on the other established risk factors that influence ideal cardiovascular health[10, 11].

It is well known, BMI has showed significant association with MI in both sexes, but not the best, and not important differences were found when compared by sex[4, 17-19, 21]. From UK Biobank results, ratio of women-to-men hazard ratios for incident MI for the comparison between BMI and WC showed higher hazard ratio of association for WC in women, and not difference in men. At once, only WC and WHR, but not BMI and WHtR were significantly associated with the risk of MI in women compared to men. Moreover, measures of central adiposity, particularly WHR as compared to BMI, showed higher ratio of hazard ratio in women than in men (0.82 vs. 0.94)[21]. However, when exploring the association between obesity and metrics novel findings have explained the reasons what both BMI and WHR are not optimal indicators in predicting MI risk, at least in men[23, 24, 27, 44]. Thereby, we could solidly think that since the musculoskeletal component may be artificially associated to MI, BMI fails to reveal the true unhealthy BC in underestimating visceral fat volume and overestimating risk from mesomorphy component. Thus, in two individuals with dominant mesomorphy and different unhealthy BC, a same BMI would underestimate the higher body fat volume in one of them. This observation makes that BMI has the importance of producing greater impact and bias in men due to that it would capture a dimension of spurious risk beyond that of women. On this basis, from the UK Biobank, the comparison between BMI and WC by sex presented bias. This was because both metrics cannot refer to the same unhealthy BC when comparing men and women, and besides WC without accounting for the whole-risk (a 1-SD WHtR was >0.5 in both sexes)[21]. To our knowledge, body weight and HC have showed low predictive ability for MI and never justifying true plausibility for the whole-risk. On the other hand, height has been inversely associated to MI with a higher relative risk, although not necessarily referring to a causal relationship[23, 24]. It is clear them that WC

would be the only one among single measurement beyond that of weight for reflecting both the cardiometabolic risk and the highest association discriminative for MI in both sexes [4, 7, 9, 12-21, 23, 24, 45]. Besides, as %BF increases in vivo, the body fat storage is homogeneously distributed, and WC becomes rather than BMI the best clinical expression of a body fat volume increased. Nevertheless, composite indices such as WHR and WHtR have always captured higher dimension of risk [4, 7, 9, 12, 16-19, 21, 23, 24, 27]. But surprisingly, most studies in predicting MI/CVD risk always showed both a WHR cutoff <1 and WHR/WHtR <2 in both sexes while selection biases were never discussed[4, 5, 7, 13, 15, 17-19, 21, 38-40, 42, 50-52]. Thus, from the INTERHEART, the median WHR in the overall population was 0.93 in cases and 0.91 in controls with significant difference between both values, and therefore between "x" values, so risk comparison was done without balancing between HC and WC[4]. Besides, WHtR as entity of whole-risk was not explored. On the other hand, the follow-up in the CONOR study showed for WHR and WC an association stronger in women and middle-aged than in men and elderly participants, respectivelly[17]. However, the higher value of "x" for middle-aged (WHR =0.79: x =21) and elderly women (WHR =0.82: x =18) respect to men counterparts (WHR =0.89: x =11, and WHR =0.92: x =8, respectively) was not kept in mind, and therefore, biases occurred respect to WC in the whole-risk comparison for unbalancing HC and WC. Additionally, WC would appear to be found with classification bias for the whole-risk in women compared to men if height do not accounted in data analysis, and WHtR as entity of whole-risk being not compared. Similarly, from the UK Biobank, a 1-SD higher WHR was significantly associated with a higher hazard ratio in women than in men, and with a corresponding women-to-men ratio of hazard ratios of 1.15. Nevertheless, the mean WHR was of <1 in both sexes (0.82: x =18 in women, 0.93: x = 7 in men)[21], so the false premise accepted in the whole-risk assignment up to 0.99 value provided selection bias for WHR when compared to WC. Thereby, having a baseline characteristic of WHR <1, a same unhealthy BC as being measured by WC will provide higher WHR-associated risk due to protective overestimation for HC there where numbers of WHR <1 received a false-risk. Besides, in data distribution and hazard ratios WHR in the top was always of <1 when WHtR in the bottom showing >0.45-0.5 in both sexes (WHR/WHtR <2), so whole-risk comparison between both indices turned out to be biased by protective overestimation for HC concerning height. Additionally, strength of association for WC was significantly higher in women than in men (1. 35 vs. 1.28) while hazard ratio for WHtR being similar in both sexes (1.34 vs. 1.33). By deduction, height differences were higher in men than in women in occurring similar whole-risk assignment for WC and WHtR in women, but not in men. This is because WC and height showed a different relationship, and WC and WHtR compared no for the same whole-risk. Indeed, the mean of WHtR at baseline in women (0.52 ± 0.1) was closer to 0.5 than that of men (0.55 ± 0.1)[21]. This means that in the stratum between 0.5 and 0.52 WC and WHtR captured similar dimension of risk in women while that in a higher range up to 0.55 only WHtR captured the highest whole-risk, as it happened in men. Thereby, height differences between sexes involve less chance of bias for WC in women when compared to WHtR, and at once, WHtR more accurately predicts whole-risk in men than it is WC[21]. By contrast, in the follow up of the Swedish

