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Review Article

Can Changes in Body Weight Indicators Affect the Atherosclerotic Cardiovascular Disease Score and Developing Cardiovascular Events? A Review

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ABSTRACT

Cardiovascular diseases are the most preventable category of non-communicable diseases (NCDs). The Atherosclerotic Cardiovascular Disease (ASCVD) risk can accurately identify patients with a high risk of developing cardiovascular diseases (CVDs) or stroke over the next ten years. This indicator has several components; however, obesity is not one of them. At the same time, several studies have reported the relationship between obesity and CVDs. This study aimed to review the relationship between obesity and ASCVD risk or the incidence of CVDs. Keywords related to obesity and ASCVD were combined and searched in three databases of Web of Science (WOS), PubMed, and Scopus. A total of 6038 articles were screened based on the title and the abstract. Seven studies investigated the relationship between obesity and ASCVD risk, and 9 assessed the relationship between obesity and CVD events. The findings showed that various obesity indicators, such as body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHR) may have different associations with development of CVDs. Obesity was demonstrated to be able to increase the risk of CVDs through the influence of other components of ASCVD. In addition, the distribution of adiposity tissue, especially visceral fat in the abdominal area, can have a more accurate relationship with the occurrence of CVDs than obesity indicators.

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Introduction

Cardiovascular diseases (CVD), principally ischemic heart disease, are the leading cause of mortality and disability worldwide (1, 2). The burden of CVDs has been steadily increasing for the last three decades in nearly all countries except those with high incomes. It mainly seems to be the result of population growth and aging. This increasing trend in CVD burden can be shown in indices like the years lived with disability (YLDs) due to CVDs

which have increased from 17.7 million in 1990 to 34.4 million in 2019. Moreover, over the last three decades, the total number of CVD cases and the number of deaths due to CVDs have increased, rising from 271 million to 523 million and from 12.1 million to 18.6 million, respectively (3, 4).

Several modifiable and non-modifiable risk factors contribute to the development and progression of CVDs. Behavioral modifiable risk factors are unhealthy diet, physical inactivity, tobacco use, and excessive alcohol consumption. These behaviors can lead to hypertension, dyslipidemia, diabetes, and obesity, which are direct precursors to CVDs (5, 6). Non-modifiable risk factors include age, gender, and genetic predisposition. Men are generally at a higher risk than women, although the risk for women increases significantly post-menopause. Additionally, CVDs account for 30-50% of total days-adjusted life years (DALYs) attributed to ambient and household air pollution, as the most important environmental risk factor (3, 7).

The burden of CVDs is not uniformly distributed across the globe. Low- and middle-income countries are experiencing a rise in CVD prevalence and mortality, driven by population growth, ageing, urbanization, changing lifestyles, and inadequate healthcare infrastructure (8, 9). According to the global burden of disease study, over 75% of CVD deaths occur in LMICs, highlighting a critical area for public health intervention (10). High-income countries have seen a decline in CVD mortality rates due to advancements in healthcare, improved management of risk factors, and better access to medical treatments. The age-standardized rate of CVDs has started to rise in some high-income countries where it was previously on the decline. This pattern can be attributed to increasing rates of risk factors such as obesity, diabetes, and hypertension, as well as disparities in healthcare access and existing health inequalities in the United States and some other Western European regions (3, 11).

Addressing the global burden of CVDs requires comprehensive public health strategies focused on prevention, early detection, and management. Prevention cannot be properly achieved unless the threat is recognized and identified in a timely manner. This allows for the identification of people at increased risk, enabling targeted dietary, lifestyle, or drug interventions to be implemented effectively. Consequently, numerous prediction models have been formulated across various populations, such as the Framingham risk score, SCORE (System for Cardiac Operative Risk Evaluation), QRISK, and others (12, 13). The American College of Cardiology and American Heart Association (ACC/AHA) Atherosclerotic Cardiovascular Disease score (ASCVD risk score), also known as the Pooled Cohort Equations, was introduced in the 2013 ACC/AHA guideline on cardiovascular risk assessment (14). It is designed to offer a thorough and personalized evaluation of cardiovascular risk, aiding clinicians in identifying the most suitable interventions to mitigate the risk of cardiovascular events, particularly in the context of statin use for dyslipidemia management. Key risk factors considered in the ASCVD risk score include age, sex, race, total cholesterol, high-density lipoprotein (HDL) cholesterol, systolic blood pressure (SBP), use of antihypertensive medication, diabetes status, and smoking status. ASCVD risk score has a pivotal role in primary prevention, patient counseling, statin therapy decisions, monitoring, and follow-up of patients (14, 15).

