



Body Mass Index (BMI) is a Risk Factor for Coronary Artery Disease (CAD)

Ghazi Daradkeh

Department of Dietetics - AL-Khor Hospital (AKH),
Hamad Medical Corporation, Qatar

Farrookh Haider

Department of Internal Medicine,
Section of Cardiology Al Khor Hospital, Hamad Medical Corporation,
Al Khor, QATAR, Department of Internal Medicine, College of Medicine,
Qatar University, Doha, QATAR

Asma Al Obahi

Department of Dietetics - AL-Khor Hospital (AKH),
Hamad Medical Corporation, Qatar

Asma Al Muhannadi

Department of Dietetics - AL-Khor Hospital (AKH),
Hamad Medical Corporation, Qatar

ABSTARCT

Background: Although excess adiposity appears to increase the risk of coronary artery disease (CAD) in the general population, its importance in patients with established coronary disease is less defined. **Aims:** We evaluate a population-based inception cohort of survivors retrospectively as a review to assess the association between body mass index (BMI) and the risk of coronary artery diseases. **Methods:** literature search in PubMed was done by using the following keywords combination: (cardiovascular diseases or heart disease or coronary artery disease) and body mass index BMI. Screened the topics and removed duplicates, papers that contained abstracts only or papers that had no access to the full article were excluded from the study. This review article has retrieved 51 papers through a PubMed search. The first screening was to remove duplicates (n = 13), followed by removing articles with only an abstract or without access to the entire research (n = 16). Finally, a complete research revision revealed non-eligible papers (n = 29). A final number of (n = 22) research was included. **Results:** all 22 articles were full-text free downloads from PubMed. **Conclusion:** Obesity is a significant component of metabolic syndrome. A greater risk of CAD is associated with an increased BMI and metabolically unhealthy people. Metabolically unhealthy obese people have a greater risk of coronary artery disease when compared to metabolically healthy obese people. Additionally, it has been proven that obese people can benefit from losing weight and physical activity.

Keywords: Obesity, Myocardial infarction, Mortality, Coronary artery disease.

BACKGROUND AND SIGNIFICANCE OF THE STUDY

Overweight and obesity is an increasing health problem worldwide. In the USA, approximately 55% of the general population are overweight or obese ^[1]. Obesity has reached epidemic proportions in the USA and Western Europe, with 65% of the population overweight and almost one-third obese, and the incidence and prevalence of obesity continue to increase ^[1,2]. Obesity is strongly associated with reduced longevity as well as with stroke, diabetes, thrombosis, and the development of coronary artery disease (CAD) ^[3-5]. In the USA, One-third of patients admitted to hospital with acute coronary syndrome are obese, and up to 50% are overweight ^[6]. Several large-scale epidemiological studies including the Framingham study documented that one of the well-known coronary heart disease risk factors is obesity, as well obese individuals' mortality rate approximately three times that of normal-weight individuals ^[7-9].

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide causing approximately one in six deaths in the United States every year ^[10]. Approximately every 25 seconds a coronary event occurs and one death every minute. The relationship between body mass index (BMI) (calculated as weight in kilograms divided by square height in meters) and cardiovascular mortality has been extensively studied. Elevated BMI is associated with an increased risk of death in several studies ^[11-17]. Cardiovascular morbidity and mortality have also been associated with elevated BMI in several studies in populations without cardiovascular disease ^[9-21]. The increased mortality rate has largely been attributed to the clustering of cardiovascular risk factors other than obesity, some of the measures that have shown consistent association to cardiovascular mortality are body mass index (BMI) and waist to hip circumference ratio (WHR) ^[22]. Body mass index as a marker of overall obesity is a strong risk factor for coronary heart disease in younger men. In older men, the fat distribution may be better at predicting the risk of coronary disease ^[23]. Recent studies have furthermore shown that waist measure alone is enough to screen overweight people for increased risk of coronary mortality ^[22,24]. Abdominal fat carries an independent risk of cardiovascular morbidity and mortality ^[25]. Individuals with abdominal obesity have a more atherogenic risk profile ^[26] as well as abdominal obesity is considered part of the metabolic syndrome ^[27]. Advising patients with coronary heart disease about the impact of different modifiable risk factors is important to increase survival, reduce the risk of further coronary and other atherosclerotic events, and improve quality of life. However, this relationship in populations with preexisting cardiovascular disease has been specifically examined by few studies.