cohort WC presented less statiscal power for a recurrent MI in the female group[45]. However, the whole-risk as WHtR measured was not explored, and therefore, the risk comparison between sexes could not be refered to the same unhealthy BC.

To our knowledge, from studies revealing bias for WHR unbalance between WC-HC, HC-height and WC-height already were pointed[23, 24, 27]. From another insight, assignation of spurious-risk for WHR in the overlapping area of their distribution of points has also been demonstrated[49]. On these bases, most of the previous large studies made bias errors when assigning the same whole-risk to subjects who had different unhealthy BC. This fact may be verified when WC-associated risk appears to be found above WHtR (cutoff >0.5) and false-positive points for WC were slanted towards cases group. It could be demonstrated if in the overlapping zone for WC above their risk cutoff a false-risk assignment were conditioned on WC >height/2 and WHtR between 0.51 and their risk cutoff receiving no true-risk, as said above. In this line, WHtR performs better than WC when height showing inverse association to status of cases and WHtR risk cutoff moving too much towards higher of 0.5 as proved in men [23, 24, 27, 49]. Conversely, whether WHtR cutoff is of ≤0.5 WC and WHtR would have the same overall performance in predicting risk. Otherwise, as being always HC <height, risk assignment for WHR and WHtR would always show unbalance, and therefore, a different BC of risk to be compared [4, 7, 9, 15, 17-21, 23, 24, 38-40, 42, 49]

Hence, when unbalancing HC vs. WC and height, or WC vs. height false-positive points for WHR and WC, respectively, might be assigned for providing association biases and underestimating the whole-risk derived from WHtR.

From a syllogistic approach, whether WHR <1 is associated to healthy individuals (first true major premise), and being HC >WC on a dataset (second true minor premise), any WHR-associated risk above WC will be a false conclusion drawn from a mathematical misconception[23, 49]. Similarly, if WHtR >0.5 is associated to MI cases, and being WC >height/2 on a dataset, any WC-associated risk beyond that of WHtR will not be a valid conclusion[24, 27, 49]. Likewise, when WHR/WHtR <2 is a natural inequality, and being HC <height in any study population, any WHR-associated risk beyond that of WHtR will draw a wrong conclusion[23, 24, 27, 49].

