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Obesity indicators and insulin resistance: a systematic review

Indicadores de obesidade e resistência à insulina: uma revisão sistemática

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ABSTRACT
The aim of this study was to verify the obesity indicators associated with insulin resistance by a systematic review. Two independent reviewers performed a search on Medline, Pubmed, LILACS, IBECS-ES and MedCarib databases up to April 2019, which included case-control, cohort or cross-sectional studies in adults. Articles' quality was assessed by Newcastle-Ottawa Scale. PRISMA guideline for conducting the review were adopted, with protocol registered at PROSPERO. Twelve articles were included in the review. All studies reported a positive association between obesity indicators and HOMA-IR. Obesity indicator most positively associated with HOMA-IR was BMI, followed by waist circumference. Obesity indicators are associated with HOMA-IR and may be a useful tool for screening insulin resistance.

Keywords: Body mass index. Obesity. Insulin resistance. Waist circumference.

RESUMO
O objetivo deste estudo foi verificar os indicadores de obesidade associados à resistência à insulina, através de uma revisão sistemática. Dois revisores independentes realizaram uma busca nas bases de dados *Medline*, *Pubmed*, *LILACS*, *IBECS-ES* e *MedCarib* até abril de 2019, incluindo estudos caso-controle, coorte ou delineamento transversal, em adultos. A qualidade dos artigos foi avaliada por meio do *Newcastle-Ottawa Scale*. Foram adotadas as normas do PRISMA para a condução da revisão, com protocolo registrado no PROSPERO. Foram incluídos na revisão 12 artigos. Associação positiva entre indicador de obesidade e HOMA-IR foi observada em todos os estudos. O indicador de obesidade que mais esteve positivamente associado ao HOMA-IR foi o IMC, seguido da circunferência da cintura. Os indicadores de obesidade estão associados ao HOMA-IR podendo ser uma ferramenta útil no rastreio da resistência à insulina.

Palavras-chave: Circunferência da cintura. Índice de massa corporal. Obesidade. Resistência à insulina.

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INTRODUCTION

Insulin resistance (IR) is defined as a condition in which target cells fail to respond to normal circulating insulin levels. Consequently, an increase in blood glucose and a compensatory increase in insulin secretion occur[1]. Central obesity, the most common cause for IR, is characterized by the accumulation of adipose tissue at the abdominal region[2]. However, the mechanism by which the accumulation of fat in the body´s central part is associated with IR is not yet fully understood[3].

Adipose tissue stores energy in the form of neutral fat and performs endocrine functions, since it synthesizes and releases bioactive proteins, called adipokines, with pro and anti-inflammatory activity[4].

Further, excess adipose tissue releases an increasing amount of free fatty acids in the blood circulation that directly affects insulin signaling, decreasing glucose uptake by skeletal muscles, stimulating the exaggerated synthesis of triglycerides and lipoproteins of very low density, and inducing increased hepatic glucose production. Consequently, blood glucose increases, closing a positive feedback cycle [1].

Obesity is therefore caused by the increase in the number and volume of adipocytes, a condition that, in recent years, has become an important public health issue in Brazil and worldwide. In fact, it affects a significant portion of the population, with an increase in the number of young people and in all socioeconomic groups. Besides being a disease, obesity is one of the most important risk factors for triggering other non-communicable chronic diseases (NCCDs)[5]. Several studies have demonstrated the association between obesity and IR in the triggering of NCCDs, such as cardiovascular diseases, Type 2 diabetes mellitus, chronic kidney disease, polycystic ovary syndrome and fatty liver disease[6-8].

IR diagnosis may be performed by Insulin Resistance Homeostasis Model Assessment (HOMA index), obtained by {[Fasting Insulin (μUI/mol) x Fasting Glucose (mg/dL)] / 22.5}, by Matthews *et al.*[9]. The above index has been a useful tool for population studies due to its easy usage and strong correlation with IR direct assessment techniques, such as the standard Frequent Sample IV Glucose Tolerance Test[10]. In spite of the calculation´s straightforwardness, the need to collect fasting blood and insulin dosage increases the procedure´s costs and impairs its application at primary health care for large population contingents[11].

Since, according to the literature, IR is related to obesity and to other NCCDs, several studies have shown that obesity indicators (OIs) feature a positive association with IR biochemical markers[12-14]. OIs depend only on anthropometric measurements and, therefore, they may be easily employed in clinical practice due to their non-invasiveness and low-cost tests. Consequently, OIs, such as body mass index (BMI), waist circumference (WC), waist-hip ratio (WHR), waist-height ratio (WHtR) and body fat percentage (%BF) have been employed[15].

Since they are easy to obtain, the OIs may be used in screening and early identification of IR, enabling a more effective prevention of diseases associated with obesity and a possible tool within primary health care. Current article verifies which OIs are associated with IR and determines the most appropriate obesity indicator (OI) to identify this condition.

