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Obesity as a risk factor for heart failure: overview of systematic reviews

Avaliação da obesidade como fator de risco para insuficiência cardíaca: overview de revisões sistemáticas

Evaluación de la obesidad como factor de riesgo de insuficiencia cardíaca: descripción general de revisiones sistemáticas

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Abstract
The overweight and population with obesity has an increased risk of mortality from HF. However, some studies point to the existence of an "obesity paradox" where there could be a protective effect on the relative risk of death by HF in these populations with high BMI. In this way, the present study aimed to investigate obesity as a risk factor for heart failure. For this, an overview of systematic reviews was performed by selecting articles from the following databases: "Pubmed", "Scopus" and "SciElo". A total of 615 articles were found from this initial search, leaving 59 articles for full-text reading, of which 22 articles were included for data extraction using the predefined inclusion criteria. From these 22 studies 73% were meta-analysis and 64% of the studies are of high methodological quality according to AMSTAR-2. Overweight and obesity have demonstrated a close relationship with the onset and increase of mortality by HF, studies have even been found that point to a gene interference in this relationship. In studies reporting on the obesity paradox, the results pointed to a momentary protection from mortality risk.
Keywords: Heart failure; Obesity; Obesity paradox.

Resumo
A população com sobrepeso e obesidade apresentam risco aumentado de mortalidade por IC. No entanto, alguns estudos apontam para a existência de um "paradoxo da obesidade" onde poderia haver um efeito protetor sobre o risco relativo de morte por IC nessas populações com IMC elevado. Dessa forma, o presente estudo teve como objetivo investigar a obesidade como fator de risco para insuficiência cardíaca. Para isso, foi realizada uma overview das revisões sistemáticas selecionando artigos das seguintes bases de dados: "Pubmed", "Scopus" e "SciElo". A partir dessa busca inicial, foram encontrados 615 artigos, restando 59 artigos para leitura na íntegra, dos quais 22 artigos

foram incluídos para extração de dados usando os critérios de inclusão predefinidos. Destes 22 estudos 73% eram metanálises e 64% dos estudos são de alta qualidade metodológica de acordo com AMSTAR-2. Sobrepeso e obesidade demonstraram uma estreita relação com o aparecimento e aumento da mortalidade por IC, até mesmo foram encontrados estudos que apontam para uma interferência gênica nessa relação. Em estudos que relatam o paradoxo da obesidade, os resultados apontam para uma proteção momentânea do risco de mortalidade.
Palavras-chave: Insuficiência cardíaca; Obesidade; Paradoxo da obesidade.

Resumen
La población con sobrepeso y obesidad tiene un mayor riesgo de mortalidad por IC. Sin embargo, algunos estudios apuntan a la existencia de una "paradoja de la obesidad" donde podría existir un efecto protector sobre el riesgo relativo de muerte por IC en estas poblaciones con IMC elevado. De esta forma, el presente estudio tuvo como objetivo investigar la obesidad como factor de riesgo de insuficiencia cardíaca. Para ello, se realizó un repaso de revisiones sistemáticas mediante la selección de artículos de las siguientes bases de datos: "Pubmed", "Scopus" y "SciElo". De esta búsqueda inicial se encontraron un total de 615 artículos, quedando 59 artículos para lectura a texto completo, de los cuales se incluyeron 22 artículos para la extracción de datos utilizando los criterios de inclusión predefinidos. De estos 22 estudios el 73% fueron metanálisis y el 64% de los estudios son de alta calidad metodológica según AMSTAR-2. El sobrepeso y la obesidad han demostrado una estrecha relación con sobre la aparición y aumento de la mortalidad por IC, incluso se han encontrado estudios que apuntan a una interferencia genética en esta relación, y en estudios que informan sobre la paradoja de la obesidad, los resultados apuntan a una protección momentánea del riesgo de mortalidad.
Palabras clave: Insuficiencia cardíaca; Obesidad; Paradoja de la obesidade.

1. Introduction

HF is an important public health problem and, despite significant improvements in its therapeutic management, it is still considered a serious syndrome associated with substantial rate of death and hospitalizations, affecting more than 23 million patients worldwide (Mozaffarian et al., 2016). After five years of diagnosis, survival rate is estimated at 35%, with prevalence increasing with age. There is an increase of 0.9% in individuals aged 55-64 years, reaching 17.4% in those aged ≥85 years. Besides the poor prognosis, HF is one of the most costly syndromes in the United States and Europe, where it accounts for about 1% to 2% of the overall healthcare budget (Bleumink et al., 2004).