Consequently, HC and height together WC should always be controlled in data analysis to preclude a different-equal risk assignment between subjects who have equal-different unhealthy BC. By contrary, a higher strength of association for WHR or WC [4, 17-21, 45] does not mean the best risk prediction, but bias and unhealthy BC not well compared for providing a misleading evidence because of the research process itself. Epidemiologically, when balanced distribution between single measurements may be checked, and the whole-risk conditioned on the true predictive variables[48, 49], WHtR should be used as optimal metric in any correct risk comparison, irrespective of the strength of association for each OA[4, 7, 9, 17-21, 23, 24, 45, 49]. Researchers have the responsibility to conduct studies in a way that makes then capable of balancing measurements and BC when comparing whole-risk. Hence, identifying and removing biases, WHtR will always provide equality and balance between groups to be used as entity of whole-risk, which allows us capture the real risk dimension, and besides, having the importance of being cheap, accessible and easy to measure.

Once revealed bias in research when predicting MI risk focus must shift.

Thereby, ethnically-based and sex-specific WHtR risk cutoff would be the easiest and definitive anthropometric tool that meets true epidemiological criteria in order to identify individuals at risk of MI, and broadly, before that a high degree of adiposity has the importance of precluding a homogenously distributed body fat volume.

Lastly, after including thousands of cases of MI, findings of this review determine the generalizability to other populations if mathematically satisfy the same observations, even when some chosen OA showing higher strength of association in women than in men. As theoretical limitation, this wont be applicable to populations not included in derivation cohort along with others not seen to be compared.

On the issue related to WHtR is also fullfilled: “Lower is better for longer, but not necessarily spending health resources and medicines”. We also believe that an evolution of findings based on a balanced weighing of potentials for false-positive biases can produce scientific knowledge to advancement of Science and Medicine.

7. Conclusion

This critical review demonstrates association biases when predicting MI risk in both sexes. Regardless of BMI, which shows not optimal risk prediction from most studies, WHR-associated risk becomes a misleading evidence derived from a generalized mathematical misconception, which overestimates the protective effect of HC concerning WC and height. The true-risk exclusively derives from enlarged WC and abdominal obesity volume, but accounting for height, and rending HC irrelevant or clinically useless, either in women or in men. Any WHR-associated risk beyond that of WC and WHtR becomes mathematically biased and anthropometrically inconsistent, and besides, epidemiologically a false one. WHtR yields no bias and it may capture a dimension of risk above WC, either by age or by sex. This only happens when height shows an inverse association and WHtR as being of >0.5 increases their discriminative ability beyond that of WC alone. The novel findings and demonstrations should be incorporated to clinical practice when rigorously handling association of anthropometrics measures and MI risk.

References

1. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388: 1459-544.
2. WHO. Obesity and overweight; 2014 [updated June 2016; accessed 21Feb 2019]. Fact sheet No 311. Available in: http//www.who.int/mediacentre/factsheets/fs311/en/
3. Cornier MA, Després JP, Davis N, et al. Assessing adiposity: a scientific statement from the American Heart Association. Circulation. 2011; 124 (18): 1996-2019.
4. Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet. 2005; 366; 1640-9.
5. Gelber RP, Gaziano JM, Orav EJ, et al. Measures of obesity and cardiovascular risk among men and women. J Am Coll Cardiol. 2008; 52 (8):605-15. doi:10.1016/j.jacc.2008.03.066
6. Zhu J, Su X, Li G, et al. The incidence of acute myocardial infarction in relation to overweight and obesity: a meta-analysis. Arch Med Sci. 2014;10 (5):855-62. doi:10.5114/aoms.2014.46206
7. Gruson E, Montaye M, Kee F, et al. Anthropometric assessment of abdominal obesity and coronary heart disease risk in men: the PRIME study. Heart. 2010; 96 (2):136-40. doi: 10.1136/hr.2009.171447.
8. Lassale C, Tzoulaki I, Moons KGM, et al. Separate and combined associations of obesity and metabolic health with coronary heart disease: a pan-European case-cohort analysis. Eur Heart J. 2018; 39 (5): 397-406. Doi.10.1093/eurheartj/ehx448.
9. Choi D, Choi S, Son JS, et al. Impact of Discrepancies in General and Abdominal Obesity on Major Adverse Cardiac Events. J Am Heart Assoc. 2019; 8 (18):e013471. doi:10.1161/JAHA.119.013471.
10. Lloyd-Jones DM, Hong J, Labarthe D, 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: 586-613. Doi: 10.1161/CIRCULATIONAHA.109.192703.
11. Fang N, Jiang M, Fan Y. Ideal cardiovascular health metrics and risk of cardiovascular disease or mortality: A meta-analysis. Int J Cardiol. 2016; 214:279-83. Doi: 10.1016/j.ijcard.2016.03.210.
12. Alberti KG, Eckel RH, Grundy SM, 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 (16): 1640-5.
13. World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation, Geneva, 8-11 December 2008. World Health Organization. 2011. http://www.who.int/iris/handle/10665/44583. (Accessed Dec 2020).
14. Ladeiras-Lopes R, Sampaio F, Bettencourt N, et al. The Ratio Between Visceral and Subcutaneous Abdominal