Those studies that included subjects with previously diagnosed cardiovascular events have not separated this population when calculating their relative risks (RRs) for subsequent fatal events ^[22,25,26]. Studies have specifically examined BMI and the rate of repeat myocardial infarction (MI) with conflicting results ^[27-29]. On the contrary, Rea et al, 2001 ^[28], found that those with a BMI of greater than 30 had an elevated RR for recurrent MI, independent of diabetes, hypertension, and dyslipidemia. Kaplan et al, 2002 ^[29], found a modest increased RR for recurrent cardiovascular events in patients with a BMI of greater than 32 compared with a reference group composed of mildly overweight patients. The prevalence of obesity has climbed sharply over the last 20 years in the United States and other parts of the industrialized world ^[12,13,30]. This increase in obesity is a considerable public health concern given the association between excess adiposity and increased morbidity and mortality ^[31,32]. Overweight people appear to be at especially high risk for the development of coronary heart disease, due

in part to obesity-related conditions, such as diabetes mellitus, systemic hypertension, and dyslipidemia [31,33]. The American Heart Association has identified obesity as an independent cardiac risk factor [34], and the National Institutes of Health (NIH) has issued guidelines to identify overweight persons for potential treatment aimed primarily at preventing coronary heart disease [35]. Although excess adiposity appears to increase the risk of coronary heart disease in the general population, its importance in patients with established coronary disease is less clearly defined. The progression of atherosclerosis leading to coronary revascularization is less clear or role of obesity to contribute acute and thrombosis-based coronary events is less clear. Few studies have examined the relationship between obesity and cardiovascular events in patients with existing CAD independent of traditional coronary risk factors [28,29,36-39]. The independent association of body mass index (BMI) and adverse cardiovascular events have been suggested to be variable and a gender difference.

Several modifiable risk factors (smoking, HDL) and non-modifiable risk factors (gender, age) have well-established associations with CAD [40], whereas other potential individual risk factors (such as obesity) are less well-established. The estimated prevalence of obesity in the United States is about 32.9% [10], and an increased body mass index (BMI) has been associated with other major health implications including hypertension (HTN), diabetes mellitus (DM), metabolic syndrome (MetS), and dyslipidemia, all independent risk factors for CAD [40-47]. The aim of this review study is to evaluate the impact of overall obesity and body fat distribution in relation to gender on long-term prognosis after acute myocardial infarction in a representative population using data from the PubMed 2020-2023

LITERATURE REVIEW

NCDs are the cause of 70% of deaths worldwide [48]. Around the globe CVDs are the main cause of hospitalization, that has economically negative effect and increasing the burden on individuals and society. To prevent interventions, have a substantial beneficial effect on public health and the economy consequently identifying risk factors is highly important. Risk factors can be modifiable or non-modifiable. Modifiable risks include sedentary lifestyle, smoking, and unhealthy diet [49]. Hypertension and diabetes are also modifiable risk factors for CVDs [50]. Non-modifiable risk factors include gender, age, and genetics [51]. The thyroid hormone has a great impact on CVD as it affects the cardiac system and function [49]. Risk factors like obesity and hypertension are among the main factors to develop CVD. Various developed countries were able to reduce CVD by 50% when reducing the associated risk factors [51]. Notwithstanding the measures and success in reducing CVDs, CVDs remain the main cause of death in adults over 35. All treatment applied for CVDs is prescribed for life, which indicates the importance of setting preventive measures as it is the most effective intervention to reduce CAD-associated morbidities and death [48]. Intervention measures should include setting policies and procedures to draw attention to preventing CVD instead of treating CVD patients. Preventive measures are more effective and require fewer resources when applying effective health promotion measures to the population [51]. Cardiovascular diseases (CVDs) are the main cause of morbidity and mortality in individuals with diabetes, reduced awareness is the reason for the unavailability of early detection and applied preventive measures [52]. For example, a study in SA revealed that only 40% of diabetic patients are aware of their higher risk of developing a CVD. CAD has high prevalence and more than 50% of studied population had more than three risk factors for developing CAD. Half of them were obese and had hypertension, and 75% had dyslipidemia. Most of participants had one or more uncontrolled risk factors that demonstrated