The effectiveness of clinical practice in health care depends on higher quality evidence-based and practices to be implemented should be discussed between health care professionals and their patients for decision making. To accomplish this process, healthcare professionals need to keep up to date. However, this is a complex challenge, due to the globalized world and the speed in which information is disseminated (Silva et al., 2012).

An alternative way to reduce the complexity of tracking, dating, and facilitating clinical decision making is to use systematic reviews (SR). One of the main functions of these studies is to summarize clinical information from multiple studies to answer a question related to diagnosis, prevention, or treatment in areas where the results may or may not agree, by critically evaluating the evidence (Green et al., 2011).

Professional updating remains a challenge, even when using SR. A possible solution to the problem has been put forward by methodologists specializing in SR: a new type of study called the systematic reviews overview, or Overview, considered to be a user-friendly "front end" to health care decision making. By definition, Overview is a study developed to integrate and produce a synthesis of existing SR information in a specific clinic, considering all available interventions to treat or prevent this condition (Silva et al., 2012; Thomson et al., 2010). In this context, the present study aimed to evaluate obesity as a risk factor for heart failure through an Overview of systematic reviews.

2. Methodology

The following oveview was performed according to the PRISMA and Cochrane Collaboration recommendations (Higgins et al., 2019; Moher et al., 2009).

Eligibility Criteria

Systematic review studies were included, with or without meta-analyses, published until March 3, 2020, in English, Portuguese and Spanish, analyzing the association of obesity with HF. Studies on the effects of drugs on these pathologies and studies with non-Roman characters were excluded. The search was performed in Pubmed / Medline; Scielo and Scopus databases. This study was updated in the same databases on November 21, 2021. 197 articles were found, but none met the eligibility criteria.

The search strategy was using the following descriptors: (("systematic review" OR “revisão sistemática” OR "meta-analysis" OR metanalysis OR “meta-análise” OR meta-analysis) AND (“Cardiac insufficiency” OR “Heart Failure” OR “Heart Decompensation” OR “Insuficiência Cardíaca” OR “Descompensação Cardíaca” OR “Falência Cardíaca” OR “Falência Cardíaca” OR “Insuficiencia cardíaca”) AND (Obesity OR Obesidad OR Obesidade)). The Boolean operators "OR" and "AND" were used in the search strategies.

Study Screening and Selection

All titles and abstracts of the studies identified by the literature search were independently reviewed by two reviewers (RF and CB). If a reviewer considered the article potentially relevant, a full-text review was conducted. Disagreements about the inclusion of the full article were resolved by a consensus discussion between the two reviewers. In case of remaining discrepancies, a third reviewer (WR) made the final decision.

Data from each included study were extracted using a pre-designed template that included variables corresponding to the study characteristics (study design, outcome assessed, data search period and number of studies included).

Evaluation of Methodological Quality and Risk of Bias

AMSTAR-2 is a popular tool for the critical appraisal of systematic reviews of randomized controlled trials, providing a broad assessment of quality, including flaws that may have impacted on poor conduct of the review. This instrument has 16 questions, 7 of which are considered critical to the validity of the systematic review and the relevance of its conclusions. Based on this, general confidence ratings can be assigned to the review results ranging from critically low, when several points of critical failure are found independent of the non-critical weaknesses, low, when one critical failure is found, moderate, when more than one non-critical weakness is observed, or high, which is when none or only one non-critical weakness is identified.

3. Results

Study selection procedure

The article selection process is shown in figure 3. A literature search in the Pubmed, Scopus and SciElo databases yielded 615 articles published up to March 3, 2020. After excluding duplicates, 555 articles remained and were then displayed with based on the evaluation of abstracts and titles. After excluding articles that did not meet the eligibility criteria, 59 full-text articles were evaluated. Of these articles, 37 articles were considered irrelevant. Finally, the remaining 22 articles were included in this Overview.