Obesity is defined by a body mass index (BMI) of 30 kg/m² or higher which has reached epidemic proportions globally (3, 16). An elevated BMI increases cardiovascular risk factors, including high SBP, fasting blood sugar (FBS), low density lipoprotein (LDL), and inflammatory markers, while also adversely affecting cardiac structure and function. This results in a higher prevalence of conditions such as hypertension, coronary heart disease, heart failure, and atrial fibrillation among obese individuals (17). In 2021, high BMI was attributed to 1.95 million cardiovascular deaths and 3.7 million overall deaths, and it accounted for 1,560 all-cause DALYs per 100,000 individuals (4). In addition to BMI, other anthropometric measures like waist circumference (WC), hip circumference (HC), and waist-to-hip ratio (WHR) represent various subtypes of obesity, such as abdominal and trunk obesity, which are specific indicators of the adverse effects of excess adiposity (18). Numerous studies have investigated which indicator or subtypes of obesity are most closely linked to CVDs. Moreover, obesity is a multifactorial disease with a complex pathogenesis influenced by biological, psychosocial, socioeconomic, and environmental factors (19, 20). This complexity and the heterogeneity in the pathways and mechanisms through which obesity leads to adverse health outcomes highlight the intricate relationship between obesity and CVD (21).

Despite the widespread use of the ASCVD risk score, which does not include obesity in its risk stratification, the significant impact of obesity on development of ASCVD score is unclear. This review aimed to explore the relationship between obesity and the ASCVD risk score, including its components, and to understand how obesity can influence this risk assessment. Furthermore, we aimed to provide a comprehensive overview of

obesity and the mechanisms by which it affects risk stratification and assessment.

Search Strategy

The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. To find relevant studies, we combined keywords related to obesity and atherosclerosis to search the Web of Sciences (WOS), Scopus and PubMed online databases until August 15, 2024. The search in the title/abstract was done using the following key words: ("Body weight" OR "Body weight change*" OR "weight change*" OR weight OR "weight loss*" OR "Weight Reduction" OR BMI OR "body mass index" OR Anthropometry OR "Waist to hip ratio" OR "Waist circumference" OR "hip circumference") AND (Atherosclerotic cardiovascular disease OR ASCVD OR "ASCVD risk" OR "ASCVD risk score" OR "arteriosclerosis"). Documents were screened using Endnote software version X9.3 by two researchers (M.E and A.M.H). Study selection included original studies such as interventional or observational studies with participants older than 18 years. Other types of studies, reviews, books were excluded.

Search Results

A total of 6038 documents were found from databases, including 1098 documents from PubMed database, 4220 documents from Scopus database and 720 documents from WOS database. After removing of 767 duplicate documents, 5270 articles remained. The title and abstract of these articles were screened to find eligible articles. At the end, 15 articles remained, among them, 7 examined associations between ASCVD risk and body weight and 8 examined ASCVD events and body weight. This process was indicated in Figure 1. Table 1 demonstrates the characteristic of eligible studies for ASCVD risk and Table 2 illustrates the characteristic of eligible studies for ASCVD events.

