

The obesity paradox revisited – influence on the results of percutaneous coronary interventions



Mohammad Reza Movahed^{1,2*}, MD, PhD; Allistair Nathan¹, MS3; Mehrtash Hashemzadeh¹, MS

**Corresponding author: University of Arizona Sarver Heart Center, 1501 N Campbell Avenue, Tucson, AZ, 85724, USA. E-mail: rmova@aol.com*

ABSTRACT

BACKGROUND: The “obesity paradox” has been seen in patients with cardiovascular disease. However, the role of the obesity paradox in patients undergoing percutaneous coronary intervention (PCI) is controversial.

AIMS: Our study aims to investigate the effect of weight categories on mortality in patients undergoing PCI.

METHODS: The National Inpatient Sample database for the years 2016-2020 was analysed using International Classification of Diseases, Tenth Revision codes in adult patients >18 years of age. Patients undergoing PCI were identified and stratified using weight categories. Univariate and multivariate analyses were performed to assess mortality.

RESULTS: We identified 10,069,454 patients who had undergone PCI. Compared to patients in the normal-weight category, cachectic patients had the highest mortality at 9.78% (odds ratio [OR] 3.88, 95% confidence interval [CI]: 3.65-4.12; $p<0.001$). Mortality was lowest in overweight patients at 1.28% (OR 0.46, 95% CI: 0.39-0.55; $p<0.001$), followed by obese patients at 1.61% (OR 0.58, 95% CI: 0.56-0.61; $p<0.001$). In the morbidly obese category, this protective effect was much less, with mortality being measured at 2.05% (OR 0.75, 95% CI: 0.42-0.78; $p<0.001$; vs 2.72% in the normal-weight category). After multivariate analysis, mortality remained high in cachectic patients (OR 3.65, 95% CI: 3.42-3.90; $p<0.001$) and remained low in overweight (OR 0.51, 95% CI: 0.43-0.61; $p<0.001$) and obese (OR 0.68, 95% CI: 0.66-0.71; $p<0.001$) patients, but the protective value of weight almost disappeared in the morbidly obese category (OR 0.96, 95% CI: 0.96-1.00; $p=0.04$).

CONCLUSIONS: The obesity paradox held only partially, with the lowest mortality in the overweight category, followed by patients with obesity, then an almost complete loss of protection in those with morbid obesity, and the highest mortality in cachectic patients.

KEYWORDS: angioplasty; obesity; obesity paradox; outcome; percutaneous coronary intervention; stenting

Coronary artery disease is a leading cause of death, with hundreds of thousands of percutaneous coronary interventions (PCI) being performed each year in the United States¹. PCI is associated with many risks, including perforation, tamponade, haemodynamic collapse, failure to recanalise the vessel, and death². Thus, it is imperative to understand patient risk factors for such complications, especially mortality. One potential risk factor that requires further investigation is the patient body habitus.

According to the Centers for Disease Control and Prevention (CDC), over 70% of adults in the United States are overweight, with over 40% being considered obese³. It is well established that obesity is a strong risk factor for the development of cardiovascular diseases, such as hypertension, as well as metabolic syndrome^{4,5}. Thus, it is commonly presumed that, since obesity is such a strong risk factor for the development of cardiovascular disease, it must also be a risk factor for poor outcomes once a patient has developed such disease. However, some studies have shown that in many cases obese patients may have better outcomes in the context of cardiovascular disease than their non-obese counterparts – termed the “obesity paradox”⁶. In particular, multiple studies have reported the obesity paradox in the context of PCI^{7–11}. Despite such evidence, the obesity paradox remains controversial, with criticisms of the paradox including failing to distinguish between metabolically healthy and unhealthy obesity as well as attributing the paradox as a whole to statistical bias in observational studies^{12,13}.

Considering the number of overweight and obese Americans, the frequency with which PCI is performed, and the persistent controversy surrounding the obesity paradox, it is clear that further investigation and evidence are needed. This study, the largest retrospective cohort investigation of the relationship between obesity and mortality following PCI, seeks to further elucidate the obesity paradox and the risk or protection conferred by increased body habitus to patients undergoing PCI.