low level of awareness about the disease, risk factors, and measures to prevent them ^[53]. MI and acute coronary syndrome can lead to CVD. MI is due to a sudden stop of blood supply to the heart and can be due to blockage in the blood vessels that supply the heart. Nevertheless, the incidence of MI is increasing with multiple risk factors including obesity, consumption of fatty food, physical inactivity, and smoking. Only 42% of the population are aware about MI risk factors, and interventions to reduce its risk. Increasing awareness of risk factors like diet and PA significantly reduces the onset, and recurrence of MI ^[54]. One of the risk factors for various chronic NCD, that leads to premature mortality is physical inactivity ^[4]. Physical inactivity is a worldwide issue and according to the WHO, people become less physically active with age ^[55]. PA boosts the immune system, safeguarding people from infectious diseases, and increases metabolism, which directly affects the risk of chronic diseases. Exercise is a structured, planned, and systematic form of PA ^[51]. PA is one vital determinant of healthy life. It maintains a proper weight and reduces the risk of many comorbidities ^[56].

Improper diet high in trans fats ^[57] that lacks fruits and vegetables, physical inactivity, and obesity are main risk factors to develop NCDs. A study in the US showed that having regular breakfast meal reduced obesity onset in 30% of adolescents ^[58]. Healthy eating habits have been shown to reduce CVDs, a main subset of NCD ^[58,59]. Conversely, low consumption of fruits and vegetables can increase hypertension, and hypercholesterolemia, which are risks to developing CVDs ^[58]. Vitamins, minerals, and fiber components of fruits, vegetables, and multi-grain products have scientifically proven roles to reduce oxidative stress, inflammation, high blood pressure, and enhance insulin sensitivity ^[60]. High fiber constituents, a low percentage of refined grains, and a low glycemic index are the main characteristics of a healthy diet. High-fiber food low in glycemic index can lower the risk of developing many chronic diseases and hence the mortality rate ^[59]. Heating liquid oil and catalyzing the oil with hydrogen to convert the liquid oil to solid fat, synthetically Trans fatty acids (TFA).

The heating step involved in the process will transform the carbon double bond to the transform. TFA has worse health consequences than saturated fatty acids and is linked to increasing CAD. In addition, TFA increases total plasma cholesterol level and the bad cholesterol low-density lipoprotein (LDL) ^[57]. Labeling is essential to inform the public about the content of their diet that could have a risk of CVD ^[57]. A proper nourishing diet greatly influences one's health and protection from illness ^[61]. A balanced diet offers vital nutrients, and the addition of dietary supplements delivers a vital source of micronutrients not provided in the diet that can protect from birth defects ^[31]. In Summary, this paper is a systematic review investigating the effect of BMI on the risk of developing CVD, risk factors of CVD collaboratively combine and increase the risk of developing a cardiac illness.

Research Questions

1. What is the effect of obesity and overweight on the risk of developing CAD

Objectives

1. Determine the risk of overweight and obesity (BMI) for developing a CVD.
2. Determine the impact of BMI on the acceleration and progression of CVD.

List of Abbreviations

CAD: Coronary Artery Disease

BMI: Body Mass Index
WHR: Waist Hip Ratio
RRS: Relative Risks
HTN: Hypertension
DM: Diabetes Millets
CVD: Cardiovascular Disease
HDL: High-Density Lipoprotein
LDL: low-Density Lipoprotein
MI: Myocardial Infarction
NCD: Non-Communicable Disease
NIH: National Institutes of Health
PA: Physical Activity
Mets: Metabolic syndrome
SA: Saudi Arabia
TFA: Trans Fatty Acids
WHO: World Health Organization
FDA: Food and Drug Administration
USA: United State of America

MATERIALS AND METHODS

This is a review of published papers, about the relationship between BMI and CVD. This review is tertiary research that does not use human material or human data and does not require IRB approval. Electronic database search for literature in PubMed was done in July 2023 by using the following keywords combination: (cardiovascular diseases or heart disease or coronary artery disease) and body mass index BMI. We followed the preferred reporting system for systematic analysis in this research. All steps from the PRISMA analysis are found below in Figure 1.

