

# Does the influence of obesity on prognosis differ in men and women? A study of obesity paradox in patients with acute coronary syndrome

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## Abstract

**Background:** Recent studies have reported the existence of obesity paradox in acute coronary syndromes (ACS). However, the occurrence of obesity paradox in men and women has not yet been thoroughly investigated, even though both genders differ in patterns and incidence of obesity.

**Aim:** Therefore, the aim of this study was to investigate whether obesity influence on outcomes of patients with ACS varies by gender.

**Methods:** This retrospective study included 341 patients admitted to hospital for treatment due to ACS in 2012. They were classified according to the World Health Organisation with use of body mass index (BMI) as normal weight, overweight, and obese. All patients received standard discharge medication. All-cause mortality was assessed during a mean follow-up time of  $212 \pm 121$  days.

**Results:** There were 82 (24%) normal weight, 160 (47%) overweight, and 99 (29%) obese patients. There were 252 (73.9%) men. All-cause mortality was lower in the obese and overweight vs. normal weight male patients (1.4% vs. 3.3% vs. 13.1%, respectively,  $p = 0.009$ ). There was a trend favouring the normal weight and obese vs. overweight women (4.8% vs. 3.6% vs. 17.5%, respectively,  $p = 0.103$ ). In the general population, after adjustment, BMI increase by one reduced risk by 15.6% ( $p = 0.015$ ), and obesity reduced risk by 50.8% ( $p = 0.056$ ). Obesity reduced risk for men by 69.4% ( $p = 0.015$ ), and BMI increase by one reduced risk for men by 22% ( $p = 0.002$ ). BMI and obesity were independent prognostic factors in men, whereas no such phenomenon was observed in women.

**Conclusions:** Only male patients seem to contribute to the obesity paradox observed in patients with ACS. The obesity paradox does not occur in female patients when considered separately. Obesity seems to have a different influence on outcomes in both genders, and this might be worthy of further studies.

**Key words:** obesity, acute coronary syndrome, gender, outcome

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## INTRODUCTION

Obesity is an established risk factor for cardiovascular diseases (CVD) [1, 2]. It is related to higher prevalence of cardiovascular risk factors and plays a major role in the development of metabolic syndrome and atherosclerosis [3–6]. Some studies published recently have demonstrated improved outcomes in obese patients. It was first observed in chronic kidney disease (CKD) and later in, among others, heart failure [7]. This phenomenon was called obesity paradox or reverse epidemiology, and it has caused many controversies since its first description.

Some authors reported data suggesting its occurrence also among patients after percutaneous coronary intervention [8] and with acute coronary syndrome (ACS) [9]. However, the occurrence of obesity paradox in men and women has not yet been thoroughly investigated, even though both genders differ in patterns and incidence of obesity [3] and women are known to differ from men in terms of risk factors, course, and prognosis in CVD [2]. Therefore, the aim of this study was to investigate whether obesity influence on outcomes of patients with ACS varies by gender.

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## METHODS

### Study group

A total of 495 patients were treated due to suspicion of ACS at a single university health care centre between January and December 2012. Body mass index (BMI) was used to classify these patients as underweight:  $< 18.5 \text{ kg/m}^2$ , normal weight:  $18.5\text{--}24.99 \text{ kg/m}^2$ , overweight:  $25\text{--}29.99 \text{ kg/m}^2$ , obese:  $30\text{--}39.99 \text{ kg/m}^2$ , and severely obese:  $\geq 40.0 \text{ kg/m}^2$ , according to the World Health Organisation criteria [10]. Body weight and height were measured at admission. Some patients were excluded from this study due to lack of height or weight records or discharge diagnosis other than ACS ( $n = 149$ ). There were very few patients with BMI  $< 18.5$  and  $\geq 40$  available to our study ( $n = 5$ ), and thus they were not included in further statistical analysis. This retrospective study eventually included 341 patients, who were diagnosed with ST-segment elevation ACS (STE-ACS), non-ST-segment elevation ACS (NSTEMI-ACS), and unstable angina (UA) according to the criteria of the European Society of Cardiology [11, 12].

### Follow up

All-cause mortality was assessed during a mean follow-up time of  $212 \pm 121$  days (min: 0, max: 436). The data on mortality was obtained from the National Personal ID Registry; the last query is dated 29 January 2014. This study was approved by the Ethical Committee of Poznan University of Medical Sciences and was conducted according to the Declaration of Helsinki. This was a retrospective study based on routine medical procedures, and additional written consent was not required. The data was processed and analysed by authorised medical personnel only, and was anonymised and de-identified prior to analysis.