Methods

DATA SOURCE

The study population was drawn from the National Inpatient Sample (NIS), a publicly available dataset provided by the Agency for Healthcare Research and Quality. The NIS dataset is one of the largest publicly available, nationally representative inpatient datasets, as it approximates a sample of about 20% of US community hospitals, and about 98% of the total US population, using discharge weights¹⁴. The NIS dataset is publicly available and includes no identifiable information, precluding the study from requiring institutional review board approval.

Impact on daily practice

Based on our report, obesity has a positive effect on mortality and therefore should not be an obstacle for performing percutaneous coronary intervention (PCI) in obese or morbidly obese patients. However, extra caution must be taken when PCI is planned in patients with cachexia. These patients should be informed about this higher risk.

STUDY POPULATION

Patient data were drawn from the NIS, for the years 2016 to 2020, and International Classification of Diseases, Tenth Revision (ICD-10) codes were used to search the database and further stratify the study populations. As outlined in the previous study by Nathan et al, the following ICD-10 procedure codes were used to identify patients who had undergone PCI: 02703(4-7)Z, 02703(D-G)Z, 02703TZ, 02713(4-7)Z, 02713(D-G)Z, 02713TZ, 02723(4-7)Z, 02723(D-G)Z, 02723TZ, 02733(4-7)Z, 02733(D-G)Z, 02733TZ, 02H(0-3)3DZ, 02H(0-3)3YZ, 027(0-3)3ZZ, 02C(0-3)3Z7, 02C(0-3)3ZZ, 02F(0-3)3ZZ¹⁵. ICD-10 diagnosis codes were then used to classify patients as cachectic (R64), overweight (E66.3), obese (E66.9, E66.8, E66.0), or morbidly obese (E66.01, E66.2).

STUDY OUTCOME AND STATISTICAL ANALYSIS

The primary study outcome was patient mortality following PCI during hospital admission. In addition to analysing mortality, patient characteristics and demographics were also analysed and incorporated into multivariate analysis of mortality. These patient characteristics include smoking history (F17.20, Z72.0, Z87.891), diabetes (E08-E13), hypertension (I10, I11.0, I11.9, I120, I129, I13.0, I13.10, I13.11, I13.2, I15.0, I15.1, I15.2, I15.9, I16.0, I16.1, I16.9), chronic obstructive pulmonary disease (COPD; J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9, J47.0, J47.1, J47.9, J684), chronic kidney disease (CKD; I13.11, I13.2, N289, Q613, N181, N182, N183, N1830, N1831, N1832, N184, N185, N186, N189, R880, N19), ST-segment elevation myocardial infarction (STEMI; I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.9, I21.A1, I21.A9, I22.0, I22.1, I22.5, I22.9), non-STEMI (I21.4, I22.2), and previous myocardial infarction (I25.2). The patient demographics considered included sex and race.

Patient demographic information and mortality are reported as means with 95% confidence intervals. Binary clinical outcomes were ascertained using logistic regression, and multivariate analysis was performed to adjust for confounders. All analysis was performed using population

Abbreviations

BMI body mass index

CKD chronic kidney disease

COPD chronic obstructive pulmonary disease

ICD-10 International Classification of Diseases, Tenth Revision

NIS National Inpatient Sample

PCI percutaneous coronary intervention

STEMI ST-segment elevation myocardial infarction

discharge weights. The reported p-values are two-sided, with $p < 0.05$ considered statistically significant. Data were analysed using Stata 17 (StataCorp).

Results

A weighted total of 10,069,454 patients were identified who had undergone PCI. Of these patients, 8,110,634 were of normal weight, 60,690 were cachectic, 55,765 were overweight, 1,134,765 were obese, and 716,085 were morbidly obese. The average age for the whole study population was 66.99 years. The average age decreased as the patient's body mass index (BMI) increased (cachectic: 74.43 years, normal weight: 70.98 years, overweight: 68.20 years, obese: 66.43 years, morbidly obese: 64.20 years). The study population was primarily comprised of males (63.67%) (Table 1).