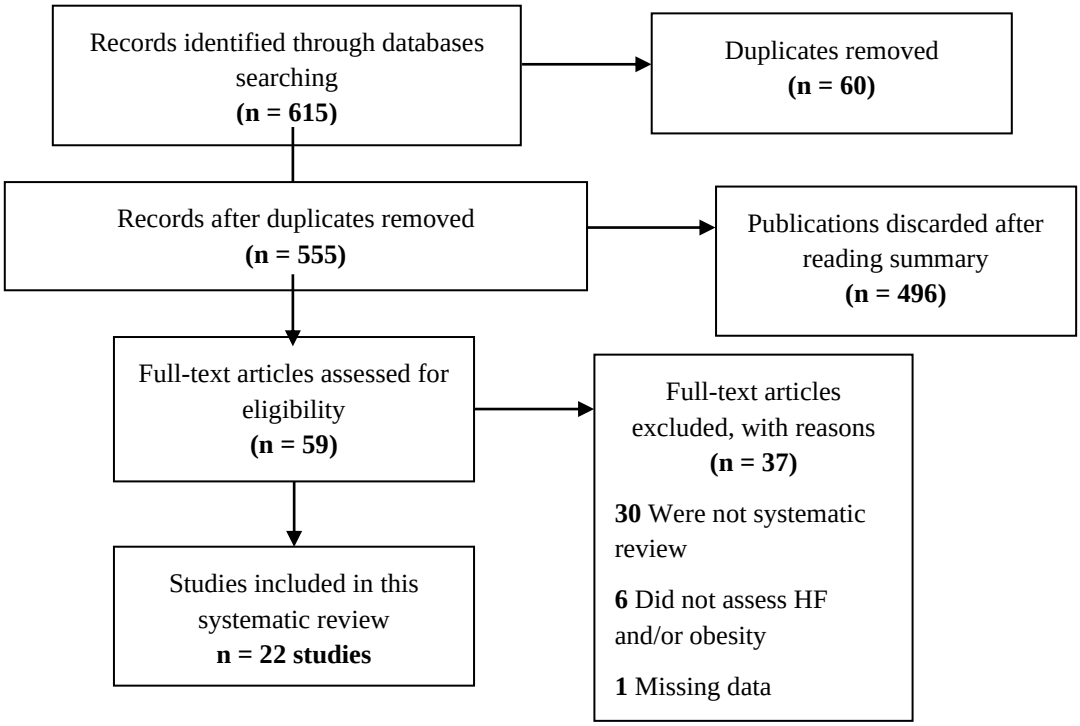
Characteristics of the included studies and synthesis of results

Figure 1 and table 1 shows that of the 22 articles that met the eligibility criteria, 73% contained meta-analyses, which shows a greater robustness of the analyzed data. The number of studies included in systematic reviews ranged from 6 to 85, with an average of 24 studies per systematic review. It also presents the outcomes found in 22 articles included and

demonstrates the global effects found in the relationship between obesity and HF. It also shows that 41% of 22 articles reported a positive, that is, a beneficial effect of the concomitant presence of obesity and HF, and 36% negative effect of obesity on HF, 18% reported positive and negative effects, and only 1 study reported no harm or benefit.

The systematic reviews ranged in quality from low to high quality according to the AMSTAR-2 quality assessment tool. However, approximately 64% of the studies are of high-quality, 27% are of moderate quality, and only 9% are considered to be of low quality.

Figure 1. Flowchart of the assessment process of Overview.



Source: Authors (2021).

Table 1. Included studies' characteristics.

Author/Year	Number of included studies	Study's methodological design	Obesity outcome in HF	Global effect
(Aune et al., 2016)	28	Systematic review and meta-analysis	For each 5-unit increase in BMI, a 41% increase in incidence and 26% increase in mortality was observed, and a 29% increase was observed for each 10 cm increase in WC and 0.1 unit increase in WHR.	↓
(Berger et al., 2018)	12	Systematic review and meta-analysis	He observed that bariatric surgery effectively improved clinical symptoms and quality of life, reducing hospitalizations for HF. It showed improvement in the NYHA class for the surgical patients, while drastic worsening for the control group.	↓
(Chang et al., 2015)	16	Systematic review and meta-analysis	It showed a higher risk of all-cause mortality for underweight patients (HR: 1.59, 95% CI: 1.32 - 1.91), while for the overweight (HR: 0.86, 95% CI: 0.78 - 0.96) and mild obesity (HR: 0.88, 95% CI: 0.78 - 1.00) groups this risk was reduced. On the other hand, morbid obesity showed no association with all-cause mortality.	↑
(Cuspidi et al., 2014)	22	Systematic review and meta-analysis	The probability of having LVH was much higher in patients with obesity than in non-obese patients (OR: 4.19, 95% CI: 2.67 - 6.53).	↓
(Fall et al., 2013)	36	Mendelian randomization	He reported a gene relationship between the FTO variant and BMI, with an estimated 0.05 and 0.74 BMI units per copy of allele A. He also observed a causal relationship between adiposity and increased incidence of HF, with a 17% increase per added BMI unit.	↓