Body Weight and ASCVD Risk

In a cohort study by Appiah *et al.* (22), a positive relationship was observed between BMI and 10-year cardiovascular risk score changes. A total of 1 kg/m^2 increase in BMI was associated with a 0.07% increase in risk. However, a small effect of BMI on the risk score trend was seen, which may be explained by other cardiovascular risk factors accounted for in the risk score. Hu *et al.* (23) investigated the association between obesity phenotypes and risk of CVDs in a Chinese cohort. Men and women with the obesity and dysmetabolic status phenotype had the highest ASCVD risk score across all phenotypes.

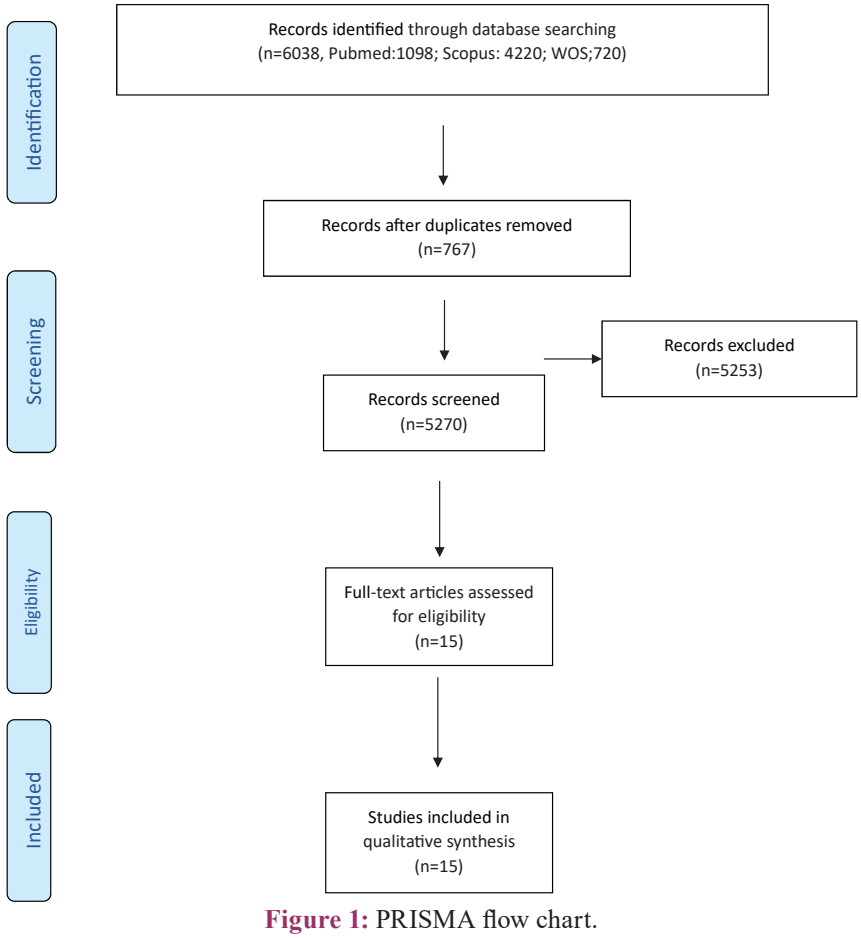

Figure 1: PRISMA flow chart.

Table 1: Characteristic of eligible studies for Atherosclerotic Cardiovascular Disease (ASCVD) risk.