When compared to patients in the normal-weight category, cachectic patients had the highest mortality at 9.78% (odds ratio [OR] 3.88, 95% confidence interval [CI]: 3.65-4.12; $p < 0.001$). Mortality was lowest in overweight patients at 1.28% (OR 0.46, 95% CI: 0.39-0.55; $p < 0.001$), followed by obese patients at 1.61% (OR 0.58, 95% CI: 0.56-0.61; $p < 0.001$). In the morbidly obese category, this protective effect was much less, with mortality being measured at 2.05% (OR 0.75, 95% CI: 0.42-0.78; $p < 0.001$; vs 2.72% in the normal-weight category) (Figure 1). After multivariate analysis adjusting for baseline characteristics and comorbidities, mortality remained high in cachectic patients (OR 3.65, 95% CI: 3.42-3.90; $p < 0.001$) and remained low in overweight (OR 0.51, 95% CI: 0.43-0.61; $p < 0.001$) and obese (OR 0.68, 95% CI: 0.66-0.71; $p < 0.001$) patients, but the protective value of weight almost disappeared in the morbidly obese category (OR 0.96, 95% CI: 0.96-1.00; $p = 0.04$) when compared with normal-weight patients (Figure 2).

Discussion

Our results demonstrate that the obesity paradox holds partially true in the context of patients undergoing PCI. Univariate analysis found that mortality after PCI for

cachectic patients was 8.5% higher than that for normal or overweight patients. However, the overweight category had the lowest mortality, followed by the obese category, with almost complete loss of protection in morbidly obese patients.

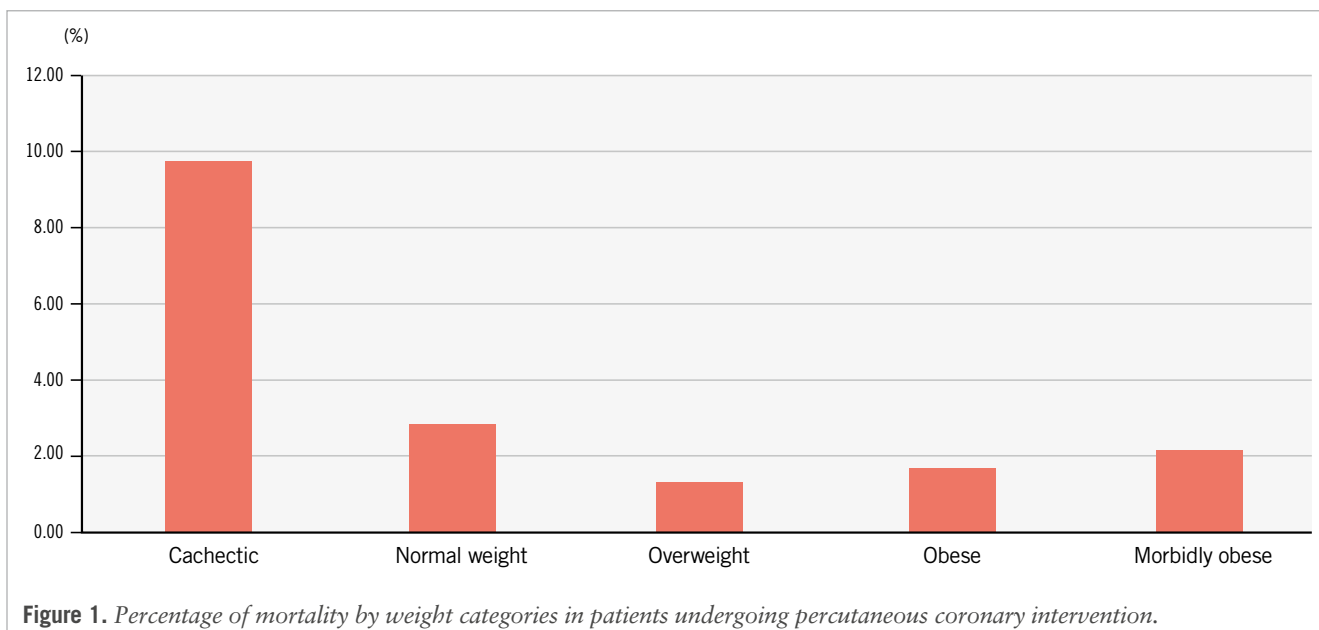
These results are consistent with multiple other studies investigating the obesity paradox in patients undergoing PCI. For example, a meta-analysis conducted by Liu et al considering over 200 studies found that overweight patients (OR 0.66) and obese patients (OR 0.60) were at lower risk of mortality following PCI for STEMI than normal-weight patients⁸. The magnitude of the risk reduction in their study is consistent with that found in this current investigation. The obesity paradox was also supported by the retrospective database investigation conducted by Li et al, which found a U-shaped relationship between BMI and mortality following coronary artery bypass grafting and an L-shaped curve in the case of PCI⁹. Thus, while the magnitude of protection conveyed by obesity and morbid obesity may be less consistent among studies, it is clear that being underweight or of normal weight conveys a higher risk of mortality following PCI than being overweight, as is further demonstrated in our study. Even studies with longer follow-up, such as that conducted by Ueshima et al with a follow-up time of 3 years, found that overweight patients had lower rates of major adverse cardiac events following drug-eluting stent placement than non-overweight patients¹¹. Considering the results of these studies and the results of this current study outlined previously, it is clear there is substantial evidence supporting the validity of the obesity paradox in the context of patients undergoing PCI. However, in our study, overweight patients had the best outcome of the weight categories, suggesting that excessive weight may have a negative effect, and morbid obesity may lose any protective effect seen in the obesity paradox.