(Hägg et al., 2015)	9	Mendelian randomization	Until then, the largest study presenting adiposity as a causal risk factor for HFCI, besides pointing out the relation of adiposity in increasing the incidence of HF. It also pointed out that the incidence of HF related to BMI is present only in women, and HFCI as an outcome only in men.	↓
(Krittanawong et al., 2018)	21	Systematic review and meta-analysis	It found that the incidence of HF was not associated with underweight, but was associated with being overweight with an increase of 33% compared to normal weight, being 23% for women, and for men it was not associated.	↓
(Lin et al., 2016)	8	Meta-analysis	It showed a racial difference in the obesity paradox, where mortality showed a higher incidence in Japanese when compared to Americans and Europeans.	↑
(Ma et al., 2018)	65	Systematic review and meta-analysis	It observed increased all-cause mortality for underweight patients, while it was reduced for overweight, obesity, and patients with severe obesity. This protective effect was also observed when the risk of major adverse cardiovascular events was analyzed.	↑
(Mahajan et al., 2020)	29	Systematic review and meta-analysis	It verified obesity associated with increased risk in the incidence of HF; however, it observed a paradoxical reduction in all-cause and CVD mortality. Another point analyzed was related to the structural and functional gain of individuals with obesity and HF who intentionally lost weight.	↑↓
(Mcdowell et al., 2018)	11	Systematic review	It suggests a benefit in survival for patients with obesity when compared to thin individuals. It also observed that overweight individuals had a lower risk of total and cardiovascular mortality when compared to normal weight patients. It also attributed the worst prognosis to underweight patients.	↑
(Milajerdi et al., 2019)	16	Systematic review and meta-analysis	A higher risk of mortality from HF was reported at the lowest end. Patients in the highest BMI categories had a 31% reduction in the risk of mortality from HF compared with the lowest BMI category.	↑

(Mirzababaei et al., 2019)	21	Systematic review and meta-analysis	It observed significant association between overweight (RR = 1.10, 95% CI: 0.60 - 2.00, P = 0.76) and obesity (RR = 0.96, 95% CI: 0.25 - 3.77, P = 0.95) metabolic phenotypes for the risk of developing HF, however they did not show increased risk for myocardial infarction.	↓
(Oga; Eseyin, 2016)	10	Systematic review	They reported better prognosis of HF with higher BMI, WC or TSF compared to normal weight categories.	↑
(Oreopoulos et al., 2008)	9	Meta-analysis	They observed an attenuated risk of all-cause and cardiovascular mortality for overweight (RR: 0.84, 95% CI: 0.79 - 0.90) and obesity (RR: 0.67, 95% CI: 0.62 - 0.73) individuals, when compared to normal BMI individuals. Moderately-severe obesity patients had decreased risk (RR: 0.62, 95% CI: 0.55 - 0.69), while underweight patients had increased risk (RR: 1.25, 95% CI: 1.19 - 1.31), when compared to normal BMI patients.	↑
(Padwal et al., 2014)	14	Meta-analysis	It found that the risk of total mortality was associated with increasing BMI for both HFpEF and HFpEF patients, with better levels for individuals with BMI between 30 and 34.9 kg/m2.	↑
(Qin; Liu; Wan, 2017)	14	Meta-analysis	He observed a linearly decreasing mortality risk of about 12% for each 5-unit increment in BMI, with a better prognosis for overweight patients. However, patients with severe obesity have higher mortality.	↑↓
(Reddy et al., 2019)	9	Systematic review and meta-analysis	It showed significant improvements in major hemodynamic derangements through weight reduction in patients without HF, projecting that weight loss interventions as a therapeutic alternative.	0
(Sharma et al., 2015)	6	Systematic review and meta-analysis	They found that the low BMI group had the highest risk of total mortality 1.27 (95% CI: 1.17 - 1.37), while the overweight 0.78 (95% CI: 0.68 to 0.89), obesity 0.79 (95% CI: 0.65 to 0.97), and with severe obesity 0.75 (95% CI: 0.57 to 0.98) groups had the lowest risks. For cardiovascular mortality, again underweight was the worst (RR: 1.20, 95% CI: 1.01 - 1.43), while overweight patients (RR: 0.79, 95% CI: 0.70 - 0.90) decreased the risk and did not differ between the other groups with overweight compared to normal weight BMI.	↑