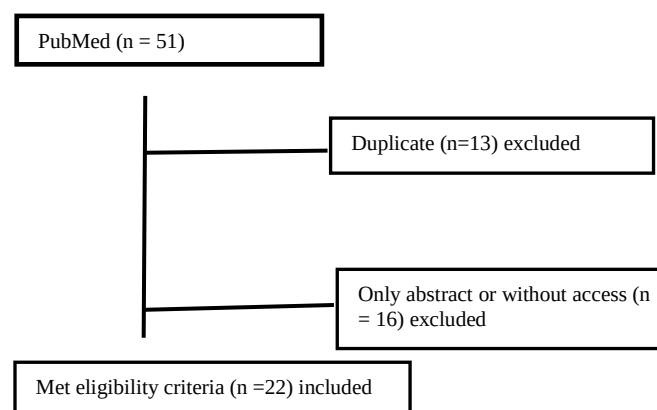


Figure 1: Prisma flow diagram for review articles

Literature Search Strategy

Electronic database search for literature in PubMed, was done in July 2022 by using the following keywords combination: (Cardiovascular diseases OR ischemic heart disease and BMI)

Study Selection

The researcher collected the literature through a PubMed search of the keywords. Screened the topics and removed duplicates. papers that contained abstracts only or papers that had no access to the full article were excluded from the study. The remaining papers with the complete article and open access to the full article were then collected and the abstract was screened. The last step included a full article screen to exclude unrelated papers.

Eligibility Criteria

Only research that satisfied the following eligibility criteria was included:

1. Papers published in the period from (2022 to 2023)
2. Papers that assess the relationship between BMI and the risk of developing CVD.

Research that did not suit these eligibility criteria was excluded. Abstract only, duplicates, and research with no access to the full articles were also excluded.

Characteristics of Included Studies

This review article has retrieved 51 papers through a PubMed search. The first screening was to remove duplicates (n = 13), followed by removing articles with only an abstract or without access to the entire research (n = 16). Finally, a complete research revision revealed non-eligible papers (n = 29), which were removed. A final number of (n = 22) research was included in this review article.

Quality of Included Studies

All studies included were of good quality.

Data Extraction

Data extracted by the sole researcher includes disease characteristics, prevalence, and risk factors. Next, extract data describing the population groups, demographic distribution, and anthropometric measurements. Finally extracting data on the effect of risk factors, awareness about risk factors, and interventions to prevent these risk factors in the population. Twenty-two papers have data on PA and its relation to CVDs in SA. Seven papers discussed the relationship between diet to increasing or decreasing the risk of developing CVDs or increasing one or more of the risk factors that lead to the development of CVDs. This systematic review has included mostly cross-sectional studies and five systematic reviews, only two clinical trials, four retrospective studies, two case-control study, one cohort study, one observational study, three articles summary, and four epidemiological studies.

RESULTS

From a preliminary screening of 51 papers, twenty-two articles were chosen for participation in the study.

All of them in this collection were full-text free downloads from PubMed. How obesity affects coronary artery syndrome and development of coronary artery disease (CAD) in obese people with and without metabolic abnormalities were described by these articles. The finalized articles are included in Table Table1 below, along with their intended audience.

Table 1: Applied Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Articles through a PubMed search	Articles not through a PubMed search
Articles from the last one year	Articles more than one year
Articles in the English language	Articles that were not in the English language
Articles includes disease characteristics, prevalence, and risk factors	Articles does not include disease characteristics, prevalence, and risk factors
Articles describing the population groups, and anthropometric measurements.	Articles does not describe the population groups, and anthropometric measurements
Articles with no duplicates	Articles with duplicates
Articles with full text and with access to the entire research	Articles with only an abstract or without access to the entire research

Table 2: study characteristics.