### Statistical analysis

Statistical analysis was performed using STATISTICA 10 Statsoft. The probability distribution of continuous variables was tested with Lilliefors and Shapiro-Wilk tests. T-student and ANOVA tests were used to compare continuous variables with normal distribution, and Mann-Whitney U and Kruskal-Wallis ANOVA tests were used for continuous variables with non-normal distribution. Chi-square tests were used for categorical variables. Univariate regression models, log rank tests, and Kaplan-Meier plots were used to assess unadjusted survival. Multivariate analysis of survival was performed using Cox proportional hazard regression models with adjustment for the parameters that significantly differed between the survivors and the patients who died (incidence of sudden cardiac arrest [SCA], CKD and history of stroke, age, left ventricular ejection fraction [LVEF], and blood haemoglobin concentration at presentation). The data is expressed as mean values with standard deviation for continuous variables and percentages for categorical variables. A  $p$  value  $< 0.05$  was considered statistically significant for all the tests.

## RESULTS

The patients' mean age was  $64 \pm 12$  years (32–92 years), there were 252 (73.9%) men, and mean BMI was  $27.93 \pm 3.93 \text{ kg/m}^2$  (18.59–39.97  $\text{kg/m}^2$ ). Twenty-two (6.45%) patients died during the follow up. 4.1% of the subjects had SCA due to ventricular fibrillation in the first 24 h after ACS. All the investigated patients received standard discharge medication, i.e. 93.8% — acetylsalicylic acid, 89.4% — statin, 85.9% — oral antiplatelet drug, 84.5% — beta-blocker, 81.5% — angiotensin converting enzyme inhibitor, 17.9% — loop diuretics, 7.9% — spironolactone, 7.6% — calcium-channel blocker, 6.8% — long acting nitrate, 4.6% — indapamide, 4.1% — angiotensin receptor blocker, and 2.4% — vitamin K antagonists. This study demonstrated significant differences between men and women in baseline characteristics — the investigated women were older, had higher prevalence of arterial hypertension, diabetes mellitus and neoplasms, and lower blood haemoglobin concentration and estimated glomerular filtration rate according to modification of diet in renal disease formula (eGFR according to MDRD). Baseline characteristics of the investigated patients are presented in Table 1, and both genders are compared in Table 2.

The patients who died had significantly lower mean BMI (25.73 vs. 28.08,  $p = 0.006$ ), higher incidence of SCA, and higher prevalence of CKD, they were older, had lower LVEF, elevated inflammatory markers, and lower haemoglobin concentration and eGFR. There were no differences as to prevalence of ACS types in these two groups (Table 3).

The obese patients showed the lowest all-cause mortality rate (Fig. 1), and log rank test used for survival probability analysis showed a trend favouring the obese (Fig. 2). Cox regression model showed hazard ratio (HR) of 0.48 for obesity (95% CI 0.26–0.87,  $p = 0.017$ ), and HR for BMI increase by one was 0.85 (95% CI 0.75–0.96,  $p = 0.007$ ). After adjustment BMI remained an independent prognostic factor with HR 0.84 (95% CI 0.74–0.97,  $p = 0.015$ ), and HR for obesity was 0.49 (95% CI 0.24–1.02,  $p = 0.056$ ).

Mortality rates were the lowest in the obese patients, regardless of gender. Among the male patients the highest mortality rates were in the normal weight, and among the female patients in the overweight (Fig. 1). Log-rank test showed significant differences in survival probability between normal weight, overweight, and obese men, which favoured the obese the most (Fig. 3), while this phenomenon was not observed in women. Among women, the overweight had the worst survival probability, although this result was statistically not significant (Fig. 4). Cox regression model showed that HR for obesity was 0.32 in men (95% CI 0.13–0.70,  $p = 0.015$ ) while it had no influence on risk for women (HR 0.88, 95% CI 0.36–2.12,  $p = 0.77$ ). Increase of BMI by one resulted in HR 0.88 for men (95% CI 0.67–0.92,  $p = 0.002$ ) while again it had no influence on risk for women (HR 0.95, 95% CI 0.79–1.14,  $p = 0.59$ ). After adjustment BMI preserved a significant influence on outcomes

**Table 1.** Baseline characteristics of patients with acute coronary syndrome ( $\chi^2$  and Kruskal-Wallis ANOVA tests)

