

Research Article

Abdominal obesity in predicting myocardial infarction risk. Waist-to-Hip Ratio: The metric that confused cardiology worldwide for a long time

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Research study

Important differences has been found in assessing the effects of obesity on cardiovascular disease (CVD) risk [1]. Interestingly, accurate estimation of the body composition (BC) is highly relevant from a public health perspective [2], and it has the importance of being essential in establishing the impact of adiposity on increased myocardial infarction (MI) risk. However, in non-randomized studies, baseline differences of BC between groups to be compared may introduce bias in results.

From INTERHEART study, waist-to-hip ratio (WHR) has been deemed as an excellent MI risk predictor [3-5], and results from UK Biobank have conferred it a greater excess risk in women than in men [6]. However, evidence supports that a higher waist circumference (WC) reflects an elevated risk of major cardiovascular outcomes [7]. Additionally, bias for WHR have been revealed due to protective overestimation for HC concerning WC and height [8,9]. Hence, *a different BC between groups with similar baseline confounding variables may provide bias in outcomes if the risk assignment does not account for the covariates that predict receiving true-risk*. Thus, as a result, risk assignment for WHR may be systematically biased if WC and hip circumference (HC) are not controlled in data analysis to preclude the same risk assignment between subjects who have equal WHR, but not necessarily referring to the same whole-risk.

Thinking about a *mathematical misconception when WHR was compared to WC in all previous studies*, our aim was to demonstrate *whether association of WHR and MI may provide bias*. Firstly, WC and HC express no equality for whole-risk as mathematical object. Secondly, in any ethnicity and sex, standard human body is formed by a HC higher than WC

More Information

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(WHR < 1) without involving any putative risk or protective effect (Figure 1). Thereby, HC > WC is a natural inequality satisfying a true premise: $HC = WC + x$, where subtracting HC by WC we calculate "x" ($x > 0$) as unit of length (cm), and being their standard value higher in women than in men. Thus, only when "x" is mathematically zero there is equality ($WC = HC$; $WHR = 1$) for whole-risk conclusion to be certain. Obviously, when "x" is < 0 ($WHR > 1$) conclusion for whole-risk holds true. Nevertheless, $WHR < 1$ is a proper fraction whose decimal value tell us the equal parts of WC that we have in HC, but it demonstrates not whole-risk beyond that of WC. Thus, in our previous research [8,9] $WHR < 1$ has always marked different individuals and proper fractions there where $HC = WC + x$, being always "x" of > 0 . As an example $94/99$ vs. $95/100$ vs. $100/105$, etc., = 0.95; $94/96.9$ vs. $98/100.9$ vs. $102/104.9$, etc., = 0.97; $94.2/94.3$ vs. $96/96.1$ vs. $100/100.1$, etc., = 0.99; there would be five type of values for WHR between 0.95 and 0.99 and infinite fractions for "x" between 5 and 0.1: $HC > WC$ in all). However, biologically there were a true-risk when WC predicted receiving whole-risk ($WC \geq$ defined cutoff: 94.4) and another one spurious when WC receiving a false-risk (WC below their cutoff). Hence, dividing WC by HC gave us a fraction, at least between the lowest and 0.99 value, there