METHODOLOGY

Current article is a systematic review and its conduction, acquisition and presentation of results complied with PRISMA guideline[16]. Review´s protocol has been registered in PROSPERO under CRD42019130849. Articles were searched in Medline, Pubmed, LILACS, IBECS-ES and MedCarib databases up to April 2019, without any language restriction or publication date. Boolean operators were used to match the following descriptors related to the OIs, IR and target age group: *obesity, overweight, body weight, body mass index, waist circumference, waist-hip ratio, abdominal obesity, body fat, anthropometry, insulin resistance, Homa-index, adults.*

Search, screening and evaluation of the articles were carried out by two independent reviewers (HCS and LOF) and a consensus was established between them, in cases of inconsistencies.

Articles were selected after the evaluation of titles and abstracts and finally their full reading. At this stage, information was retrieved on the publications, which included authors, the year of publication, study site, population under analysis, study aims, obesity and IR measures collected, the mode measures were evaluated and classified (cutoff points), the association measures, adjustments and main results.

Inclusion criteria comprised studies on adults (between 18 and 65 years old), both sexes, and cross-sectional, case-control or cohort designs. Studies were excluded whether they were conducted with specific groups or people with special/hospitalized clinical conditions, such as pregnant women, postpartum women, postmenopausal women, patients with cardiovascular conditions, psychiatric diseases, diabetics, patients with some type of cancer and others.

The Newcastle-Ottawa Scale (NOS) was employed to evaluate the studies´ methodological quality. Total score assigned for each study corresponded to the number of positive items, with a maximum of 9 points for case-control or cohort studies, and 10 points for cross-sectional studies[17, 18].

RESULTS

The databases search revealed 3,515 articles, of which 3,276 came from Pubmed, 220 from Medline, 11 from LILACS, 7 from IBECS-ES and 1 from MedCarib. Due to duplication, 45 articles were removed. After evaluation by titles and abstracts, 29 articles were selected for full reading. Seventeen articles were excluded and the remaining 12 articles have been included in current systematic review[19-30] (Figure 1).