First author (Reference)	Country	Design	Participants (N)	Health status	Results
Appiah *et al.* (22)	United States of America	Cohort study	1691	Coronary Artery Risk Development in Young Adults (CARDIA) Study participants	There was a positive association between BMI trends and a 10 year increase in ASCVD risk scores (0.07% per 1 kg/m2).
Ponce de Leon-Ballesteros *et al.* (26)	Mexico	Cohort study	113	Patients who underwent bariatric surgery	One year after bariatric surgery, 92.9% of the patients showed a significant reduction in the estimated 10-year ASCVD risk when compared to baseline.
Hollerbach *et al.* (27)	United States of America	Cross-sectional study	644	Firefighters	The association of body weight with increased ASCVD risk was significantly higher among older firefighters.
Hu *et al.* (23)	China	Cohort study	10826	Adults aged 40-79 years	Compared to normal participants, men and women with obese and dysmetabolic status had a significantly higher ASCVD score. Men and women with obesity and dysmetabolic status had a significantly higher odds of reporting ASCVD risk than those with obesity and normal metabolic status. Additionally, men and women with the overweight-dysmetabolic status phenotype had a significantly lower ASCVD risk than those with the overweight-normal metabolic phenotype.
Hassan *et al.* (30)	United States of America	Cohort study	1617	Adults aged 40 years and older	Increased body mass index and waist circumference were not associated with ASCVD risk. The results indicate that the waist-hip ratio (WHR) is a more accurate indicator of ASCVD risk associated with obesity than BMI.
Ke *et al.* (25)	China	Retrospective cohort study	684	Patients with type 2 diabetes mellitus	Over 5 years of follow-up, bariatric surgery was associated with a lower calculated of ASCVD risk in patients with T2D and low BMI than medical therapy.
Zheng *et al.* (29)	China	Retrospective observational study	6997	Patients with type 2 diabetes mellitus	In patients with T2DM, subjects with normal-weight visceral obesity had the highest 10-year ASCVD risk. Normal-weight visceral obesity subjects had a 2-fold or 3-fold higher risk for ASCVD than overweight or obese subjects without visceral obesity.

When BMI was classified as overweight, it played a more significant role in determining ASCVD risk. However, when BMI was classified as obese, metabolic status played a more important role in ASCVD risk determination.

He *et al.* (24) designed a serial cross-sectional survey study that estimated US trends in cardiovascular risk factors from 1999 through 2018. They found that non-Hispanic blacks tended to have higher levels of BMI, blood pressure, and blood glucose levels than non-Hispanic white individuals, and were also at a higher 10-year risk of developing ASCVD. These changes were eliminated after accounting for factors such as educational level, income, home ownership, employment status, health insurance, and access to health care.

Table 2: Characteristic of eligible studies for Atherosclerotic Cardiovascular Disease (ASCVD) events.

First author (Reference)	Country	Design	Participants (N)	Health status	Major Results
Fan *et al.* (32)	China	Longitudinal study	3950	Elderly Shanghai community residents (aged≥65 years)	Among the indices of abdominal obesity, WHtR and waist circumference predicted ASCVD, but body mass index was not associated. The odds ratio of weight to height ratio was greater than that of waist circumference. The optimal Weigh to height ratio cut-off value for predicting ASCVD risk was WHtR ≥0.53. High glucose, triglycerides, and hsCRP levels were predicted by all three indices, but only weight to height ratio≥0.53 was associated with physical activity.
Lin *et al.* (31)	Taiwan	Cohort study	166	Hemodialysis patients (60±12 years old)	40 patients had an incident ASCVD event during the median follow-up period of 4.3 years. Patients with central obesity did not display a significantly higher risk of ASCVD. In this study, central obesity determined by dual-energy X-ray absorptiometry (DXA)
Pagidipati *et al.* (33)	Several countries	Cohort study	14,534	Type 2 diabetes mellitus	11.4 % of participants with ASCVD and T2D were overweight or obese. Those in class I obesity (30≤BMI≤34.9) had a lower risk of cardiovascular disease than those who were underweight /normal weight (body mass index<25). Obesity was not associated with worse glycemic control.
Patel *et al.* (35)	United States of America	Randomized controlled trial study	5103	Healthy subjects	Decline in fat mass and waist circumference, but not lean mass, were each significantly associated with lower risk of heart failure but not myocardial infarction. Furthermore, decline in waist circumference was significantly associated with lower risk of heart failure with preserved ejection fraction but not heart failure with reduced ejection fraction.
Ardissino *et al.* (36)	United Kingdom	Cohort study	1186	Obese subjects without history of ASCVD	The rate of ASCVD was significantly lower for who underwent bariatric surgery. Rates of coronary artery disease, cerebrovascular disease, and peripheral arterial disease were not significantly different across cohort. However, the bariatric surgery group experienced a decreased rate of all-cause mortality.
Kumar *et al.* (34)	Pakistan	Cross-sectional study	1099	Patients candidate for primary percutaneous coronary intervention (PCI)	Obesity is paradoxically protective against hospital morbidity after surgery. The morbidity rate in obese patients was significantly higher than non-obese patients, but mortality rate in obese was significantly lower than non-obese patients.
Paulin *et al.* (38)	United Kingdom	Cohort study	319,866 UK Biobank participants	Healthy individuals	Unlike body mass index, waist-to-hip circumference had a dose-response relationship with ASCVD risk. Women and men had similar results.
Zhou *et al.* (37)	United Kingdom	Cohort study	404,332 UK Biobank participants	Healthy individuals	Obesity was associated with a higher risk of ASCVD and HF compared to non-obese individuals after adjusting for sociodemographic and lifestyle factors and medications for cholesterol, blood pressure and insulin.