#	Title	link	conclusion
1.	Obesity and Cardiovascular Disease [62].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8493650/	The dramatic increase in the proportion of young patients with severe obesity invokes the need for more upstream interventions for the primary prevention and better treatment of obesity as a chronic disease.
2.	Body Mass Index and Association with Cardiovascular Outcomes in Patients with Stable Coronary Heart Disease [63].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9238503/	Patients with stable coronary heart disease showed a graded increase in cardiometabolic and inflammatory risk factors with increasing BMI category >25 kg/m ² . All-cause and cardiovascular mortality were lowest at BMI of 25 to 35 kg/m ² . Underweight with BMI of <20 kg/m ² and very high BMI of ≥35 kg/m ² were strong risk markers for poor prognosis.
3.	Relationship of body mass index to clinical outcomes after percutaneous coronary intervention [64].	https://onlinelibrary.wiley.com/doi/10.1111/eci.13789	The lean BMI category was associated with adverse outcomes in CAD patients who underwent PCI. The obesity paradox regarding the independent association of elevated BMI with reduced mortality after PCI remains evident in both male patients and female patients.
4.	Associations between Body Mass Index, Waist Circumference, and Myocardial Infarction in Older Adults Aged over 75 Years: A Population-Based Cohort Study [65].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9783624/	WC is a more appropriate indicator for predicting the risk of MI in the older population.
5.	Effect of body mass index and abdominal obesity on mortality after percutaneous	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8009155/	The mortality showed a U-shaped curve, and the cut-off value of lowest mortality was 29 in case of BMI and 78 cm of WC.

	coronary intervention: a nationwide, population-based study [66].		The abdominal obesity may be associated with poor prognosis in Korean patients who underwent PCI.
6.	Exploration of an alternative to body mass index to characterize the relationship between height and weight for prediction of metabolic phenotypes and cardiovascular outcomes [67].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8804920/	Considering an individual's height and weight opposed to BMI is a better method for quantifying individual disease risk.
7.	Identification of potentially common loci between childhood obesity and coronary artery disease using pleiotropic approaches [68].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9663585/	The common molecular mechanisms underlying the association of childhood obesity and CAD provide a theoretical direction for early disease prevention and potential therapeutic targets.
8.	Association of Lean Body Mass and Fat Mass With 1-Year Mortality Among Patients with Heart Failure [69].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8918916/	Higher LBM, not FM, was associated with lower 1-year mortality among HF patients.
9.	Effect of a phase 2 cardiac rehabilitation program on obese and non-obese patients with stable coronary artery disease [70].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7790927/	Cardiac rehabilitation programs lead to an improvement in cardiovascular disease risk factors with more reduction in BMI, BP, and LDL-C levels in obese patients compared to non-obese ones.
10.	Body Mass Index Is Independently Associated with the Presence of Ischemia in Myocardial Perfusion Imaging [71].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9332284/	BMI was an independent predictor of ischemia in our patient population.
11.	Effect of a nut-enriched low-calorie diet on body weight and selected markers of inflammation in overweight and obese stable coronary artery disease patients: a randomized controlled study [72].	https://www.nature.com/articles/s41430-020-00819-9	Energy-restricted diet containing mixed nuts has an improving effect on the plasma concentration of ICAM-1 and IL-6. Overall beneficial anti-inflammatory effect of the weight loss and nut consumption observed in these high-risk individuals may have a beneficial impact on the secondary prevention of CVD of these patients.
12.	Obesity in patients with established coronary artery disease over a 20-year period (1997-2017) [73].	https://www.mp.pl/paim/issue/article/15742/	Gradual increase in BMI and waist circumference in patients with established CAD over a period of 3 decades. The trend is independent of age, sex, and the educational level of patients.
13.	Body weight and physical fitness in women with ischemic heart disease: does	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9440958/	Physical fitness may have an important role in the obesity paradox in women