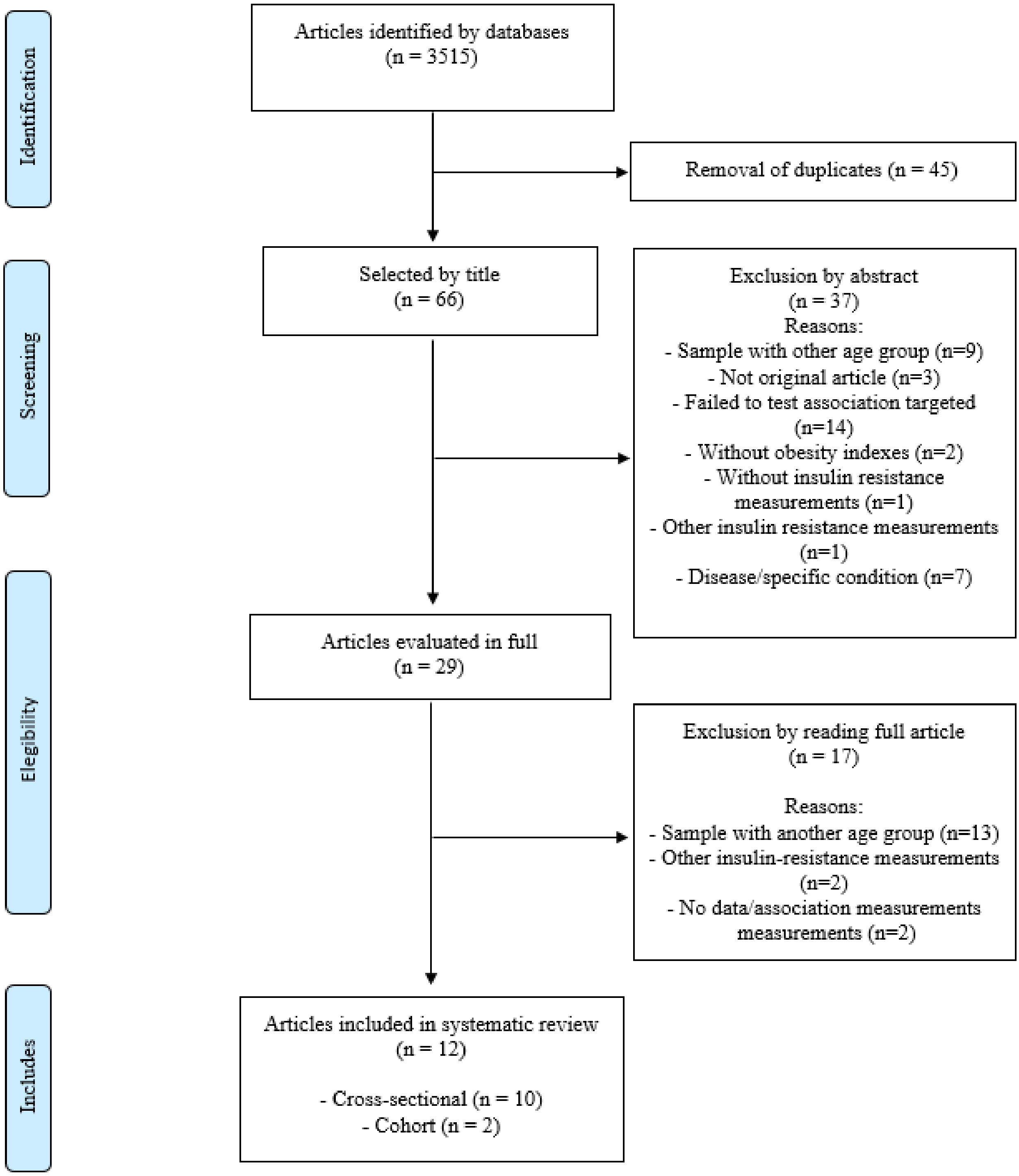

Figure 1. Flowchart of articles included in the systematic review

All articles were published since 2009, at different databases (12/12), with samples ranging between 60 and 12,018 participants, from different continents, particularly from Asia (5/12). Most had a cross-sectional design (10/12) and people of both sexes (9/12) (Table 1).

The most employed OIs comprised BMI, WC, %BF and WHtR (10/12, 9/12, 6/12 and 4/12, respectively). Most articles presented data with more than one indicator (10/12) in their analyses. Only four studies used cutoff points to classify OIs according to established evaluation standards. As an IR measure, in six studies, the authors themselves established cut-off points in the IR assessment when using HOMA-IR (Table 1).

The relationship between OIs and IR occurred in all articles under analysis, although each had a different aim. While several articles verified the direct association between OIs and IR (7/12), others evaluated the association between OIs and cardiometabolic risk factors (5/12), with IR included in the latter. Most articles featured more than one association test (7/12) and, consequently, presented more than one measurement. In the case of association measurements, the correlation coefficients (8/12) were determined, followed by β of the regressions (5/12) and by Odds Ratio (OR) (3/12). Adjustments and stratification of the comparison groups also differed (Table 2).

In the case of dispersion measurements and central tendency of OIs compared to HOMA-IR, Lim *et al.*[25] reported significantly higher mean rates in weight, WC, BMI and WHtR when people with and without IR were compared (Table 2). This was similar to that observed by Kurniawan *et al.*[21] when assessing body weight, BMI, WC and %BF between insulin non-resistant and resistant people. Park *et al.* [26] analyzed quartiles of change of WC and HOMA-IR in 20 years and Vasques et al. [29] checked WC, BMI, %BF, WHR and WHtR among HOMA-IR quartiles (data not shown in table).

On the other hand, Zhang *et al.* [30] assessed mean HOMA-IR index among classification categories of nutritional status for different OIs and reported significantly higher HOMA-IR index among obese men and women by BMI, when compared with overweight and normal weight ones, and obese by %BF, WHtR and WHR, when compared with normal classification. Janssen[20] investigated the prevalence of IR among BMI and WC classifications for different age groups and detected that the prevalence of IR was higher in the groups with high BMI and WC, regardless of age group (data not shown in table).

When Hsieh *et al.* [19] assessed the relationship between insulin sensitivity and body fat distribution, they found no correlation between total body fat (TBF) and HOMA-IR (Table 2). Moreover, Kurniawan *et al*.[21], Pourshahidi *et al.*[27], Sasaki *et al.*[28] and Vasques *et al.*[29] detected a moderate correlation between %BF and HOMA-IR ($r=0.438$ $p=0.00$; $r=0.33$ $p<0.0035$; $r=0.369$ $p<0.0001$; $r=0.394$ $p<0.001$, respectively). Zhang *et al.* [30] also found a moderate correlation between these measurements, when assessing separately by sex (men $r=0.390$ $p<0.001$; women $r=0.345$ $p<0.001$) (data not shown in table).

Lacerte et al. [22] investigated the co-relationship between changes in anthropometric measurements and HOMA-

IR levels in 48-month cohort and detected a high correlation rate between %BF and HOMA-IR ($r=0.54$ $p<0.01$) among people with alterations in the OIs analyzed (n=60). However, the correlation was moderate ($r=0.44$ $p=0.01$) when they evaluated people who increased their %BF by more than 1% over the period. In the case of other OIs, a high correlation was found between BMI and HOMA-IR ($r=0.54$ $p<0.01$) and moderate correlation between WC and HOMA-IR ($r=0.38$ $p<0.01$) for those who had an OI increase in 48 months. In the group with an increase in fat percentage by more than 1% in 48 months, the correlation between BMI and HOMA-IR was moderate ($r = 0.44$ $p=0.01$) and low ($r = 0.25$ $p=0.18$) between WC and HOMA-IR (data not shown in table).

The same authors also investigated the correlation between weight gain (delta BMI) and HOMA-IR during four years and found that BMI increase was associated with an increase in HOMA-IR, verified by moderate correlation ($r=0.54$; $p<0.01$) (data not shown in table).