(Sommer; Twig, 2018)	85	Systematic review	It suggests that childhood and adolescent obesity is associated with increased risk of cardiovascular morbidity, mainly from ischemic heart disease or stroke.	↓
(Wawrzeńczyk et al., 2019)	75	Systematic review	He presented obesity, especially severe, long-lasting, and abdominal obesity as an increased risk factor for HF by 15 to 70%. However, he reported that overweight and obesity are associated with reduced mortality by 24 to 59% and 15 to 65%, respectively, while malnutrition is an aggravating factor for mortality and hospitalization.	↑↓
(Zhang et al., 2019)	10	Systematic review and dose-response meta-analysis	It found that for every 5-unit increment in BMI, the risk of all-cause mortality was attenuated in patients with HFpEF (HR: 0.93, 95% CI: 0.89 - 0.97), and in patients with HFpEF (HR: 0.96, 95% CI: 0.92 - 0.99). The meta-analysis dose-response showed lower mortality for BMI of 32 kg/m2 in patients with HFpEF.	↑↓

Source: Authors (2021). Caption: (↑) Positive or beneficial effect; (↓) Negative or deleterious effect; (0) Null effect; (AVCI) Ischemic stroke; (CABG) Coronary artery revascularization; (CC) Waist circumference; (CQ); (CAD) Coronary artery disease; (CVD) Cardiovascular disease; (FTO) Fat mass and obesity-associated gene; (HR) Hazard Ratio; (LVH) Left ventricular hypertrophy; (CI) Confidence interval; (HF) Heart failure; (CHF) Chronic heart failure; (HFpEF) Heart failure with preserved ejection fraction; (HFpEF) Heart failure with reduced ejection fraction; (PCI) Percutaneous coronary intervention; (MI) Myocardial infarction; (BMI) Body mass index; (OR) Odds Ratio; (WHR) Waist-to-hip ratio; (RR) Relative Risk; (TSF) Triceps skinfold thickness.

4. Discussion

Overweight is related to hemodynamic and anatomic alterations of the cardiovascular system. Recent evidence suggests that the relationship of overweight with changes in metabolism, inflammatory profile, and hormonal changes (such as insulin resistance), may help to understand the relationship between obesity and HF (Comitê, 2018). In the systematic review and meta-analysis of prospective studies by Aune et al., (2016), it was found that for every 5 unit increment in BMI there was a significant increase of 1.41 (95% CI: 1.34 - 1.47; I2 = 83%) for incidence and increase of 1.26 (95% CI: 0.85 - 1.87; I2 = 95%) for mortality by CI. It was also observed that the risk was maintained with the increase of 10 cm in waist circumference, being 1.29 (95% CI: 1.21 - 1.37; I2 = 89%) and through the increase of 0.1 unit in waist-to-hip ratio the risk was also 1.29 (95% CI, 1.13 to 1.47; I2 = 82%). Demonstrating, then, that both overweight and obesity can increase the risk of HF incidence and mortality.

Corroborating with the findings of the previous study, the systematic review and meta-analysis conducted by Krittanawong et al., (2018), noted that being overweight increased the incidence of HF by 1.33 (95% CI 1.16 to 1.52; p <001, I2 = 83.6%) when compared to the normal group, representing an increase of about 33%. However, the increase in incidence risk differs among patients, with female patients being more impaired with a risk of 1.23 (95% CI 1.13 to 1.34; p <001, I2 = 0%), i.e., a 23% increased risk, while male patients showed no significant association (1.07, 95% CI 0.69 to 1.64; p = 0.772, I2 = 0%). Another important finding of this study was the quantification of incidence risk according to obesity classes, being 73% for class I obesity (1.73, 95% CI 1.52 to 1.98; p < 001, I2 = 83.2%), 85% for class II obesity (1.85, 95% CI 1.43 to 2.38; p < 001, I2 = 91. 1%) and 189% for class III obesity (2.89, 95% CI 1.94 to 4.31; p. < 001, I2 =95.9%) compared to the normal weight group.