Fat Assessed by Computed Tomography Is an Independent Predictor of Mortality and Cardiac Events. Rev Esp Cardiol (Engl Ed). 2017; 70 (5): 331-7.
15. Chen Y, Jiang J, Shi J, et al. Association of Visceral Fat Index and percentage Body Fat and Anthropometric Measures with Myocardial Infarction and Stroke. J Hypertens. 2016; 5: 235.doi: 10.4172/2167-1095.1000235.
16. Brown JC, Harhay MO, Harhay MN. Anthropometrically-predicted visceral adipose tissue and mortality among men and women in the third national health and nutrition examination survey (NHANES III). Am J Hum Biol. 2017; 29:e22898. doi:10.1002/ajhb.22898
17. Egeland GM, Igland J, Vollset SE, et al. High population attributable fractions of myocardial infarction associated with waist-hip ratio. Obesity. 2016; 24 (5):1162-9.
18. Nilson G, Hedberg P, Leppert J, et al. Basic Anthropometric Measures in Acute Myocardial Infarction Patients and Individually Sex- and Age-Matched Controls from the General Population. J Obes. 2018; 2018: 3839482. doi: 10.1155/2018/3839482.
19. Cao Q, Yu S, Xiong W, et al. Waist-hip ratio as a predictor of myocardial infarction risk. A systematic review and meta-analysis. Medicine. 2018; 27-30 (e11639). doi.org/10.1097/MD.0000000000011639
20. Joseph P, Yusuf S, Lee SF, et al. Prognostic validation of a non-laboratory and a laboratory based cardiovascular disease risk score in multiple regions of the world. Heart. 2017; 0: 1-7. Doi: 10.1136/heartjnl-2017-311609.
21. Peters SAE, Bots SH, Woodward M. Sex Differences in the Association Between Measures of General and Central Adiposity and the Risk of Myocardial Infarction: Results From the UK Biobank. J Am Heart Assoc. 2018; 7(5). pii: e008507. Doi: 10.1161/JAHA.117.008507.
22. Nicklas BJ, Penninx BH, Cesari M, et al. Association of Visceral Adipose Tissue with Incident Myocardial Infarction in Older Men and Women The Health, Aging and Body Composition Study. Am J Epidemiol. 2004; 160:741-9. Doi: 10.1093/aje/kwh281.
23. Martín-Castellanos A, Cabañas-Armesilla MD, Barca-Durán FJ, et al. Obesity and risk of Myocardial Infarction in a Sample of European Males. Waist To-Hip-Ratio Presents Information Bias of the Real Risk of Abdominal Obesity. Nutr Hosp. 2017; 34 (1): 88-95. doi.org/10.20960/nh.982.
24. Martin-Castellanos A, Cabañas MD, Martín-Castellanos P, et al. The body composition and risk prediction in myocardial infarction men. Revealing biological and statistical error bias for both general obesity and waist-to-hip ratio. Card Res Med. 2018; 2: 13-20.
25. Song X, Jousilahti P, Stehouwer CD, et al. Comparison of various surrogate obesity indicators as predictors of cardiovascular mortality in four European populations. Eur J Clin Nutr. 2013; 67 (12): 1298-302. doi: 10.1038/ejcn.2013.203.
26. Rost, S, Freuer D, Peters A, et al. New indexes of body fat distribution and sex-specific risk of total and cause-specific mortality: a prospective cohort study. BMC Public Health. 2018;18(1):427. Doi: 10.1186/s12889-018-5350-8.
27. Martin-Castellanos A, Martin-Castellanos P, Cabañas MD, et al. Adiposity-Associated Anthropometric Indicators and Myocardial Infarction Risk: Keys for Waist to-Height-Ratio as Metric in Cardiometabolic Health. AJFNH. 2018; 3 (5): 100-7.