When Janssen *et al.* [20] stratified sample by sex and age group (20-39 years n=922; 40-59 years n=781) to verify whether the relationship between high WC and cardiometabolic risk markers decreased by aging, they detected a high correlation between BMI and HOMA-IR and between WC and HOMA-IR for both sexes. Kurniawan *et al.* [22] stratified their sample between resistant and non-resistant to insulin and detected a moderate correlation for these same OI and HOMA-IR (data not shown in table).

Moderate correlations were also found between OIs and HOMA-RI in studies by Pourshahidi *et al.* [27], Vasques *et al.* [29] (Table 2) and Sasaki *et al.* [28] (BMI and HOMA-IR $r = 0.422$ $p<0.0001$ and WC and HOMA-IR $r = 0.386$ $p<0.0001$). Zhang *et al.* (2018) [30] evaluated the correlation between BMI and HOMA-RI for both sexes and reported moderate correlation in women ($r = 0.484$ $p<0.001$) and high correlation in men ($r = 0.552$ $p<0.001$) (data not shown in table).

The authors also assessed the correlation between WHR and WHtR and HOMA-IR for both sexes and detected moderate correlations in both (men $r = 0.440$ $P<0.001$; $r = 0.495$ $P<0.001$ / women $r = 0.410$ $p<0.001$; $r = 0.424$ $P<0.001$, respectively). Similar results were observed by Vasques *et al.* [29] and by Pourshahidi *et al.* [27]. They also detected a moderate correlation in their evaluations, except for WHR and HOMA-RI in the study by Pourshahidi *et al.* [27], where correlation was low and not significant, whilst OI was taken only for men (Table 2).

Only Kurniawan *et al.* [21] analyzed the correlation between body weight and HOMA-IR and observed a moderate correlation between the measurements ($r = 0.480$ $p=0.00$) (data not shown in table).

Among the studies that evaluated the association by multiple linear regression, Lacerte *et al.* [22] detected a significant result between a shift from HOMA-IR to a BMI unit, even after adjustments. Association is stronger when variables related to lifestyle and metabolic capacity were added. Lajeunesse-Tremp *et al*. [23] and Lara *et al*. [24], who assessed BMI and the association WC - HOMA-IR, also found a significant association between these variables. Park *et al*. [26] also verified the association between WC and HOMA-IR and obtained significant results. Only Sasaki *et al*. [28] assessed the association between %BF and HOMA-IR and detected a significant association regardless of adjustment used. These authors also evaluated the relationship between BMI and WC - HOMA-IR. However, the association was only significant for BMI in Model 2 adjustment (Table 2).

In the case of associations measured by OR, all authors insisted on a positive association between OIs and HOMA-IR. Janssen[20] stated that people with higher BMI and WC rates were more likely to be insulin resistant. Kurniawan *et al.* [21] found a positive association for the same indicators and weight and %BF. Similarly, Zhang *et al.* [30] detected a positive association for BMI, WHtR and WHR and HOMA-IR measurements in both sexes, but not for %BF.

Table 3 gives an evaluation of the articles´ methodological quality. Total scores ranged from five to ten points. Only 2/10 of the cross-sectional studies scored on all quality items evaluated. On the other hand, only 1/2 of cohort studies had maximum score. The main limitation among cross-sectional studies was the non-presentation of the non-response rate, followed by sample representativeness and sample size.

DISCUSSION

Current systematic review revealed that BMI was the OI most positively associated with HOMA-IR, not only because it was the most evaluated indicator but due to more robust associations. Association between BMI and HOMA-IR remained significant even after different adjustments. Lacerte *et al.* [22] stated that association was strongest when variables related to lifestyle and aerobic capacity were added. Further, higher mean rates and prevalence of BMI and WC among insulin-resistant people or with higher HOMA-IR index were also reported. WC was the second most evaluated and positively associated index with HOMA-IR. On the other hand, the positive association between %BF and HOMA-IR was ambiguous since it was not significant in all studies. This may be due to different methods of body composition assessment carried out in different studies. Body weight and WHtR were the OIs least evaluated in the studies.

It is noteworthy that for this review, articles published in different databases were included, without any restriction on the date of publication and language. Most studies evaluated individuals of both sexes, from different parts of the world, featuring good-sized samples. Most presented good scores in methodological evaluation and guaranteed the quality of the results found in current review. Moreover, it is actually one of the few systematic reviews aimed at identifying which IO had the most robust association with IR. A meta-analysis and a bibliographic survey addressing a similar theme were found. Carried out by Zhang *et al*. [31], the meta-analysis evaluated the association between different deposits of adipose tissue with IR. Results similar to those in current present review were reported. HOMA-IR was correlated with total body fat (r = 0.492, 95% CI: 0.407-0.570), BMI (r = 0.482, 95% CI: 0.445-0.518) and WC (r = 0,466, 95% CI: 0.432-0.500). The bibliographic survey made by Vasques *et al*. [32] reported that WC had a better predictive capacity for IR, with more consistent results than the other indicators evaluated. WHtR showed a positive result, but the authors pointed out that more studies were needed to consolidate it as an IR predictor. On the other hand, results with BMI and WHR were more inconsistent.