Childhood obesity is an important factor for the development of risk factors for cardiovascular morbidity and mortality in adulthood. In general, excessive BMI in childhood is believed to be associated with an increased risk of coronary artery disease in adulthood. On the other hand, high BMI in adolescence was independently associated with angiography-confirmed coronary heart disease, and the risk of atherosclerosis in adulthood is affected by the cumulative exposure time of overweight or obesity (Sommer; Twig, 2018).

The systematic review by Sommer and Twig (2018), concluded that childhood obesity leads to considerable consequences in adulthood, being associated with adult hypertension and dyslipidemia, resulting in high cardiometabolic risk. Additionally, it appears to induce changes in myocardial geometry and function, demonstrating a worrying and early onset of potentially adverse changes in the myocardium. This way, childhood and adolescent obesity has been associated with increased risk of cardiovascular morbidity, mainly from ischemic heart disease or stroke. Therefore, as the prevalence of overweight and children and adolescents with obesity continues to grow, the risk of weight-related cardiovascular disease and death in adults may increase. From this, it is pointed out that a successful reduction in the incidence and prevalence of obesity in children and adolescents will lead to a reduction in cardiometabolic sequelae in adulthood.

In the largest Mendelian randomization study to date by Fall et al., (2013) corroborated the studies already mentioned in this study, where obesity is pointed out as a causal factor for the development of HF. The meta-analysis also revealed a relationship in the locus portion of the fat mass and obesity-associated gene (FTO), responsible for increased BMI, with increased incidence of HF and adiposity, and increased concentrations of the liver enzymes ALT and Gamma GT. The study further estimates that a 1-unit increase in BMI will increase the incidence of heart failure by 17%. In another Mendelian randomization study carried later by the same research group, the association between BMI and genetic score was confirmed. Through observational meta-analysis found that high BMI corresponded to increased risk of coronary artery disease 1.20 (95%

CI, 1.12 to 1.28, p = 1.88.10-7), CI 1.47 (95% CI, 1.35 to 1.60, p = 9.27.10-19) and ischemic stroke 1.15 (95% CI, 1.06 to 1.24, p = 0.00076). It was also pointed out evidence of the relationship of BMI in the incidence of HF, however only in women 3.33 (95% CI,1.60 to 6.93, p = 0.001) and of ischemic stroke only in men 2.01 (95% CI, 1.02 to 3.98, p = 0.04). However, the z-test showed little support for a significant difference between genders for both incidence of HF and ischemic stroke (Hägg et al., 2015).

Another systematic review and meta-analysis of prospective cohort studies was performed and observed a significant positive association between all metabolic phenotypes of overweight 1.10 (95% CI, 0.60 to 2.00, p = 0.76) and obesity (RR = 0.96, 95% CI: 0.25-3.77, p = 0.95) metabolically healthy and the risk of developing HF, it was further observed that for patients with obesity of weakened metabolic phenotype, a risk of infarction 1.82 (95% CI, 1.50 to 2.22, p <0.001), when compared to normal weight and metabolically healthy phenotype patients. Demonstrating, thereby, that a genetic relationship exists, where obesity exerts an influence on the incidence of HF, the article further highlights that the profile of metabolically healthy patients is not completely protected from cardiovascular events (Mirzababaei et al., 2019).

The phenomenon of the obesity paradox, characterized by the protective effect on survival of patients with overweight or obesity who concomitantly have HF and having lower BMI as a marker of poor prognosis 29, was evidenced in 13 of 22 systematic review studies, 8 of these with meta-analysis, the U-shaped graphical association with all-cause mortality according to all BMI categories, confirming the increased risk in patients with low BMI, and attenuated risk for patients with BMI category compatible with overweight or obesity, some studies also highlighted the importance of the protective effect of overweight in mortality from cardiovascular events (Chang Et Al., 2015; Chrysant; Chrysant, 2013; Ma Et Al., 2018; Mahajan Et Al., 2020; Milajerdi Et Al., 2019; Oga; Eseyin, 2016; Oreopoulos Et Al., 2008; Padwal Et Al., 2014; Qin; Liu; Wan, 2017; Sharma Et Al., 2015; Shirley; Davis; Carlson, 2008; Wawrzeńczyk Et Al., 2019; Zhang Et Al., 2019).

