



THE RELATIONSHIP BETWEEN BODY MASS INDEX AND RISK OF ACUTE CORONARY SYNDROME IN PATIENTS WITH TYPE 2 DIABETES

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Abstract

Introduction: Body mass index, the risk of cardiovascular events, and all-cause mortality are related in diabetics is a debatable matter. Diabetes patients are more likely to experience cardiovascular complications. It is commonly known that obesity raises the risk of cardiovascular disease (CVD) in the general population. Little is known about the relationship between BMI and major adverse cardiovascular events, despite the fact that these are important health outcomes for individuals with diabetes. The connection between a person's BMI and mortality in those with diabetes has been the subject of continuous discussion. "Obesity paradox" in diabetics is often documented, suggesting that the mortality rates of individuals with diabetes who have elevated BMIs are lower than those of individuals whose BMIs are thought to represent normal weight.

Aim of the Study: The purpose of the present review is to understand the relationship between body mass index (BMI) and cardiovascular complications like acute coronary syndrome in patients with Type -2 Diabetes.

Methodology: The review is a comprehensive research of PUBMED from 1997 to 2023.

Conclusion: Despite the debate, it is suggested that patients who do not receive insulin therapy and have type 2 diabetes mellitus also maintain the obesity paradox. The lowest and highest mortality rates were found in class I obese patients and the normal weight population, respectively, when examining the relationship between BMI and all-cause mortality in patients with type 2 diabetes mellitus and ACS. The benefit of obesity for survival was eliminated for patients on insulin therapy.

Keywords: Body mass index, Type-2 diabetes, Acute coronary syndrome, obesity, etc.

Introduction

Overweight and diabetes mellitus are recognised risk factors for mortality from all causes as well as those specific to the cardiovascular system. Weight control is advised as a treatment recommendation for type 2 diabetes mellitus because it is closely linked to the onset and course of the disease. Moreover, any increase in weight brought on by antidiabetic medication is regarded as an undesirable side effect. However, there is still uncertainty regarding the relationship between BMI and mortality in patients with type 2 diabetes mellitus and obesity is not always linked to worse outcomes. The

"obesity paradox" states that in certain patients, such as those with heart failure, stable coronary artery disease, acute coronary syndrome (ACS), and so on, obesity is linked to a lower mortality than normal weight.^[1-3]

The secondary prevention guidelines for coronary artery diseases recommend weight maintenance or reduction because ACS is one of the leading causes of death in patients with diabetes mellitus. Nevertheless, there isn't any concrete data to support this advice, particularly for ACS patients. Few researchers have suggested the relationship between BMI and death in individuals with type 2 diabetes mellitus after ACS manifestation. Due to their variable effects on body weight, cardiovascular events, and death rates, antidiabetic drugs may introduce bias into studies examining body weight and mortality.^[4-6]

A higher body mass index (BMI) causes adipose tissue to behave differently, favoring the development of ischemic cardiopathy by causing insulin resistance and predisposition to type-2 diabetes, arterial hypertension, dyslipidemia, and proinflammatory and prothrombotic states.^[7]

Risk Factors and Prevalence

It is anticipated that the global diabetes patient population will continue to rise, especially in Asia. Despite making up over 30% of the global population, the majority of large-scale research on diabetes and cardiovascular illnesses has been carried out in populations with a predominance of white people. The incidence, severity, complications, and responsiveness to treatment of diabetes might vary throughout populations. Dietary variations, insulin sensitivity, obesity prevalence, illness severity, and cytochrome P450 enzyme polymorphisms may impact the efficacy of treatment among East and Southeast Asian populations. As a result, a patient's genealogy could be important for both diagnosis and care.^[8]

Insulin resistance and obesity influence the onset and course of type 2 diabetes. Insulin resistance⁵, which is linked to atherosclerosis, is correlated with body mass index (BMI).⁶ A higher risk of cardiovascular disease and all causes of death is linked to obesity.^{7,8} However, among Asians, insulin secretion disruption rather than insulin resistance is linked to the onset of diabetes.⁹ The risk of diabetes-related coronary artery disease varies according to ethnicity.¹⁰ Asians with diabetes in the US are less likely than Whites to have coronary artery disease.^[9]