When the methodological quality of the articles was assessed, most of which presented a good score. It was decided to analyze the articles with lower scores and indicate their methodological weaknesses, as only 12 articles met the inclusion criteria and were included in the review. Although most studies evaluated people of both sexes, three articles included only men. This fact limited the comparison between the findings and the extrapolation of the results. It is well-known that men and women differ in terms of body composition and regions of adipose tissue accumulation[33,34]. Further, women have several specificities which depend on the age group. In pre-menopause women, fat accumulation occurs mainly in the subcutaneous region, while men accumulate more adipose tissue in visceral deposits, regardless of age. On the other hand, postmenopausal women have an increase in visceral adiposity due to the reduction of endogenous estrogen production[35], which contributes to an increase in cardiometabolic risk, which includes IR[36,37].

Due to the above factors, women are at higher risk in developing IR than men, albeit depending on life stage. However, Lajeunesse-Tremp *et al*. [23] and Zhang *et al*. [30] detected no differences between men and women when evaluating the association between OI and IR. Similar results in both sexes may be due to the fact that women have healthier lifestyle habits, regardless of health status, with lower drinking and smoking trends[38,39]. The latter are factors with a direct impact on OI and, consequently, on HOMA-IR.

Ethnicity is an other factor that influences IR. Studies conducted in the USA and South Africa have shown that, when compared to white women, black women have less visceral fat and greater fat accumulation in the gluteus-femoral region, albeit more resistant to insulin[40,41]. In addition, the differences in health between ethnic groups derive from complex relationships, such as biological, socioeconomic, environmental, behavioral, and geographic characteristics, influencing the pattern of body fat distribution[42]. It is actually an important variable in studies investigating this relationship. In current review, two studies included ethnicity as an adjustment measure[20,26], although no association was made with this aim in view. Further, only one study comprised exclusively black individuals[23].

Janssen[20] detected a positive association between high BMI and WC rates with cardiometabolic risk (including IR) markers. When young people were compared with older ones, OR were attenuated by age, or rather, young people with high BMI and WC rates were more likely to develop IR when compared to older ones. Consequently, in the association between IOs and HOMA-IR, age is an important factor. When the adjustment variables used in the studies included in this review were analyzed, it was reported that most authors included age in their model.

On the other hand, differences in the association between IO and HOMA-IR according to age were not reported by Kahn *et al*.[43] When the risk of increased BMI and WC measurements among individuals with higher HOMA-IR index was compared, no significant difference was reported between age groups (20-49 years and 50 years or more). However, relative risks tended to be lower among older individuals. It was not possible to include this specific article in current review since analyses were made only by comparing the association of interest between the age groups, which included people over 65 years of age.

Limitations of current review comprised the inclusion of only two cohort studies which prevented the establishment of a causal relationship between the variables under analysis. Moreover, measurements which were part of the objective of this study have already been widely explored for various purposes. Consequently, it was difficult to determine the search strategy. In fact, search resulted in many publications that did not aim in evaluating the relationship between IOs and IR. When searching the databases, many articles were excluded due to their lack of stratification of samples by age group, evaluating similarly adults and elderly people. However, the literature shows that adults and elderly people differ physiologically and, therefore, they have to be evaluated separately, which justifies the establishment of this exclusion criterion in the selection of articles[44,45].

Finally, data showed the need for cohort and case-control studies to verify which OI could predict the risk of developing IR. In fact, this finding would facilitate clinical practice and could be used as a preventive strategy for cardiometabolic diseases. Further, no study exclusively on women or that controlled the women population according to the reproduction period was extant. Such deficits impair analysis on the relationship investigated due to the influence of hormonal factors in such relationship.

CONCLUSION

Current review detected a positive association between IO and IR measured by HOMA-IR, in studies conducted in different parts of the world, with diversified sample size, for both sexes and, for the most part, with good methodological quality.

There was a recent interest in the theme in adults and the need to conduct other studies, especially with a longitudinal design, to better elucidate the causal relationship between obesity and IR. In fact, OI may be an important tool in the screening and prevention of IR.

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Table 1. Main characteristics and obesity indicators of the articles included in the systematic review