http://www.aascit.org/journal/ajfnh. (Accessed Dec 2020).
28. Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med. 2008; 359:2105-20.
29. Ashwell M, Gunn P, & Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. Obes Rev. 2012; 13 (3), 275-86.
30. Guasch-Ferré M, Bulló M, Martínez-González MA, et al. Waist-to-Height Ratio and Cardiovascular Risk Factors in Elderly Individuals at High Cardiovascular Risk. PLoS ONE. 2012; 7 (8):e43275. Doi: 10.1371/journal.pone.0043275.
31. Kang SH, Cho KH, Park JW, et al. Comparison of waist to height ratio and body indices for prediction of metabolic disturbances in the Korean population: the Korean National Health and Nutrition Examination Survey 2008-2011. BMC Endocr Disord. 2015; 15:79. doi: 10.1186/s12902-015-0075-5.
32. Lam BC, Koh GC, Chen C, et al. Comparison of Body Mass Index (BMI), Body Adiposity Index (BAI), Waist Circumference (WC), Waist-To-Hip Ratio (WHR) and Waist-To-Height Ratio (WHtR) as predictors of cardiovascular disease risk factors in an adult population in Singapore. PLoS One. 2015; 16; 10 (4): e0122985. doi: 10.1371/journal.pone.0122985.
33. Swainson MG, Batterham AM, Tsakirides C, et al. Prediction of whole-body fat percentage and visceral adipose tissue mass from five anthropometric variables. PLoS One. 2017; 12 (5): e0177175. Doi: 10.1371/journal.pone.0177175
34. Hajian-Tlaki K, Heidari B. Comparison of abdominal obesity measures in predicting of 10-year cardiovascular risk in an Iranian adult population using ACC/AHA risk model: A population based cross sectional study. Diabetes Metab Syndr. 2018; 12 (6):991-7. doi: 10.1016/j.dsx.2018.06.012.
35. Howell CR, Mehta T, Ejima K, et al. Body Composition and Mortality in Mexican American Adults: Results from the National Health and Nutrition Examination Survey. Obesity (Silver Spring). 2018; (8):1372-80. doi: 10.1002/oby.22251.
36. Segura-Fragoso A, Rodríguez-Padial L, Alonso-Moreno FJ, et al. Anthropometric measurements of general and central obesity and discriminative capacity on cardiovascular risk: RICARTO study. Semergen. 2019; 45 (5): 323-32. Doi: 10.1016/j.semerg.2019.02.013.
37. Ramírez-Vélez R, Pérez-Sousa MÁ, Izquierdo M, et al. Validation of Surrogate Anthropometric Indices in Older Adults: What Is the Best Indicator of High Cardiometabolic Risk Factor Clustering? Nutrients. 2019;11 (8):1701. doi: 10.3390/nu11081701.
38. Czernichow S, Kengne AP, Stamatakis, E, et al. Body mass index, waist circumference and waist-hip ratio: which is the better discriminator of cardiovascular disease mortality risk?: evidence from an individual-participant meta-analysis of 82 864 participants from nine cohort studies. Obes Rev. 2011; 12 (9):680-7. Doi: 10.1111/j.1467-789X. 2011. 00879.x.
39. Nalini M, Sharafkhah M, Poustchi H, et al. Comparing Anthropometric Indicators of Visceral and General Adiposity as Determinants of Overall and Cardiovascular Mortality. F. Arch Iran Med. 2019; 22 (6):301-9.
40. Liu J, Tse LA, Liu Z, et al. PURE (Prospective Urban Rural