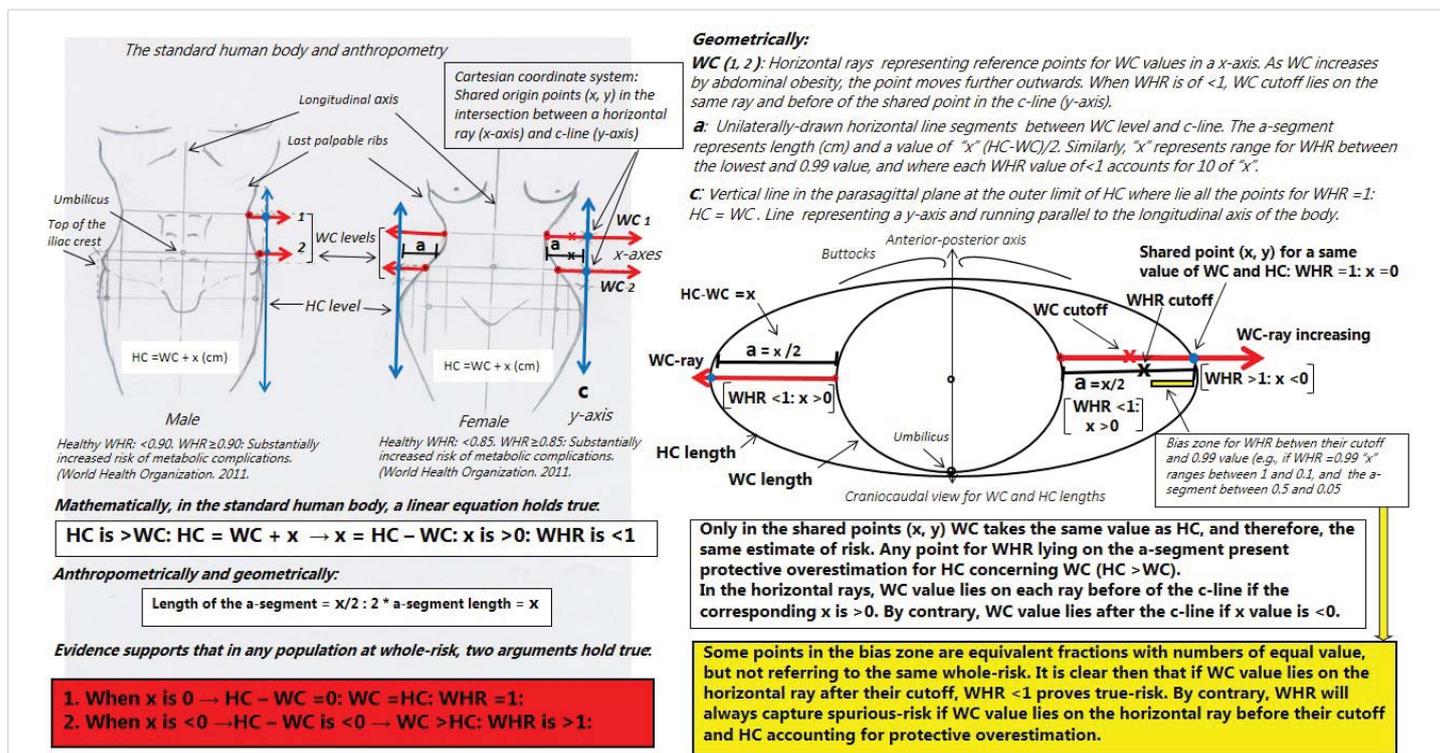


Figure 1: Original assembly from anthropometric models and geometric lines on the standard human body. Geometrical and mathematical demonstrations for a correct anthropometric assessment of the abdominal obesity and CVD risk. Drawings representing the human body (both sexes) where metrics would be sample mean values per standard deviation for WC, HC and WHR being actually valid for any anthropometrically healthy population and ethnicity. In the respective lines drawn would lie points of increased abdominal obesity representing mean values for thousands of cases of CVD as well as biological changes pointing towards greater excess risk of CVD as WC increases. Similarly, the corresponding cut-off points associated per standard deviation, or quintiles, quartiles/tertiles or Receiver Operating Characteristic analysis for WC and WHR will always lie before of the c-line. The anthropometric models and schemes are valid for both case-control and cohort studies, and any type of cardiovascular event. Explanations for understanding, in text. Names of lines and rays, where appropriate. The origin of the horizontal rays represent the same level of measurement for WC. CVD, cardiovascular disease; HC, hip circumference; WC, waist circumference; WHR waist-to-hip ratio.

where WHR was simply a way of representing size that was not whole-risk. On this approach, WHR would be a confounding variable with whole-risk conditioned on WC "x" distance and the estimate of risk for HC concerning WC [9].