In other words, the initial differences in cardiovascular risk factors between non-Hispanic Black and non-Hispanic White individuals were largely explained by differences in socioeconomic status.

In another study with object of comparing the long-term CVD risk in Chinese patients with type 2 diabetes and low BMI who underwent bariatric surgery versus those who received medical therapy, using the China Prediction for ASCVD Risk equations and the United Kingdom Prospective Diabetes Study risk engine, showed that compared to the medical therapy group, patients who underwent bariatric surgery showed a significant improvement in their 10-year and lifetime risk of ASCVD using the China Prediction for ASCVD Risk equation at a 5-year follow-up period. Furthermore, the bariatric surgery group had a significantly lower risk of coronary heart disease, fatal coronary heart disease, stroke, and fatal stroke when assessed using the United Kingdom Prospective Diabetes Study risk engine at the 5-year mark (25).

In another study that examined the effect of bariatric surgery on the 10-year estimated risk of ASCVD, twelve months after surgery, a significant reduction in the 10-year estimated risk of ASCVD compared with preoperative levels was observed in 92.9% of patients (26). Hollerbach *et al.* examined ASCVD risk scores by age and weight status in professional firefighters. This study found that the risk of CVDs among firefighters increased with age. In addition, among older firefighters, the association between weight status and increased ASCVD risk was stronger (27). Based on pooled cohort equations, overweight or obese but active individuals had a similar or potentially lower risk of ASCVD event compared to normal-weight but inactive individuals in the next decade (28).

In a China multicenter study, Zheng *et al.* demonstrated that in individuals with type 2 diabetes, those who were normal-weight, but with visceral obesity, had a significantly higher 10-year risk of developing ASCVD compared to those who were overweight or obese but did not have visceral obesity. This risk was more than double or triple for persons with normal weight but visceral obesity (29). Another study examined the relationship between anthropometric measures and 10-year CVD risk in Eastern Caribbean adults. There was no significant relationship between BMI (over 30 kg/m^2) and WC with CVD risk. In contrast, a WHR above 0.9 and 0.85 for men and women, respectively and a WHR ratio above 0.5 were strongly associated with CVD risk. Furthermore, this study identified increased WHR as a significant predictor of CVD risk (30).

Body Weight and CVD Events

In a cohort study, Lin *et al.* investigated the association between central obesity and ASCVD among maintenance hemodialysis patients. Central obesity was defined as a fat mass ratio (android to gynoid) higher than the average value. The results illustrated that patients with central obesity had higher BMI, total fat mass, triglyceride and high-sensitivity C-reactive protein (CRP), and lower HDL cholesterol levels compared to those without central obesity. However, the ASCVD risk of patients with central obesity was not significantly higher than those without central obesity (31). Fan *et al.* examined the relationship between body fat and abdominal fat measurements with ASCVD risk in Shanghai community subjects (65 years or older). The results revealed that a WHR above 0.53 was significantly associated with the prevalence of ASCVD and its risk factors. This relationship was more significant than WC and BMI in this elderly Chinese population (32).