Epidemiology) study in China. Predictive Values of Anthropometric Measurements for Cardiometabolic Risk Factors and Cardiovascular Diseases among 44 048 Chinese. J Am Heart Assoc. 2019; 8 (16):e010870. doi: 10.1161/JAHA. 118.010870.

41. Davidson FE, Matsha TE, Erasmus RT, et al. The discriminatory power of visceral adipose tissue area vs anthropometric measures as a diagnostic marker for metabolic síndrome in South African women. Diabetol Metab Syndr. 2019; 11:93. doi:10.1186/s13098-019-0483-1
42. Gavriilidou NN, Pihlsgard M, Elmstahl S. Anthropometric reference data for elderly Swedes and its disease related pattern. Eur J Clin Nutr. 2015; 69 (9):1066-75.
43. Tchernof A, Despres JP. Pathophysiology of human visceral obesity: an update. Physiol Rev. 2013; 93:359–404.
44. Williams SR, Jones E, Bell W, et al. Body habitus and coronary heart disease in men. A review with reference to methods of body habitus assessment. Eur Heart J. 1997; 18: 376-93.
45. Mohammadi H, Ohm J, Discacciati A, Sundstrom J, et al. Abdominal obesity and the risk of recurrent atherosclerotic cardiovascular disease after myocardial infarction. Eur J Prev Cardiol. 2020; 27 (18):1944-52.
Doi: 10.1177/2047487319898019.
46. Fox CS, Massaro JM, Hoffmann U, 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.
47. Woolcott OO, Bergman RN. Relative fat mass (RFM) as a new estimator of whole-body fat percentage ─ A crosssectional study in American adult individuals. ScientificReports. 2018; 8 (1):10980.doi:10.1038/s41598-018-29362-1.
48. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivariate Behavioral Research. 2011; 46: 399-424.
Doi: 10.1080/00273171.2011.568786
49. Martin-Castellanos A, Martin-Castellanos P, Martin E, et al. Abdominal obesity and myocardial infarction risk: We demonstrate the anthropometric and mathematical reasons that justify the association bias of waist-to-hip ratio. Nutr Hosp. 2021. English. doi: 10.20960/nh.03416. Epub ahead of print. PMID: 33757289. https://www.nutricionhospitalaria.org/articles/onlinefirst. (Accessed March 2021)
50. Lee HW, Hong TJ, Hong JY, et al. Korea Working Group on Myocardial Infarction Investigators. Waist-hip ratio and 1-year clinical outcome in patients with non-ST-elevation myocardial infarctions. Coron Artery Dis. 2016; 27 (5):357-64. Doi: 10.1097/MCA.0000000000000369.
51. Medina-Inojosa JR, Batsis JA, Supervia M, et al. Relation of Waist-Hip Ratio to Long-Term Cardiovascular Events in Patients With Coronary Artery Disease. Am J Cardiol. 2018; 121 (8): 903-9. doi: 10.1016/j.amjcard.2017.12.038.
52. Dhar S, Das PK, Bhattacharjee B, et al. Predictive Value of Waist Height Ratio, Waist Hip Ratio and Body Mass Index in Assessing Angiographic Severity of Coronary Artery Disease in Myocardial Infarction Patients. Mymensingh Med J. 2020; 29 (4): 906-13.