	Normal weight	Overweight	Obese	P
Number	82 (24%)	160 (46%)	99 (29%)	
Mean age [years]	66 ± 12	64 ± 12	63 ± 11	0.19
Mean BMI [kg/m <sup>2</sup> ]	23.1 ± 1.5	27.5 ± 1.4	32.7 ± 2.3	
Men	61 (74.4%)	120 (75.0%)	71 (71.7%)	0.84
Sudden cardiac arrest	7 (8.5%)	4 (2.5%)	3 (3.1%)	0.07
Arterial hypertension	41 (50.0%)	120 (75.0%)	81 (83.5%)	< 0.001
Diabetes	11 (13.4%)	36 (22.5%)	34 (35.1%)	0.003
Chronic kidney disease	6 (7.3%)	11 (6.9%)	2 (2.1%)	0.19
Neoplasm	2 (2.4%)	13 (8.1%)	5 (5.0%)	0.16
History of ACS	29 (35.4%)	57 (35.6%)	35 (35.4%)	0.99
Chronic heart failure	6 (7.3%)	11 (6.9%)	10 (10.1%)	0.64
History of stroke	5 (6.1%)	6 (3.8%)	7 (7.2%)	0.45
Chronic obstructive pulmonary disease	2 (2.4%)	3 (1.9%)	6 (6.0%)	0.19
Mean LVEF [%]	48 ± 11	48 ± 11	49 ± 9	0.81
Mean eGFR (MDRD) [mL/kg/1.73 m <sup>2</sup> ]	77 ± 23	73 ± 23	75 ± 20	0.52
Haemoglobin [mmol/L]	8.6 ± 1.2	9 ± 1	9.1 ± 0.9	0.052
Indication:				0.92
STE-ACS	46 (56.1%)	76 (47.5%)	48 (50.0%)	
NSTE-ACS	24 (29.3%)	51 (31.9%)	32 (31.3%)	
Unstable angina	12 (13.4%)	33 (20.6%)	19 (20.8%)	
Angiographic findings:				0.94
One-vessel disease	48 (58.0%)	85 (52.8%)	55 (55.3%)	
Multi-vessel disease	24 (29.6%)	56 (35.2%)	33 (32.9%)	
No significant changes	10 (12.4%)	19 (11.9%)	11 (11.7%)	
Treatment:				0.67
PCI	66 (80.5%)	128 (80.0%)	81 (81.4%)	
CABG	4 (4.9%)	13 (8.1%)	4 (4.1%)	
Conservative	12 (14.6%)	19 (11.9%)	14 (14.4%)	

ACS — acute coronary syndrome; BMI — body mass index; eGFR (MDRD) — estimated glomerular filtration rate (modification of diet in renal disease formula); CABG — coronary artery bypass graft; LVEF — left ventricular ejection fraction; NSTE-ACS — non-ST-elevation acute coronary syndrome; PCI — percutaneous coronary intervention; STE-ACS — ST-elevation acute coronary syndrome

in men with HR 0.82 (95% CI 0.69–0.97,  $p = 0.019$ ), and HR for obesity was 0.39 (95% CI 0.16–0.98,  $p = 0.044$ ).

## DISCUSSION

This study investigated outcomes of patients with ACS, and its main findings are that the obese and overweight patients demonstrated improved outcomes in comparison with the normal weight subjects, with the best outcomes of the obese, in spite of the better baseline clinical profile of the normal weight patients. To our knowledge, the new finding is that the obesity paradox may be observed only in men, and not in women, with ACS. Obesity seems to have a different influence on outcomes in women and men.

The existence of the obesity paradox in patients with coronary artery disease (CAD) and ACS remains controversial. Angeras et al. [9] confirmed the existence of the obesity

paradox in patients after ACS in their study of the Swedish Coronary Angiography and Angioplasty Registry, and Diercks et al. [13] reported similar results in patients after NSTE-ACS included in the CRUSADE study, along with Schechter et al. [14] in their study of an Israeli population. They found a U-shaped relationship between mortality and BMI, with peak mortality rates in underweight and severely obese patients, and the best outcomes in overweight and obese. Other authors also reported improved short-term survival rate of the obese and a trend favouring the obese in long term; however, they included patients with various types of CAD, and percentages of ACS varied between 30% and 70% of all patients [15, 16]. Some authors investigating patients after NSTE-ACS reported worse outcomes of the underweight patients [13, 17]. The above-mentioned studies differ in follow-up: from in-hospital to six-year. They show improved short-term out-