Acute Coronary Syndrome and Body Mass Index:

People who are overweight or obese had a lower incidence of ACS and all-cause mortality in people with diabetes, according to a review of nationwide follow-up data on adult Koreans. Individuals who were underweight compared to those who were classified as normal-weight had a greater risk of cardiovascular death and myocardial infarction based on the specific subtype. On the other hand, those who were overweight or obese had a decreased risk of stroke and cardiovascular death.^[10]

Obesity has been linked to CVD harmful effects, according to prior research. In individuals with type 2 diabetes mellitus (T2DM), underweight BMI (<18.5 kg/m²) and obese BMI (≥25.0 kg/m²) were linked to an increased risk of CVD in China.⁷ In England, individuals with T2DM who were classed as overweight or obese (BMI ≥25.0 kg/m²) were more likely than those who were normal-weight (BMI 18.5–24.9 kg/m²) to experience cardiac events, such as acute coronary syndrome and heart failure. People who were overweight or obese (BMI ≥25.0 kg/m²) in the Swedish National Diabetes Register research had a greater risk of cardiovascular disease (CVD) than people who were classed as normal-weight.^[11-13]

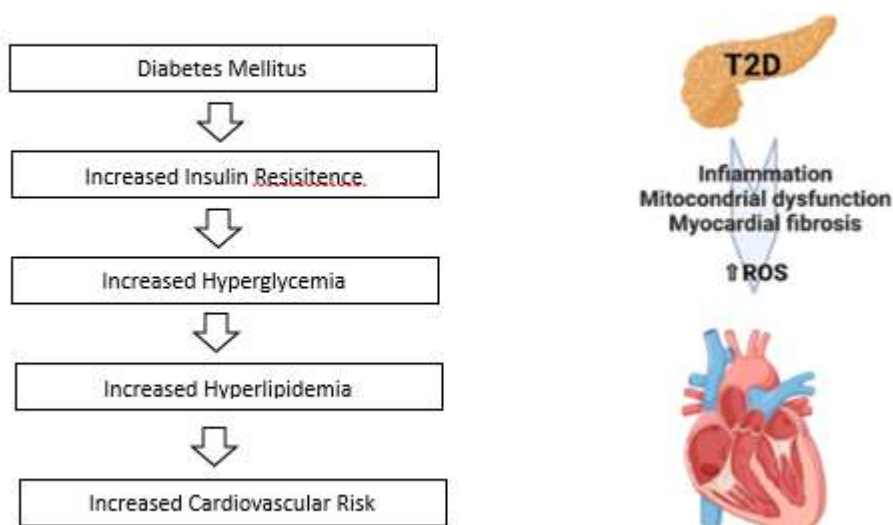
Numerous studies point to an obesity paradox in which those who are overweight or obese have a better prognosis for CVD than those who are underweight, despite the fact that being overweight or obese has a negative impact on CVDs. It's unknown what mechanisms underlie this conundrum.

Nonetheless, a lower risk of CVD may be explained by some traits shared by obese individuals, such as their younger age, lower smoking prevalence, and usage of heart medicines to treat high blood pressure. Additionally, our research revealed that those who were obese were less likely to smoke, younger, had higher blood pressure, and were more likely to take anti-platelet, statin, or anti-hypertensive medications. Therefore, even though we adjusted for these variables, drug usage, and lifestyle changes made by obese individuals may have an impact on their risk of ACS.^[14]

The reported increased risk for ACS linked to underweight BMI may be explained by a number of factors:- ^[10]

1. There are certain advantages to having more fat provided it is distributed appropriately. There may be a cardioprotective benefit to subcutaneous peripheral fat, according to several studies. It might eliminate dietary triglycerides by acting as a "metabolic sink."
2. Second, having more muscle mass protects against CVD by preventing insulin resistance. However, as BMI and muscle mass are positively connected, especially in the elderly, underweight individuals may also have low muscle mass. In one study, the groups with lower BMIs and those with higher BMIs engaged in less physical activity.^[10]
3. The advantages seen in the fat group can be explained by genetic theories. Individuals with diabetes who are underweight or have a normal BMI may be genetically predisposed to a higher risk of cardiovascular events.