Completing our research line, a case-control study to demonstrate biases was evaluated on a sample of MI men (n = 252). The minimum sample size for calculating was of 90 cases and at least 1 control per case, with obesity exposition and statistical power of 22% and 0.99, respectively. Measurements, strength of association and risk cutoffs for WC (≥ 94.4 cm), WHR (≥ 0.95) and WHtR (≥ 0.54) were consonant with those of large studies [3-9,12]. However, for the first time stratification as approach for removing bias effect was used. We created a baseline covariate (WHR_{0.95-0.99}) from a new matched sample in the stratum between 0.95 and 0.99 value for coinciding on the overlap area of the distribution and there where all subjects had a similar propensity score, and therefore, they should have the same risk distribution. Consequently, we considered other baseline covariate with binary outcomes for a spurious-risk assignment (WHRs). It was conditioned defining spurious-risk there where WC took a value below their cutoff, and besides, being lower than HC.

From results, WHR showed the strongest association, but WHR_{0.95-0.99} presenting no significant between-group difference. By contrast, WHRs showed double prevalence in cases, what indicated a risk assignment wrong due to slanted arithmetic data in an artificial direction. WHR < 1 and "x" > 0 were independently associated to control group as anthropometrically expected. Thereby, accepting WHR < 1 as entity of whole-risk was a false premise. Besides, in a Cartesian system WC and HC only may coincide on the same estimate of risk when WC takes the same value as HC (WHR = 1, Figure 1). Accordingly, selected risk points for WHR < 1 yielded a misclassification respect to WC because HC did not account for the same estimate of risk as WC, and only when WC (numerator) proved whole-risk WHR < 1-assigned risk had solid validity. Anthropometrically, between WHR cutoff and 0.99 value we always find protective overestimation for HC, and therefore, systematic bias occurs for making impossible the validity of WHR above WC alone, even when "x" being between 0.1 and 1 and WHR = 0.99 accounting for 10 values of "x".

Surprisingly, most studies in predicting MI and mortality risk always showed a WHR cutoff < 1 in both sex, while selection biases were never discussed [3-6,10-12]. Indisputably, "x" was



always a higher positive value in women and middle-aged than in men and elderly, respectively [2-5,10,12], and therefore, WHR cutoffs were always lower in the first two compared to the seconds. This means longer range up to 0.99 for involving higher possibility of bias in women and middle-aged due to a higher number of fractions where selection bias for WHR will always occurred [3-6,10-12]. In this line, WC and WHR would mathematically be equivalent for the same whole-risk, if and only if $HC = WC$, and therefore, $WHR = 1$ would be the entity of whole-risk exclusively depending on WC, and besides, HC taking the same value as WC. If not, error of estimate for the true-BC at risk may occur in comparing WC alone with WHR, and either by age or by sex. Therefore, if $HC > WC$ (WHR risk cutoff < 1) protective overestimation occurs for HC respect to WC, and the lower the WHR cutoff (e.g. in women), the higher the risk overestimation for WHR as compared to WC. It is mathematically clear, in any anthropometric-risk evaluation where baseline characteristics for WHR and WHR risk cutoff are of < 1 WC alone turn out to be the entity of whole-risk to be compared, but never WHR performing better than WC, except accepting biased results.

This research has the strength of demonstrating bias for WHR when mathematically thinking about risk cutoffs < 1 . These findings determine the generalizability to other ethnically-based or sex-specific populations if mathematically satisfy the same observation for WHR-associated risk, even finding higher hazard ratio in women compared to men [4,6,12]. As theoretical limitation, this won't be *applicable to populations not included in derivation cohort along with others not compared. Nevertheless, all WHR-associated risk above WC, as being mathematically incorrect* provides to cardiology false epidemiological conclusions worldwide. It is time of avoiding an unnecessary and confounding anthropometric where HC renders clinically useless.

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