While the evidence for the existence of the obesity paradox is strong, the cause of the paradox remains uncertain. One proposed mechanism is that overweight and obese patients are often younger at presentation and may be managed with more aggressive medical therapy. For example, a study conducted by Bundhun et al, which lends support to the

Table 1. Patient demographic information, overall and by BMI class.

2016-2020	Total PCI	Normal weight	Cachectic	Overweight	Obese	Morbidly obese
Total population, n	10,069,454	8,110,634	60,690	55,765	1,134,765	716,085
Age, years	66.99±12.20	70.98±12.15	74.43±10.94	68.20±12.03	66.43±11.51	64.20±11.11
Mortality	2.58	2.72	9.78	1.28	1.61	2.05
Sex						
Male	63.67	81.63	0.58	0.60	11.15	6.12
Female	36.33	78.64	0.65	0.48	11.48	8.85
Race						
White	77.00	80.52	0.59	0.55	11.35	7.06
Black	10.63	78.02	0.78	0.53	11.81	8.98
Hispanic	7.10	80.35	0.48	0.59	11.75	6.93
Asian/Pacific Islander	2.13	89.95	0.74	0.60	6.25	2.48
Native American	0.52	79.85	0.53	0.46	11.34	7.89
Other	2.62	83.99	0.54	0.67	9.64	5.21

Values are % or mean±standard deviation, unless otherwise indicated. BMI: body mass index; PCI: percutaneous coronary intervention



obesity paradox, found that overweight patients were more likely to have intensive use of medications than non-obese patients¹⁶. More intense medication use post-PCI in obese patients following discharge was also observed by Tan et al in their meta-analysis¹⁷.

Beyond more intense medical management of obese patients, age alone may contribute to the observed paradox. A Swedish study investigating outcomes of out-of-hospital cardiac arrest found that obese patients were significantly younger at the time of arrest than non-obese patients¹⁸. While their study investigating out-of-hospital cardiac arrest did not support the obesity paradox, our results do demonstrate that obese and overweight patients are significantly younger at the time of PCI than normal-weight patients. As reported in the results section, the average age decreased as patient BMI increased (cachectic: 74.43 years, normal weight: 70.98 years, overweight: 68.20 years, obese: 66.43 years, morbidly obese: 64.20 years). While decades of research have demonstrated that obesity plays a strong role in the development of cardiovascular disease, the notion that overweight and obese patients develop such disease at a younger age may be an advantage when it comes to surviving cardiac procedures, contributing to the observed obesity paradox.