Fig. 1 Pharmacological options for Type 2 Diabetes and cardiovascular risk.^[15]



Role of Antidiabetic Therapy

Individuals diagnosed with type 2 diabetes mellitus are at a higher risk of cardiovascular morbidity and mortality. Research has demonstrated variations in cardiovascular outcomes and mortality when examining the impact of various antidiabetic medicines. Moreover, these anti-diabetic medications differ in their effects on changes in body weight: SGLT2 (sodium-glucose cotransporter 2) inhibitors and glucagon-like peptide-1 agonists decrease body weight, metformin, and dipeptidyl peptidase-4 inhibitors do not alter it, and insulin, sulfonylurea, meglitinides, and thiazolidinediones increase it.^[16] A major complication that needs more research is the shift in body weight brought on by anti-diabetic medications, which have been suggested as a potential mechanism by which they exert survival effects. The inverse link between BMI and mortality persisted only in individuals taking oral antidiabetic medicines, not in those receiving insulin therapy, according to our subgroup analyses of

antidiabetic therapies. Our data may help to explain some of the contradictory findings found in the German population-based registry study (47 percent of patients received insulin therapy, and no survival benefit was observed in the high-BMI group) and the previous DIAMOND registry study (12% of patients received insulin therapy and the obesity paradox was present).^[17]

A variety of reasons in insulin therapy may alter the link between BMI and mortality. Patients on insulin therapy typically have long-term diabetes mellitus, diminished pancreatic reserve, increased insulin resistance, and a higher number of comorbidities associated with diabetes mellitus. Therefore, the benefits of obesity may be mitigated by an advanced stage of disease. Furthermore, it has been demonstrated that insulin therapy lowers the amounts of adiponectin in obese people, which may have cardioprotective effects. It was suggested by Nolan et al. that exogenous insulin may be able to overcome the physiologic protective effect of insulin resistance in the myocardium in patients who are overweight or obese, particularly in those who gain weight after receiving insulin therapy or are unable to manage their caloric intake.^[18]

Arrhythmias and a decline in myocardial contractility can result from such metabolic stress. A further potential mechanism could be weight gain associated with insulin, particularly in obese patients. This could exacerbate hemodynamic and metabolic abnormalities, as well as glucose regulation, necessitating higher insulin dosages and the use of additional preventive medication. As a result, high-dose insulin may make severe hypoglycemia crises more common. All of the previously stated variables may have an impact on patients' mid- and short-term mortality during the post-ACS phase.^[19]

Conclusion

A substantial fraction of individuals with Acute coronary syndrome have diabetes mellitus, which is linked to unfavorable short- and long-term outcomes. Research on the prevalence of cardiovascular diseases such as acute coronary syndrome and risk factors like obesity in individuals with type 2 diabetes is scarce. However, it can be suggested that for individuals with T2DM, ACS is a significant cause of comorbidity and death, with the highest frequency. In terms of BMI, the underweight population is more prone to develop ACS than the obese population.

References

1. American Diabetes Association (2017). Standards of medical care in diabetes—2017. *Diabetes care*, 40(1), 1.
2. Tobias D K, Pan A, Jackson C L, O'Reilly E J, Ding E L, Willett W C, & Hu F B (2014). Body-mass index and mortality among adults with incident type 2 diabetes. *New England Journal of Medicine*, 370(3), 233-244.
3. Gruberg L, Weissman N J, Waksman R, Fuchs S, Deible R, Pinnow E E, & Lindsay J (2002). The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox?. *Journal of the American College of Cardiology*, 39(4), 578-584.
4. Smith Jr S C, Benjamin E J, Bonow R O, Braun L T, Creager M A, Franklin B A, & Taubert K A (2011). AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation*, 124(22), 2458-2473.
5. Colombo M G, Meisinger C, Amann U, Heier M, von Scheidt W, Kuch B, & Kirchberger I (2015). Association of obesity and long-term mortality in patients with acute myocardial infarction with and without diabetes mellitus: results from the MONICA/KORA myocardial infarction registry. *Cardiovascular diabetology*, 14, 1-10.
6. Paneni F, & Lüscher T F (2017). Cardiovascular protection in the treatment of type 2 diabetes: a review of clinical trial results across drug classes. *The American journal of cardiology*, 120(1), S17-S27.