	physical fitness contribute to our understanding of the obesity paradox in women? [74].		with IHD by 38–40% lower risk of long-term all-cause mortality.
14.	Visceral Adiposity in Relation to Body Adiposity and Nutritional Status in Elderly Patients with Stable Coronary Artery Disease [75].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8308712/	This study has shown a high rate of misclassification of visceral ATD by BMI and BAI. Notably, ATD and malnutrition were common in patients with CAD. Likewise, each of the BMI-defined and BAI-defined weight categories included patients with all forms of ATD. In addition, most patients with normal nutritional status had some form of ATD, and as many as one-third of patients with moderate or severe malnutrition did not have any ATD.
15.	Fat-to-muscle Ratio: A New Indicator for Coronary Artery Disease in Healthy Adults [76].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8579285/	Our results showed that a high FMR was significantly associated with CAD. This association persisted even after adjusting for covariates, including BMI and waist circumference. This result may support FMR as a predictive marker of early coronary atherosclerosis, although further large-scale prospective studies on the relationship of FMR with coronary atherosclerosis are necessary to validate the former as an indicator of CAD.
16.	[Relationship of visceral obesity and coronary calcinosis in ischemic heart disease] [77].	2021 Dec 15;93(12):1428-1434. doi: 10.26442/00403660.2021.12.201277	The index of the ratio of VAT to subcutaneous adipose tissue (VAT/SAT), but not BMI, had a direct correlation with CC. Morphology of VAT may be a significant diagnostic sign of massive CC in patients with CAD, as a factor affecting treatment and prognosis.
17.	Clinical Significance of Body Fat Distribution in Coronary Artery Calcification Progression in Korean Population [78].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8024146/	Body fat distribution is important in CAC progression. Predominance of VAT over SAT at $\geq 30\%$ is the strongest predictor of CAC progression, even with normal BMI or WC in apparently healthy Korean population. Assessment of body fat distribution may provide further risk stratification over known clinical risk factors and traditional obesity surrogate markers.
18.	Is obesity a risk factor for coronary atherosclerosis? [79].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9588166/#:~:text=Metabolically%20healthy%20obe	Obesity is a significant component of metabolic syndrome; a greater risk of CAD is associated with metabolically unhealthy people when compared to metabolically healthy subjects. A

		se%20subjects%20have,compared%20to%20normal%2Dweight%20individuals.	common association that inflammation and further endothelial damage caused by the release of pro-inflammatory cytokines play a vital role in the development of coronary artery disease in obese people.
19.	Causal relationship of excess body weight on cardiovascular events through risk factors [80].	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8960828/	Excess body weight is a major health problem in Thailand and likely a cause of CVE occurrences. Participants who were overweight or obese trended to develop T2DM and HT leading to occurrence of CVEs during long-term follow-up. It is important that healthy overweight and obese people should reduce their BMIs to prevent T2DM and HT. Concurrent reduction in the magnitude of all conventional risk factors is the key for successfully reducing the occurrence of CVEs.
20.	Obesity paradox in patients with chronic total occlusion of coronary artery [81].	https://onlinelibrary.wiley.com/doi/10.1111/eci.13698	Higher BMI was associated with better survival in patients with CTO at 3 years follow up. The obesity paradox in patients with CTO warrants further larger study.
21.	Coronary circulatory function with increasing obesity: A complex U-turn [82].	https://onlinelibrary.wiley.com/doi/10.1111/eci.13755	The U – turn of hyperemic from obesity to morbid obesity is likely to reflect contrasting effects of abdominal versus subcutaneous adipose tissue on coronary circulatory function indicative of two different disease entities but needing further investigations.
22.	[Impact of different obesity patterns on coronary microvascular function in male patients with non-obstructive coronary artery disease] [83].	2022 Nov 4;50(11):1080-1086. doi: 10.3760/cma.j.cn112148-20220914-0071.	In male patients with non-obstructive coronary artery disease, abdominal obesity is associated with decreased coronary microvascular function. Male patients with simple abdominal obesity face the highest risk of CMD.

DISCUSSION

The incidence of cardiovascular diseases has been significantly affected by adipocytokines. The hormones like peptides and other molecules secreted from the adipose tissue likely act as pro-atherogenic markers [84]. Adiponectin, leptin, resistin, vascular endothelial growth factor (VEGF), and pro-inflammatory cytokines, such as TNF, IL-1, IL-6, and monocyte chemoattractant protein-1 (MCP-1) are the main components of Adipokines that are released from adipocytes. In obesity, the endocrine function of adipocytes is changed, with decreased adiponectin and increased levels of leptin, resistin, IL-6, and tumor necrosis factor (TNF) [85]. During the prolonged follow-up periods, it was observed that patients who had been obese at baseline stayed obese and infrequently turned lean. This was true for both young adults and