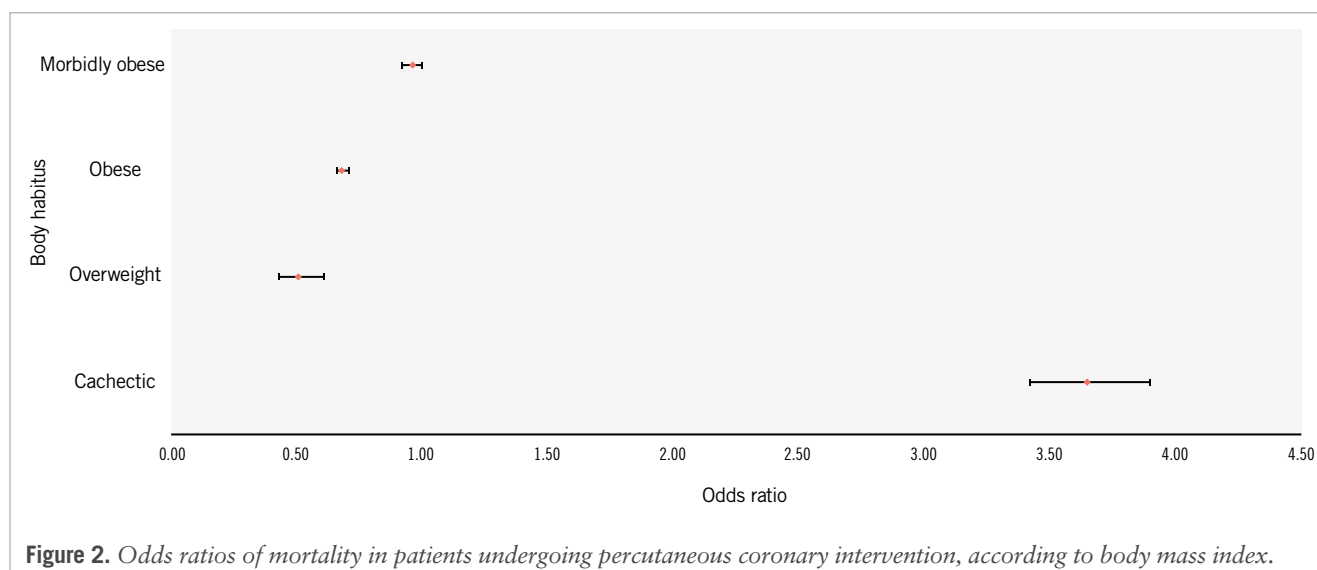
Another factor potentially involved in the aetiology of the obesity paradox is the difference between metabolically healthy and unhealthy obesity and the distinction between visceral versus subcutaneous adiposity. It is well established that central adiposity carries a higher metabolic risk than peripheral adiposity¹⁹. One study investigating obesity in the context of Takotsubo syndrome found that subcutaneous adiposity was protective, leading to better in-hospital outcomes and overall clinical course. The author continued to discuss the observed benefits contributing to lower autonomic sympathetic nervous system activity in patients with subcutaneous obesity, leading to lower stress placed on the damaged heart²⁰. With this in mind, it is possible the observed obesity paradox may be due, in part, to benefits experienced by patients with subcutaneous obesity, versus

those with central and visceral adiposity. However, the NIS database does not provide information regarding fat distribution, thereby limiting our results.

Critics of the obesity paradox often claim it is merely correlation and not causation, citing statistical bias as the underlying cause¹². Additionally, more specific criticism of studies supporting the obesity paradox includes failing to control for smoking status as a confounding variable, as not only does smoking increase cardiac risk, but it is often associated with lower body mass due to its effects on metabolic rate¹¹. While a valid concern, our study has controlled for not only smoking status, but also COPD, CKD, hypertension, diabetes, race, sex, and age; when such a control is considered alongside the sheer size and representativeness of the NIS database, our results are strongly supported.