In a cohort study, Pagidipati *et al.* evaluated the relationship between BMI and ASCVD in patients with type 2 diabetes and a history of ASCVD. In this study, a paradoxical relationship between obesity and health outcomes was observed such that the risk of cardiovascular outcomes was lower in overweight or obese individuals, especially with BMI of 30-34.9 kg/m^2. In addition, obesity was not associated with poor glycemic control (33). In another cohort study, Kumar *et al.* examined the phenomenon called the "obesity paradox" in patients with severe ST-elevation heart attacks (STE-ACS) and found obesity to be associated with a lower risk of postoperative complications (in-hospital complications) after primary percutaneous coronary intervention (PCI) in patients with ST-ACS. However, obesity was an independent predictor of in-hospital mortality that, although it may not worsen immediate complications, was still associated with a higher risk of death following PCI (34).

Another study assessed the association of baseline and longitudinal changes in body composition (fat mass, lean mass, and waist circumference) measures with the risk of heart failure and myocardial infarction in type 2 diabetes. The researchers showed that of 5103 participants, 257 participants experienced heart failure over 12.4 years. This study showed that, over a period of one year, fat mass and waist circumference reduction was associated with a reduction in the risk of heart failure. In contrast, the reduction of lean mass was not significantly related to the risk of heart failure. Long-term four-year changes in body composition also showed similar patterns of association. Interestingly, changes in body composition were not significantly associated with myocardial infarction risk (35).

In a nested propensity-matched cohort study, Ardissino *et al.* displayed that patients who underwent bariatric surgery had a significantly lower risk of developing new ASCVD compared to other groups. Although there were no significant differences in rates of individual cardiovascular conditions, such as coronary artery disease, cerebrovascular disease, or peripheral arterial disease, the bariatric surgery group did experience a lower overall rate of mortality (36). In a prospective cohort study involving 404,332 White participants from the UK Biobank, Zhou *et al.* measured the extent of increased risk of ASCVD and heart failure associated with obesity. In comparison to individuals without obesity, those who were obese exhibited a higher risk of ASCVD and heart failure. The primary mediators for ASCVD included renal function, blood pressure, triglycerides, and hyperglycemia. Together, these factors accounted for a higher proportion of the excess risk associated with ASCVD to heart failure. However, without weight management, the heart failure burden does not decrease (37).

Another UK Biobank study examined the impacts of BMI, lifestyle, and cardiometabolic risk factors on the incidence of ASCVD. A cardiovascular health score (CVHS) based on four lifestyle and six cardiometabolic parameters was developed. Participants with a high CVHS (8-10) and BMI ≥35.0 kg/m^2 had no significantly higher ASCVD risk in comparison to those with a normal BMI (18.5 to 24.9 kg/m^2). Also, normal BMI and lower CVHS (0-2) had a higher effect on ASCVD risk than a higher CVHS (8-10). When the WHR was utilized instead of BMI, a dose-response relationship between the WHR and the risk of ASCVD was observed in healthier participants (38).

Discussion

Since cardiovascular diseases are the most important cause of death and disability in the world, investigating the role of various risk factors such as dyslipidemia, inflammation, hypertension, diabetes, smoking, obesity, and lifestyle factors is important (39-41). Nutritional ingredients were demonstrated to play a pivotal role in cell function and subsequently in most of diseases including CVD too (42-45). According to the Global Burden of Disease (GBD) study, the burden of elevated BMI has risen, with high BMI being responsible for 4 million deaths in 2015 (46). A significant majority of these deaths (over two-thirds) were attributed to CVD, even after taking into account smoking and other health issues (46, 47). In other words, obesity is directly related to the development of CVD risk factors such as dyslipidemia, type 2 diabetes, and hypertension (47, 48). Furthermore, it increases the risk of CVDs and mortality regardless of other underlying risk factors (49).