Author /Year	Country	Study	Study design	Population	Obesity Indicators/ Cut points	Insulin resistance/ cut points
Hsieh et al. (2014)	Taiwan	-	Cross-sectional	328 participants: 179 men and 149 women, 41 - 59 years old	BF (cm^3)	HOMA-IR
Janssen (2009)	USA	NHANES	Cross-sectional	5,222 participants: 2,642 men and 2,580 women, ≥ 20 years old	BMI WC	HOMA-IR (Matthews et al., 1985) RI ≥ 4.28(men) ≥ 4.09(women)
Kurniawan et al. (2018)	Indonesia	-	Cross-sectional	140 adult men, 18-25 years old	BMI WC %BF	HOMA-IR: RI ≥75 percentile (RI ≥3.75)
Lacerte et al. (2014)	Canada	-	Cohort	60 participants: 42 men and 18 women	BMI WC %BF	HOMA-IR (Matthews et al., 1985)
Lajeunesse-Tremp et al. (2019)	Kenya	-	Cross-sectional	1,405 participants (rural area: 450 men and 708 women; urban area: 131 men and 116 women), 32 – 42.1 years old	BMI WC	HOMA-IR (Matthews et al., 1985)
Lara et al. (2012)	Chile	-	Cross-sectional	999 participants: 437 men and 562 women, 22 - 28 years old	BMI WC	HOMA-IR (Matthews et al., 1985) RI ≥ 2.53 (Acosta et al., 2002)
Lim et al. (2019)	Korea	KNHANES	Cross-sectional	11,149 participants: 4,777 men (45.2 ± 15.0 years old) and 6,372 women (44.3 ± 14.6 years old)	BMI WC WHR	HOMA-IR: RI >75 percentile (Lee et al., 2006; Radikova et al., 2006)
Park et al. (2010)	USA	CARDIA	Cohort	3,331 participants both sexes, 18 - 30 years old	WC	HOMA-IR (Matthews et al., 1985)
Pourshahidi et al. (2016)	North Ireland	-	Cross-sectional	192 participants: 160 men and 32 women, 18 - 40 years old	BMI: Adequate <25.0 kg/m^2 Overweight 25.0–29.9 kg/m^2 Obesity ≥30.0 kg/m^2 WHR WHtR %BF	HOMA-IR (Matthews et al., 1985) RI >5.13 (Blake et al., 2010)
Sasaki et al. (2016)	Japan	-	Cross-sectional	167 adult men	BMI: Low ≤18.5 and <22.,0 Adequate ≤22.0 and <25.0 WC: Adequate <85.0 cm High ≥85.0 cm %BF	HOMA-IR (Matthews et al., 1985)
Vasques et al. (2009)	Brazil	-	Cross-sectional	138 men, 20 - 59 years old	BMI: Adequate <25 kg/m^2 High ≥25 kg/m^2 WC: Adequate <94 cm High ≥94 cm Very High ≥102 cm WHR:	HOMA-IR (Matthews et al., 1985)

					Adequate <0.92 High ≥0.92 WHR: Adequate <0.48 High ≥0.48 %GC: Adequate <25% High ≥25%	
Zhang et al. (2018)	China	-	Cross-sectional	12,018 participants: 7,185 men (46.0 ± 8.8 years old) and 4,833 women 46.4 ± 9.4 years old)	BMI: adequate ≥18.5 and ≤24.0 Overweight >24.0 and <28.0 Obesity ≥28.0 %BF: Adequate <28%(men) <35%(women) Obesity ≥28%(men) ≥35%(women) WHR: Adequate <0.96(men) <0.85(women) Obesity ≥0.96(men) ≥0.85(women) WHtR: Adequate <0.54(men) <0.51(women) Obesity ≥0.54(men) ≥0.51(women)	HOMA-IR: High ≥2.9(men) ≥2.2(women)

Abbreviations: BF: body fat; BMI: Body Mass Index; %BF: body fat percentage; WC: waist circumference; WHtR: waist-height ratio; WHR: waist-hip ratio; IR: insulin resistance; HOMA-IR: *Insulin Resistance Homeostasis Model Assessment*.