Shirley; Davis; Carlson, (2008) found a temporal relationship in the protective effect promoted by the paradox, where the higher level of BMI was not associated with improved survival in the first 12 months and in 5 years, showing beneficial effect only in the second year, when the calculation of ideal weight percentage was used instead of BMI the same relationships held to be true. However, it also demonstrated several reports of improved survival for patients with increased BMI, with adjusted hazard ratios of 0.88 (95% CI: 0.80 to 0.96) and 0.81 (95% CI: 0.72 to 0.92) for overweight and patients with obesity, respectively, and increased risk of death for patients with underweight BMI 1.21 (95% CI: 0.95-1.53) compared to normal BMI patients. He also observed the highest percentage of major clinical events such as cardiovascular death or urgent transplant were related to patients with low body surface area percentage (2.0 m2), BMI (27.7 kg/m2), body fat (22.5%), total fat (19.7 kg) and lean body weight (65.5 kg), whereas patients with higher body fat percentage was the strongest predictor of survival reported in the study.

In order to prove the existence of the obesity paradox and clarify the questions regarding the gaps left by BMI, Oga and Eseyin (2016) verified articles that measured, in addition to BMI, the thickness of the triceps skinfold (TSF), waist-to-hip ratio (WHR), and waist circumference (WC), and after the analyses pointed out that patients with the highest BMI, TSF and WC parameters had a better prognosis when compared to normal weight categories, added to this the study found that the paradox existed even for survival after 2 years.

In the systematic review and meta-analysis conducted by Lin et al., (2016) in order to investigate the association between BMI and HF mortality the East Asian region found that all-cause mortality, cardiovascular and noncardiovascular mortality increased with decreasing BMI categories compared to normal weight, underweight showed higher risk of all-cause mortality and cardiovascular mortality, and obesity showed lower risk of noncardiovascular mortality, compatible with the

obesity paradox also for eastern populations, however an ethnic difference of the paradox was observed, where at each increment of 5 kg/m2 the risk of noncardiovascular mortality was shown to increase in European and American patients than in Japanese.

The systematic review and meta-analysis conducted by Cuspidi et al., (2014) argues that obesity is a powerful risk factor for systolic and diastolic dysfunction, since their findings were consistent with a much higher incidence of HF in patients with obesity when compared to non-obese patients, therefore the authors argue that prevention and/or treatment may have an important favorable impact on HF.

Corroborating these data, in the systematic review conducted by McDowell et al., (2018), the authors argued that although the obesity paradox was present in the sample studied, with greater survival and lower mortality risk for the population with obesity, intentional weight loss in patients who coexisted with obesity and HF demonstrated improvement in exercise capacity, NYHA classification, and quality of life. Similarly, the meta-analysis conducted by Mahajan et al., (2020) also argues that intentional weight reduction, since it showed a reduction in left ventricular mass index, improvement in diastolic function, and reduction in left atrial size, resulting in improvement of structural and functional cardiac indexes in individuals with obesity affected with HF.

Reddy et al., (2019) conducted a systematic review and meta-analysis, noted that weight loss is associated with significant reductions in biventricular filling pressures, pulmonary arterial pressure, heart rate, cardiac output, systemic arterial pressure, and whole-body oxygen consumption. That is, the authors hypothesize that weight reduction interventions could then be effective in mitigating the hemodynamic derangements that contribute to morbidity and mortality in people with the obese phenotype and with HF. However, they warn that weight loss alone without aerobic exercise training may result in a loss of lean body mass, which can be detrimental in older patients with PFEI.

5. Conclusion

Given the results obtained, it can be inferred that overweight, as well as obesity, represents an important risk factor contributing to the increase in mortality. Mendelian randomization studies have also been found that point to this close relationship across gene loci associating increased BMI with increased HF. However, studies have reported the phenomenon known as the "obesity paradox", where obesity, despite aiding in the development of HF, for some patients would serve as a protective effect against mortality. It was also observed that the intentional weight reduction,when associated with aerobic physical activity, it is an important management to be performed with patients, as studies point to an improvement in the clinical picture. Based on the results obtained from this overview, further evidence-based health research can be carried out on the influence of other comorbidities, such as coronary artery disease, kidney disease and dyslipidemia, as well as their implications for the development and morbidity and mortality of HF.

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