Although in epidemiological studies, BMI is frequently used to categorize individuals as overweight or obese, however, BMI has limitations, as it can be insensitive to individual variations in body composition and does not accurately reflect body fat percentage. This is because BMI does not account for the significant differences in body fat distribution that can occur due to age, gender, and race (49-51). Researchers suggest that measuring WC and WHR as central obesity determinants may be more effective in identifying individuals with CVDs and its risk factors (52-54). Examining the combination of BMI and measures of abdominal obesity is a more accurate predictor of CVDs and its related risk factors than considering BMI alone (55, 56).

It was shown that WC is a more reliable indicator of body fat distribution than BMI, and is closely linked to visceral adipose tissue (VAT) (57, 58). Importantly, visceral obesity is an emerging risk factor for CVDs and is significantly related to coronary atherosclerosis which is strongly associated with the worldwide risk of cardiovascular mortality (57, 59). Furthermore, because an increase in the ratio of fat to lean body mass, even in individuals with normal weight, can contribute to metabolic obesity, the location of excess fat, particularly in VAT and ectopic reservoirs such as muscle and liver, is associated with a higher cardiometabolic risk (60). Therefore, to reduce the burden of atherosclerosis and maintain human health, it is crucial to pay attention to visceral obesity as a risk factor in ASCVD and CVDs. In a recent multicenter study in China, patients with type 2 diabetes who had normal-weight, visceral obesity demonstrated the highest 10-year risk of CVDs. This group had a significantly higher risk than those who were overweight or obese based on their BMI, but did not have any visceral obesity. The odds ratio for this group was more than twice or three times higher than the other groups, and this difference was statistically significant (29).

Based on the mentioned studies that quantify fat deposits, including ectopic fat, also showed that excessive visceral adiposity is an independent predictor of poor cardiovascular outcomes (49). Despite the established link between visceral obesity and cardiovascular risk, the relationship between visceral obesity and 10-year ASCVD risk remained a topic of ongoing debate. In a cohort study by Koulii *et al.*, visceral obesity, independently of lifestyle factors, was associated with a 10-year risk of CVD. This relationship was more in men than women (61). Another cohort study showed no

significant association between visceral obesity and 10-year CVD risk (62). Also, the results of the National Health and Nutrition Examination Survey (NHANES) cross-sectional study revealed a significant correlation between visceral obesity and the 10-year ASCVD risk, and this relationship was more pronounced in males, which was similar to the findings of Koulii *et al.* (61, 63). This gender difference in the occurrence of risk can be due to the difference in the accumulation of fat tissue so that men were more prone to the accumulation of visceral fat tissue than women (64).

As discussed before, another factor that can be explored is the association between obesity and CVD risk factors, including dyslipidemia, hypertension, insulin resistance, and systemic inflammation. Several possible mechanisms proposed the association between visceral obesity and the 10-year ASCVD risk (65). Visceral fat is associated with ASCVD-related risk factors such as insulin resistance, dyslipidemia, inflammation, and hypertension (63, 66). Factors released from visceral adipose tissue, such as mesenchymal stem cells, fatty acids and cytokines including leptin and adiponectin, can influence inflammation and insulin resistance (67-69). In addition, macrophages in visceral adipose tissue can produce proinflammatory cytokines, including tumor necrosis factor-alpha (TNF-a) and interleukin-6 (IL-6), which can disrupt insulin sensitivity after accumulation and lead to insulin resistance (70-72).

A complex interplay of glucotoxicity, lipotoxicity, and inflammation caused by insulin resistance creates an environment that selectively disrupts PI3K-dependent insulin signaling pathways and ultimately contributes to the pathogenesis of atherosclerosis and the development of ASCVD (73). Increased amounts of leptin and insulin in people with visceral obesity can lead to the promotion of the sympathetic nervous system, and activation of the renin-angiotensin-aldosterone system, which increases blood pressure (74, 75). Visceral obesity also leads to the kidneys reabsorbing sodium through the sympathetic nervous system, aldosterone and insulin, and changes in the renal vasculature (angiotensin II). This increased sodium reabsorption contributes to elevated blood pressure (63, 76).