7. Bays H E (2011). Adiposopathy: is “sick fat” a cardiovascular disease?. *Journal of the American College of Cardiology*, 57(25), 2461-2473.
8. Tishkoff S A, & Kidd K K (2004). Implications of biogeography of human populations for race and medicine. *Nature genetics*, 36(Suppl 11), S21-S27.
9. Lanting L C, Joung I M, Mackenbach J P, Lamberts S W, & Bootsma A H (2005). Ethnic differences in mortality, end-stage complications, and quality of care among diabetic patients: a review. *Diabetes care*, 28(9), 2280-2288.
10. Lee D H, Ha K H, Kim H C, & Kim D J (2018). Association of body mass index with risk of major adverse cardiovascular events and mortality in people with diabetes. *Journal of obesity & metabolic syndrome*, 27(1), 61.
11. Wan E Y F, Fung C S C, Fong D Y T, Chan A K C, & Lam C L K (2016). A curvilinear association of body mass index with cardiovascular diseases in Chinese patients with type 2 diabetes mellitus—A population-based retrospective cohort study. *Journal of Diabetes and its Complications*, 30(7), 1261-1268.
12. Costanzo P, Cleland J G, Pellicori P, Clark A L, Hepburn D, Kilpatrick E S, & Atkin S L (2015). The obesity paradox in type 2 diabetes mellitus: relationship of body mass index to prognosis: a cohort study. *Annals of internal medicine*, 162(9), 610-618.
13. Eeg-Olofsson K, Cederholm J, Nilsson P M, Zethelius B, Nunez L, Gudbjörnsdóttir S, & Eliasson B (2009). Risk of cardiovascular disease and mortality in overweight and obese patients with type 2 diabetes: an observational study in 13,087 patients. *Diabetologia*, 52, 65-73.
14. Lavie C J, McAuley P A, Church T S, Milani R V, & Blair S N (2014). Obesity and cardiovascular diseases: implications regarding fitness, fatness, and severity in the obesity paradox. *Journal of the American college of cardiology*, 63(14), 1345-1354.
15. Andreadi A, Muscoli S, Tajmir R, Meloni M, Muscoli C, Ilari S, & Lauro D (2023). Recent pharmacological options in type 2 diabetes and synergic mechanism in cardiovascular disease. *International Journal of Molecular Sciences*, 24(2), 1646.
16. American Diabetes Association. (2018). 8. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes—2018. *Diabetes care*, 41(Supplement_1), S73-S85.
17. Colombo M G, Meisinger C, Amann U, Heier M, von Scheidt W, Kuch B, & Kirchberger I (2015). Association of obesity and long-term mortality in patients with acute myocardial infarction with and without diabetes mellitus: results from the MONICA/KORA myocardial infarction registry. *Cardiovascular diabetology*, 14, 1-10.
18. Nolan C J, Ruderman N B, Kahn S E, Pedersen O, & Prentki M (2015). Insulin resistance as a physiological defense against metabolic stress: implications for the management of subsets of type 2 diabetes. *Diabetes*, 64(3), 673-686.
19. Yki-Järvinen H, Ryysy L, Kauppila M, Kujansuu E, Lahti J, Marjanen T, & Taskinen M R (1997). Effect of obesity on the response to insulin therapy in noninsulin-dependent diabetes mellitus. *The Journal of Clinical Endocrinology & Metabolism*, 82(12), 4037-4043.