young-older adults who were obese [86]. The prognosis of CAD can sometimes be evaluated with the serum level of adipokines, which is used in screening, diagnosing, and predicting atherosclerosis [84]. Increased body mass leads to increased metabolic requirements. In "uncomplicated" obesity, enlarged left ventricular mass might be an early adaptation of cardiac function, compensating for the greater hemodynamic and metabolic demand in obesity [85]. Inflammatory processes linked to obesity occur in both vascular and non-vascular tissues, and endothelial cells are activated by the vasoactive chemicals secreted by adipocytes, such as resistin and leptin [84]. Adipokines such as resistin, leptin, and adiponectin have adverse effects on coronary arteriolar dilation in obesity which in turn is related to the development of coronary artery disease as reported and conducted by certain studies. These effects are supported by the loss of NO and increased reactive oxygen species (ROS) production in the coronary arteries of obese subjects [85]. Obesity relates to inflammation, evidenced by increased C-Reactive protein (CRP) levels. Studies have proved that inflammation associated with elevated levels of resistin and leptin has a significant role at the beginning of the mechanism of inflammation and leads to the advancement of atherosclerotic disease, as a known factor that CRP is an important marker determining the degree of inflammation, this elevated levels of resistin and leptin, in turn, induces CRP production in coronary endothelial cells that promotes vascular thrombosis which might be involved in the acute coronary syndrome pathophysiology process. In that same study, it has shown that leptin and resistin are linked with coronary artery disease regardless of CRP [84]. Obesity and overweight are the major determinants of metabolic syndrome and contribute to the development of cardiovascular diseases [87]. Obesity is also a significant risk factor for both DM and metabolic syndrome, and increased cases of obesity have been seen due to the prevalence of DM [88]. Combination of anthropometric, hemodynamic, and metabolic alterations is a metabolic syndrome constitutes. Several organizations in 2009, stated that clinical diagnosis of metabolic syndrome was released by a joint interim. This statement comprises a cluster of components such as central obesity, elevated blood pressure and triglycerides, low high-density cholesterol, and altered glucose metabolism [89]. Metabolic syndrome has a stronger association with developing atherosclerotic cardiovascular disease [90] both genetic and acquired factors are involved in the pathogenesis of metabolic syndrome, which in turn leads to the final pathway of inflammation contributing to coronary vascular disease [91]. When metabolic syndrome is identified early, patients should be actively encouraged to make lifestyle changes, and physicians can take steps to reduce the risk of type 2 diabetes mellitus. The management of patients already diagnosed with T2DM-associated metabolic syndrome is crucial because it helps to overcome the known cardiac complications associated with T2DM [89].

The Obesity Paradox

Although there is a greater risk of acquiring CVD in obese people, recently, it has been stated that once CVD gets established in overweight or obese individuals, they have lower mortality when compared with normal-weight people, which is termed as 'obesity paradox' as discussed above from various studies. Many cardiovascular diseases, such as CAD, atrial fibrillation, and heart failure have been explained this paradox. The highly fit normal-weight reference group Mortality rates were comparable to those of overweight and obese men, typically lower mortality rates was found among patients with high levels of fitness than those with lower levels and adding fitness to other conventional risk factors seems to reduce cardiovascular mortality [88]. Defining obesity based on BMI might be one of the reasons for this paradox, as it does not take into consideration lean mass [92]. Positive caloric balance causing adiposity leads

to pathologic changes in the adipose tissue causing metabolic diseases has been proposed before a CVD event. Alternatively, negative caloric balance as it may occur during a CV event where adipose tissue responds with enhanced function has been observed to improved clinical outcome. Increased muscle strength in obesity has also been associated with a better prognosis [88]. In this evaluation of the obesity paradox, BMI is a protective factor in both lower and higher CRP groups [93]. Endogenous regenerative capacity can be measured by using cell progenitor counts is another explanation of obesity paradox in obese people with CAD. The relation of obesity with adverse outcomes in CAD is indirectly proportional to those with a preserved endogenous regenerative capacity which is higher cell progenitor cell counts [94].