While our study did consider smoking as a possible confounding variable, it still had multiple limitations. First, the NIS database did not allow for the specification of whether mortality was due to a cardiac or non-cardiac cause. This is an important implication and should be further studied in future investigations. Additionally, while previously discussed studies considered medication differences between overweight and non-overweight patients, the NIS database does not provide such information. Finally, the NIS database does not include any information related to long-term survival or quality of life following discharge, which should be further investigated.

The cause of the obesity paradox is not known. Metabolic reserve appears to be the most important reason for the obesity paradox. Patients in critical conditions have high metabolic demands that could protect obese patients from nutritional-related mortality²⁰. The fact that cachexia has the highest mortality is consistent with this hypothesis. There are some data indicating that obese patients may present at an earlier stage in the course of their illness, and therefore, they are less sick²¹. Furthermore, the definition of normal weight versus overweight may need adjustment as many overweight patients may have better fitness than patients defined in the



normal-weight definition of a BMI between 18.5 and 25. If a slightly higher BMI were categorised as normal weight, we could show a lower mortality in the normal-weight category. Furthermore, at the lower end of the normal-weight category, many patients could be closer to the cachexia category, despite being called normal weight. This could result in high-risk cachectic patients being included in the normal-weight category, falsely elevating the mortality rate in this population^{22,23}.

Limitations

Our study is a retrospective analysis and not a randomised trial, limiting our results. We used ICD-10 coding for weight categories and did not have true BMI. However, ICD-10 coding followed recorded BMI and therefore should be accurate. We analysed the inpatient population; therefore, our results cannot evaluate any effect of obesity in a stable outpatient population. We had no access to medication data, preventing us from adjusting for medication used. Furthermore, our mortality data only included total mortality without the ability to assess cardiac mortality.

Conclusions

The “obesity paradox” held only partially, with the lowest mortality in the overweight category followed by the obese category, with an almost complete loss of protection in morbidly obese patients; mortality was highest in cachectic patients. The partial confirmation of the obesity paradox, with loss of protection with increasing weight, suggests that we should continue to advise against obesity and morbid obesity in our population. The cause of the most protective effect of overweight status in PCI patients is unknown and warrants further investigation.

Authors' affiliations

1. University of Arizona, Phoenix, AZ, USA; 2. University of Arizona Sarver Heart Center, Tucson, AZ, USA

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

- Ahmad M, Mehta P, Reddivari AKR, Mungee S. Percutaneous Coronary Intervention. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. <http://www.ncbi.nlm.nih.gov/books/NBK556123/> (Last accessed 23 May 2025).
- Doll JA, Hira RS, Kearney KE, Kandzari DE, Riley RF, Marso SP, Grantham JA, Thompson CA, McCabe JM, Karpalotis D, Kirtane AJ, Lombardi W. Management of Percutaneous Coronary Intervention Complications: Algorithms From the 2018 and 2019 Seattle Percutaneous Coronary Intervention Complications Conference. *Circ Cardiovasc Interv.* 2020;13:e008962.
- Obesity and Overweight. FastStats. CDC. Published December 27, 2023. <https://www.cdc.gov/nchs/fastats/obesity-overweight.htm> (Last accessed 23 May 2025).
- Mandviwala T, Khalid U, Deswal A. Obesity and Cardiovascular Disease: a Risk Factor or a Risk Marker? *Curr Atheroscler Rep.* 2016;18:21.
- Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation.* 1983;67:968-77.
- Amundson DE, Djurkovic S, Matwiyoff GN. The obesity paradox. *Crit Care Clin.* 2010;26:583-96.
- Wolny R, Maehara A, Liu Y, Zhang Z, Mintz GS, Redfors B, Madhavan MV, Smits PC, von Birgelen C, Serruys PW, Mehran R, Leon MB, Stone GW. The obesity paradox revisited: body mass index and -long-term outcomes after PCI from a large pooled patient-level database. *EuroIntervention.* 2020;15:1199-208.
- Liu SH, Lin YZ, Han S, Jin YZ. The obesity paradox in ST-segment elevation myocardial infarction patients: A meta-analysis. *Ann Noninvasive Electrocardiol.* 2023;28:e13022.
- Li C, Han D, Xu F, Zheng S, Zhang L, Wang Z, Yang R, Yin H, Lyu J. Obesity Paradox of All-Cause Mortality in 4,133 Patients Treated with Coronary Revascularization. *J Interv Cardiol.* 2021;2021:3867735.
- Shirahama Y, Tabata N, Sakamoto K, Sato R, Yamanaga K, Fujisue K, Sueta D, Araki S, Takashio S, Arima Y, Hokimoto S, Sato K, Sakamoto T, Nakao K, Shimomura H, Matsumura T, Tayama S, Fujimoto K, Oshima S, Nakamura S, Tsunoda R, Hirose T, Kikuta K, Sakaino N, Yamamoto N, Kajiura I, Suzuki S, Yamamoto E, Kaikita K, Matsushita K, Tsujita K; Kumamoto Intervention Conference Study (KICS) Investigators. Validation of the obesity paradox by body mass index and waist circumference in patients undergoing percutaneous coronary intervention. *Int J Obes (Lond).* 2022;46:1840-8.
- Ueshima D, Yoshikawa S, Sasaoka T, Hatano Y, Kurihara K, Maejima Y, Isobe M, Ashikaga T. Obesity paradox in the era of percutaneous coronary