Another mechanism that can be mentioned is dyslipidemia, which increases the risk of atherosclerotic ASCVD through several factors, including abnormal fat metabolism, insulin resistance, inflammation, and vitamin D deficiency (77, 78). In addition, various mechanisms that obesity causes, such as increased production of VLDL, impaired breakdown of triglycerides, damage to the absorption of fatty acids, and the formation of dense and small LDL can cause abnormal blood lipids that can increase the risk of CVDs (79). Also, the enlargement of visceral fat cells leads to an increase in the production of pro-inflammatory cytokines, a decrease in the production of anti-inflammatory adiponectin, and cell death, which can lead to the invasion of macrophages, an increase in inflammation, and a decrease in production of adiponectin. Harmful products produced by the interaction between macrophages and visceral fat cells play a role in developing ASCVD (80-82).

WHR as a new measurement index has been considered in identifying individuals at risk of cardiometabolic disorders (83). Unlike BMI, WHR provides a more accurate assessment of obesity because it accounts for variations in height, sex, and race. It was shown that a global WHR threshold of less than 0.5 was effective in prevention of CVDs and type 2 diabetes. This index may enhance public health efforts by providing a more detailed understanding of obesity risk (84, 85). A study examined the relationship between various anthropometric measurements and three cardiovascular risk conditions (metabolic syndrome, dyslipidemia, and type 2 diabetes) in a primary care population. This study showed that compared to other measurements such as WC, WHR, it was the best predictor of mortality and cardiovascular risk factors. Also, it suggests that the superior performance of WHR may be due to its ability to account for differences in body height (86). Some researchers have also suggested that WHR may be a valuable indicator of cardiovascular risk due to its association with an increased probability of cardiovascular events (87-89). Furthermore, several studies suggested that a higher HC can demonstrate a protective effect against cardiovascular events, such as CVDs, CHD, and myocardial infarction (90-92).

Due to the high number of studies on younger and middle-aged populations, there is very little data and research on older people, especially people older than 80 years. A study in Spanish elderly showed that abdominal obesity was a better predictor of diabetes, hypertension, and metabolic syndrome than BMI (93). Notably, the results of other studies indicated that overweight and abdominal obesity did not increase the risk of death in some elderly populations, including those aged 90 years and older (94-96). These findings showed the inconsistency between overweight/obesity and the risk of cardiovascular events and mortality in the elderly population. Because BMI does not differentiate between fat and muscle or account for different fat distributions, it can lead to inaccurate identification of adipose

tissue and cardiovascular risk in older adults (32). Despite this, some studies of older people have seen a contradictory relationship between higher BMI and better results, which have different results depending on the general health status. It was found that the background health status of elderly people can be different in the relationship between BMI and their mortality. In subjects with poor health, higher BMI, it was associated with better outcomes and worse outcomes were seen in individuals with good health (97). A study in Taipei revealed the lowest mortality rate in people who were mildly overweight or obese (BMI 25-35 kg/m^2); while being underweight or severely obese resulted in higher mortality rates (98).

Conclusion

Obesity was shown to be a complex condition characterized by different metabolic and CVD profiles among individuals with similar BMI. Based on findings, various measures of obesity, including BMI, WC, and WHR may have specific associations with development of CVDs. Obesity can heighten the risk of CVDs by impacting other factors related to ASCVD risk. Moreover, the distribution of adipose tissue, particularly visceral fat in the abdominal region, may have a more precise correlation with the onset of CVDs compared to conventional obesity indicators. With the increasing prevalence of obesity, it is necessary to investigate the cause and find effective treatments for people with obesity and CVDs. In addition, the growing number of severely obese youth calls for more preventive efforts to prevent obesity, especially during the early stages of development.

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Authors' Contribution

Conceptualization: MM and HBD; Search and article screening: ME, AMH and MMN; writing the draft: AMH and FPZ; Review and editing: HBD and MM. All authors reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no competing interests.

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