Obesity as a Risk Factor for Coronary Artery Disease (CAD)

The adverse effects of obesity are due to pathogenesis involving psychosocial, biological, environmental, and socioeconomic factors [95]. The association between obesity and cardiovascular diseases has been exclusively studied, but the question is still not understood and remains complex. Obesity with comorbidities such as hypertension, dyslipidemia, and glucose intolerance increase the risk of coronary vascular diseases [96]. When compared to BMI, the measurement of waist circumference was also found to be a marker for cardiometabolic risk [97]. Obesity can cause CAD, and researchers are looking into the genes that contribute to the development of obesity to see if there is a link to CAD development [98]. one of the molecular mechanisms responsible for early life obesity is an epigenetic modification of genes through methylation, histone modification, chromatin remodeling, and non-coding RNA alterations. This epigenetic modification increases the risk of getting adult obesity and which can be transmitted to future generations, thereby responsible for the obesity epidemic [99]. The majority of obesity cases are polygenic and come about as a result of a complicated interaction between the environment and the genotype, while certain types of obesity are brought on by solitary mutations [98]. Coronary artery calcium scores (CACS) can be measured using CT to measure the degree of calcification in the coronary arteries. This CACS score is one of the indicators of atherosclerosis [100], a positive association between high BMI and risk of CAD has been demonstrated, which showed that every 1kg/m² increase in BMI led to a 5%-7% increase in the incidence of CAD across all BMI categories. BMI may sometimes overestimate body fat for very muscular people, and for those who have lean muscle mass, BMI may underestimate body fat. General adiposity may be measured by either BMI of more than 30kg/m². while central adiposity and its association with CAD may be measured by using a waist-hip ratio of more than 0.90 for males and 0.85 for males [101].

The shorter survival rate for CHD is mainly linked with greater levels of abdominal obesity, either predicted through waist circumference or waist-to-hip ratio has been concluded by using the use of G-estimation for assessment of obesity and CHD. In G-estimation, three criteria were used to calculate the impact of obesity on CHD and compare it to accelerated failure time models. All indices of obesity were associated with an elevated risk of CHD in the first model that was adjusted for baseline variables while removing metabolic mediators of obesity. Based on waist circumference and waist-to-hip ratio, respectively, the hazard ratios derived by G-estimation for general obesity were 1.15 (95%CI: 0.83-1.47), 1.65 (95%CI: 1.35-1.92), and 1.38 (95%CI: 1.13-1.99) for abdominal obesity, indicating that abdominal obesity enhanced the risk of coronary heart disease [102]. The risk factors of CAD can be moderately reduced, evidenced by low body fat and body mass, low blood pressure, low triglycerides, and increased high-density cholesterol with regular physical activity and aerobic exercise, [103]. Improves insulin sensitivity

and endothelial function regardless of weight loss. The general idea of this weight loss management is to reduce body weight so as to prevent further weight gain and maintain a lower body weight [95]. Overweight or obese individuals with weight loss targets of 5% to 10% have been shown to significantly improve the health outcome of obesity-associated complications. Losing weight can aid in the prevention of T2D in people who are obese and have prediabetes, and it has a favorable long-term effect on cardiovascular mortality [104]. The efficacy of weight loss treatment can be determined by measuring BMI and WC [95]. The causes of the discrepancies between the outcomes of weight loss trials using medical and surgical methods are likely distinguish the degree of weight loss obtained with medical weight loss (5-10 kg) versus with surgery (10-40 kg) and the reduction in risk factors seen with bariatric surgery [95]. Fitness seems to improve prognosis, and therefore, physical activity and exercise training are recommended as it is accompanied by purposeful weight loss with CAD [88].

CONCLUSION

The relationship between obesity and the development of coronary artery disease has been explained by the pathophysiology involved as a sedentary lifestyle is becoming more prevalent nowadays. Adipokines from adipose tissue, such as resistin, leptin, adiponectin, and TNF, play a vital role in the inflammation process, which is the main reason for the development of atherosclerosis. Obesity is a significant component of metabolic syndrome. A greater risk of CAD is associated with metabolically unhealthy people when compared to metabolically healthy subjects. The articles that were shortlisted and included in this study have a common association that inflammation and further endothelial damage caused by the release of pro-inflammatory cytokines play a vital role in the development of coronary artery disease in obese people, and further, these articles show that metabolically unhealthy obese people have a greater risk of coronary artery disease when compared to metabolically healthy obese people. Additionally, it has been proven that obese people can benefit from losing weight. Even though so many studies have supported the notion put forth above. Future research, and more randomized controlled trials should be conducted because most studies currently available are only observational studies.

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