intervention with 2nd-generation drug-eluting stents: an analysis of a multicenter PCI registry. *Heart Vessels*. 2019;34:218-26.

12. Samuels JD, Lui B, White RS. Clearing Up the Obesity Paradox in Cardiac Surgery. *J Cardiothorac Vasc Anesth*. 2021;35:959-60.
13. Donataccio MP, Vanzo A, Bosello O. Obesity paradox and heart failure. *Eat Weight Disord*. 2021;26:1697-707.
14. Gacutan K. Healthcare Cost and Utilization Project (HCUP). Published online 2020. <https://www.ahrq.gov/data/hcup/index.html> (Last accessed 23 May 2025).
15. Nathan A, Hashemzadeh M, Movahed MR. Percutaneous Coronary Intervention of Chronic Total Occlusion Associated with Higher Inpatient Mortality and Complications Compared With Non-CTO Lesions. *Am J Med*. 2023;136:994-9.
16. Bundhun PK, Li N, Chen MH. Does an Obesity Paradox Really Exist After Cardiovascular Intervention?: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies. *Medicine (Baltimore)*. 2015;94:e1910.
17. Tan XF, Shi JX, Chen AM. Prolonged and intensive medication use are associated with the obesity paradox after percutaneous coronary intervention: a systematic review and meta-analysis of 12 studies. *BMC Cardiovasc Disord*. 2016;16:125.
18. Hjalmarsson A, Rawshani A, Råmunddal T, Rawshani A, Hjalmarsson C, Myredal A, Höskuldsdóttir G, Hessulf F, Hirlekar G, Angerås O, Petursson P. No obesity paradox in out-of-hospital cardiac arrest: Data from the Swedish registry of cardiopulmonary resuscitation. *Resusc Plus*. 2023;15:100446.
19. Zhang X, Ha S, Lau HC, Yu J. Excess body weight: Novel insights into its roles in obesity comorbidities. *Semin Cancer Biol*. 2023;92:16-27.
20. Madias JE. "Obesity paradox" and takotsubo syndrome. *Int J Cardiol Cardiovasc Risk Prev*. 2022;15:200152.
21. Carbone S, Lavie CJ, Arena R. Obesity and Heart Failure: Focus on the Obesity Paradox. *Mayo Clin Proc*. 2017;92:266-79.
22. Soto ME, Pérez-Torres I, Rubio-Ruiz ME, Manzano-Pech L, Guarner-Lans V. Interconnection between Cardiac Cachexia and Heart Failure-Protective Role of Cardiac Obesity. *Cells*. 2022;11:1039.
23. Ortega FB, Sui X, Lavie CJ, Blair SN. Body Mass Index, the Most Widely Used But Also Widely Criticized Index: Would a Criterion Standard Measure of Total Body Fat Be a Better Predictor of Cardiovascular Disease Mortality? *Mayo Clin Proc*. 2016;91:443-55.