Table 2. Main aims and results of the articles included in the systematic review

Author / Year	Aim (s)	Measurement (s)	Main results
Hsieh et al. (2014)	- Evaluate relationship between sensitiveness to insulin, chronic inflammation and central fat distribution	Pearson´s Correlation Coefficient (r)	*- Adjusted by age and sex* GCT and HOMA-IR: r = 0.18 p=0.075
Janssen (2009)	- Determine whether relation between high WC and cardiometabolic risk markers is lowered with age	Odds Ratio (OR) and confidence interval (CI 95%)	*- Adjusted by sex, ethnicity and smoking* **20-39 years:** moderate BMI and IR: OR = 4.85 IC 95% 2.11-11.17 High BMI and IR: OR = 37.99 IC 95% 17.94-80.46 (p<0.05) Moderate WC and IR: OR = 4.95 IC 95% 2.99-8.22 High WC and IR: OR = 30.41 IC 95% 17.58-52.34 (p<0.05) **40-59 years:** Moderate BMI and IR: OR = 4.50 IC 95% 2.21-9.15 High BMI and IR: OR = 17.48 IC 95% 9.57-31.91 (p<0.05) Moderate WC and IR: OR = 4.49 IC 95% 2.25-8.93 High WC and IR: OR = 17.11 IC 95% 9.13-32.09(p<0.05)
Kurniawan et al. (2018)	- Evaluate the association between five obesity indicators (body weight, BMI, WC, %BF, Visceral Fat) with IR - Stratify diagnose rates to predict IR	Odds Ratio (OR) and confidence interval (CI 95%)	Weight and IR: OR = 1.065 IC 95% 1.037-1.095 p=0.00 BMI and IR: OR = 1.114 IC 95% 1.065-1.228 p=0.00 WC and IR: OR = 1.076 IC 95% 1.041-1.112 p=0.00 %BF and IR: OR = 1.227 IC 95% 1.116-1.349 p=0.00
Lacerte et al. (2014)	- Evaluation of influence of weight gain and changes in the distribution of fat in IR and in the circulating variations of adiponectin during 4 years in young adults with adequate weight	Linear regression (β) e standard deviation (SD)	**- BMI changes associated with HOMA-IR change** *-without adjustment:* β = 0.44 EP = 0.16 p=0.01 *-Adjusted by sex:* β = 0.51 EP = 0.19 p=0.01 *-Adjusted by sex and age:* β = 0.50 EP = 0.19 p=0.02 *-Adjusted by sex and parents´ schooling:* β = 0.51 EP = 0.20 p=0.02 *-Adjusted by sex, age, parents´ schooling and consumption of fruits and vegetables:* β = 0.53 EP = 0.23 p=0.03 *-Adjusted by sex, age, parents´ schooling. consumption of fruits and vegetables and physical activities:* β = 0.64 EP = 0.25 p=0.02 *-Adjusted by sex, age, parents´ schooling. consumption of fruits and vegetables. physical activities and aerobic capacity:* β = 0.83 EP = 0.25 p<0.01
Lajeunesse-Tremp et al. (2019)	- Comparing association between anthropometric features and risk factors for cardiometabolic diseases	Multiple linear regression (β)	*- Adjusted by age, smoking, alcoholic beverages, physical activities, energy and urban area* **Men** – BMI and HOMA-IR: β = 0.091 p<0.05 / WC and HOMA-IR: β = 0.019 p<0.05 **Women** – BMI and HOMA-IR: β = 0.055 p<0.05 / WC and HOMA-IR: β = 0.018 p<0.05
Lara et al. (2012)	- Verify which measure of obesity, BMI or WC is the best to assess cardiovascular risk factor	Multiple Linear Regression (β) and confidence interval (CI 95%)	*- Adjusted by age and sex* BMI and HOMA-IR: β = 0.14 IC 95% 0.12-0.16 WC and HOMA-IR: β = 0.06 IC 95% 0.05-0.06
Lim et al. (2019)	- Investigate efficiency of various combinations of glucose-triglyceride index and obesity indicators for IR	Mean ± standard deviation	**- Comparison between groups: Non-IR and IR** (p<0.001) Weight (kg): 60.2 ± 10.5 e 67.6 ± 12.7 / CC (cm):77.9 ± 8.8 e 85.0 ± 9.9 BMI (kg/m²): 22.6 ± 2.9 e 25.2 ± 3.5 / RCE: 0.48 ± 0.05 e 0.52 ± 0.06
Park et al. (2010)	- Association between WC and IR (HOMA-IR), by linear models employing three WC: WC at base, linear changes at WC and fluctuation of WC, during 20 years follow-up	Multiple linear regression (β) and standard error (EP)	*- Adjusted by other two measurements of WC, age, sex, ethnicity, study centers, schooling and HOMA-IR in year 15* **WC from year 0 and HOMA-IR in year 20** men ≥85cm and women ≥78cm: β = 0.1213 EP = 0.0200 men 80 - <85cm and women 70 - <78cm: β = 0.0442 EP = 0.0182 men 75 - <80 cm and women 66 - <70cm: β = 0.0113 EP = 0.0180 men <75 cm and women <66 cm: Reference (p<0.0001) **Changes in WC (cm) from year 0 to year 15 and HOMA-IR in year 20** +1.113 a +3.895: β = 0.1669 EP = 0.0204 / +0.675 a +1.112: β = 0.1290 EP = 0.0181 +0.322 a +0.674: β = 0.0749 EP = 0.0172 / -2.770 a +0.321: Reference (p<0.0001)

			- Adjusted WC by other two WC measurements, age, sex, ethnicity, study center, smoking, physical activity, consumption of alcoholic beverages, schooling and HOMA-IR in year 15. All co-variables except WC were measured at year 15. **WC at year 0 and HOMA-IR at year 20** men ≥85cm and women ≥78 cm: β = 0.1211 EP = 0.0199 men 80 - <85cm and women 70 - <78 cm: β = 0.0427 EP = 0.0182 men 75 - <80cm and women 66 - <70cm: β = 0.0130 EP = 0.0180 **Changes in WC (cm) from year 0 to year 15 and HOMA-IR at year 20** +1.113 - +3.895: β = 0.1628 EP = 0.0206 / +0.675 - +1.112: β = 0.1274 EP = 0.0182 +0.322 - +0.674: β = 0.0739 EP = 0.0171 / -2.770 a +0.321: Reference (p<0.0001)
Pourshahidi et al. (2016)	- Determine which body composition index is the best predictor for metabolic risk - Investigate the relation between inflammatory markers related to obesity and cardiometabolic risks	Pearson´s Correlation Coefficient (r)	*- Adjusted by age and sex* BMI and HOMA-IR: r = 0.32 p<0.0035 / %GC and HOMA-IR: r = 0.33 p<0.0035 WC and HOMA-IR: r = 0.34 p<0.0035 / RCE and HOMA: r = 0.36 p<0.0035 *- Adjusted only by age: men* **–** WHR and HOMA-IR: r = 0.18 (not significant)
Sasaki et al. (2016)	- Investigate the relation between WC and body fat with IR in men with tolerance to glucose and adequate BMI	Multiple linear regression (β)	*- Adjusted by age, BMI, WC, WH, body fat, SAP, DAP, aspartate aminotransferase, alanine aminotransferase, total cholesterol, triglycerides, HDL-cholesterol, e GFR, adiponectin, HbA1c and family history in diabetes* BMI and HOMA-IR: β = 0.112 p<0.294 / WC and HOMA-IR: β = 0.147 p<0.176 %GC and HOMA-IR: β = 0.211 p<0.016 *- Adjusted by age. BMI. WC. HC and %GC* BMI and HOMA-IR: β = 0.239 p<0.020 / WC and HOMA-IR: β = 0.096 p<0.375 %GC and HOMA-IR: β = 0.208 p<0.015
Vasques et al. (2009)	- Evaluate of behavior of obesity indicators with regard to levels of HOMA-IR and determine which indicators are the most efficient to identify IR	Spearman´s Coefficient of Correlations (r)	WC and HOMA-IR: r = 0.464 p<0.001 / WHR and HOMA-IR: r = 0.406 p<0.001 BMI and HOMA-IR: r = 0.377 p<0.001 / %BF and HOMA-IR: r = 0.394 p<0.001 WHR and HOMA-IR: r = 0.379 p<0.001
Zhang et al. (2018)	- Identify association between different indicators of body composition (MBI. %GC. WHR and WHtR) and metabolic parameters - Identify which index is the best predictor for metabolic parameters	Odds Ratio (OR) and confidence interval (IC 95%)	*- Adjusted by age. SAP. MBI. %GC. WHtR and WHR* **Men** – adequate BMI and HOMA-IR: OR = 3.44 IC 95% 2.90-4.91 p<0.001 High BMI and HOMA-IR: OR = 7.53 IC 95% 5.85–9.69 p<0.001 %GC and HOMA-IR: OR = 1.03 IC 95% 0.87-1.22 p=0.712 WHtR and HOMA-IR: OR = 1.48 IC 95% 1.28–1.74 p<0.001 WHR and HOMA-IR: OR = 1.46 IC 95% 1.24–1.71 p<0.001 **Women –** adequate BMI and HOMA-IR: OR = 2.60 IC 95% 2.19–3.09 p<0.001 High BMI and HOMA-IR: OR = 3.59 IC 95% 2.05–6.28 p<0.001 %BF and HOMA-IR: OR = 1.04 IC 95% 0.84–1.28 p=0.731 WHtR and HOMA-IR: OR = 1.56 IC 95% 1.30–1.88 p<0.001 WHR and HOMA-IR: OR = 1.25 IC 95% 1.01–1.53 p=0.037

Abbreviations: BMI: Body Mass Index; WC: waist circumference; %BF: body fat percentage; IR: insulin resistance; HOMA-IR: *Insulin Resistance Homeostasis Model Assessment*; WHR:waist hip ratio; WHtR: waist height ratio; TBF: total body fat; SAP: systolic arterial pressure; DAP: diastolic arterial pressure.

Table 3. Evaluation of articles' methodological quality according to study design: Cross-sectional, cohort and control case

Cross-sectional

Author / Year	Selection				Comparison	Outcome		Total score
	Representativity of sample	Sample size	Non-response rate	Determination of exposure	Control by important or additional factor	Assessment of outcome	Statistic test	
Hsieh et al. (2014)	0	0	0	2	1	2	1	6
Janssen (2009)	1	1	1	2	2	2	1	10
Kurniawan et al. (2018)	0	0	0	2	1	2	1	6
Lajeunesse-Tremp et al. (2019)	1	1	0	2	2	2	1	9
Lara et al. (2012)	1	1	1	2	2	2	1	10
Lim et al. (2019)	1	1	0	2	2	2	1	9
Pourshahidi et al. (2016)	0	0	0	2	1	2	1	6
Sasaki et al. (2016)	0	0	0	2	2	2	1	7
Vasques et al. (2019)	0	0	0	2	0	2	1	5
Zhang et al. (2018)	1	1	0	2	2	2	1	9

Cohort

Author / Year	Selection				Comparison	Outcome			Total score
	Representativity of exposure	Selection of non exposure	Determination of exposure	Absent outcome at start of the study	Control by important or additional factor	Assessment of outcome	Sufficient following time	Adequacy of follow-up	
Lacerte et al. (2014)	0	1	1	1	2	1	1	1	8
Park et al. (2010)	1	1	1	1	2	1	1	1	9