**Table 2.** Comparison of baseline characteristics of investigated men and women ( $\chi^2$  and U Mann-Whitney tests)

	Women	Men	P
Number	89 (26.1%)	252 (73.9%)	
Mean age [years]	68 ± 11	63 ± 12	< 0.001
Mean BMI [kg/m <sup>2</sup> ]	28 ± 4	28 ± 4	0.45
Sudden cardiac arrest	5 (5.5%)	9 (3.6%)	0.44
Arterial hypertension	73 (80.2%)	172 (68.3%)	0.030
Diabetes	29 (31.9%)	53 (21.0%)	0.040
Chronic kidney disease	4 (4.4%)	15 (5.9%)	0.58
Neoplasm	10 (11.2%)	10 (3.9%)	0.012
History of ACS	32 (35.2%)	89 (35.3%)	0.98
Chronic heart failure	9 (10.1%)	18 (7.1%)	0.51
History of stroke	4 (4.4%)	14 (5.6%)	0.67
Chronic obstructive pulmonary disease	2 (2.3%)	9 (3.6%)	0.54
Mean LVEF [%]	50 ± 12	48 ± 10	0.039
Mean eGFR (MDRD) [mL/kg/1.73 m <sup>2</sup> ]	68 ± 21	77 ± 22	< 0.001
Haemoglobin (mmol/L)	8.4 ± 0.8	9 ± 1	< 0.001
Normal weight	21 (23.6%)	61 (24.2%)	0.84
Overweight	40 (44.9%)	120 (47.6%)	
Obese	28 (31.5%)	71 (28.2%)	
Indication:			0.78
STE-ACS	47 (52.8%)	123 (49.3%)	
NSTEMI-ACS	25 (28.1%)	80 (32.1%)	
Unstable angina	17 (19.1%)	49 (18.6%)	
Angiographic findings:			0.11
One-vessel disease	44 (49.4%)	130 (52%)	
Multi-vessel disease	32 (36%)	102 (40.6%)	
No significant changes	13 (14.6%)	20 (7.4%)	
Treatment:			0.20
PCI	66 (74.2%)	207 (82.8%)	
CABG	7 (7.8%)	14 (5.6%)	
Conservative	16 (18%)	31 (11.6%)	

Abbreviation as in Table 1

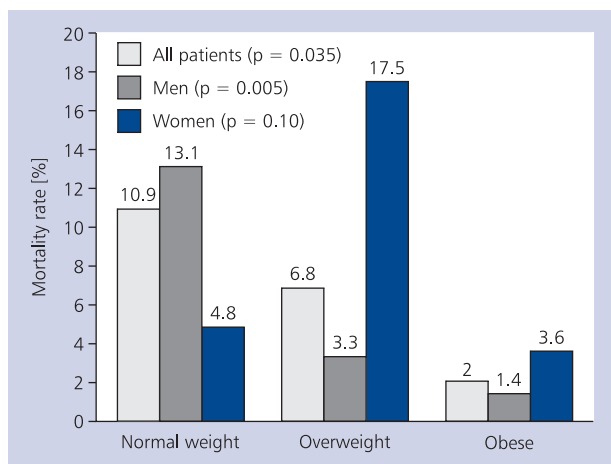
comes of the overweight and obese while there are no clear proofs for this phenomenon in the long term. Kadakia et al. [18] reported improved short-term outcomes of the obese and no significant influence of obesity on long-term survival, and they suggested the existence of a reverse effect in the longer term. Moreover, they reported increased risk for lean patients with large waist circumference. The present study provides intermediate follow-up and confirms the existence of the obesity paradox. No influence of age or sex on prognosis was demonstrated, and there were no differences between the mortality rates in different types of ACS.

**Table 3.** Comparison of baseline characteristics of survivors and deceased ( $\chi^2$  and U Mann-Whitney tests)

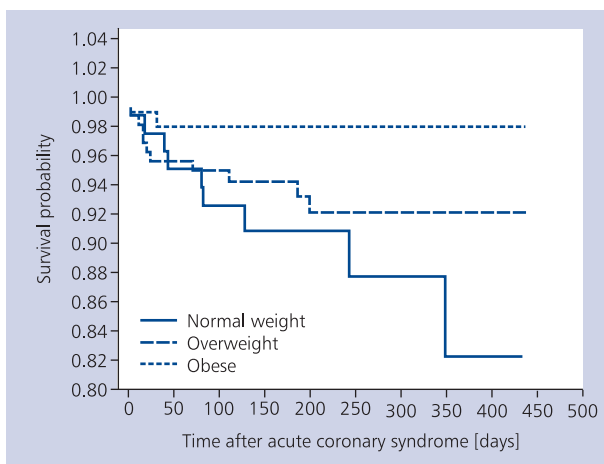
	Survivors	Deceased	P
Number	319	22	
Men	239 (74.9%)	13 (59.1%)	0.10
Mean age [years]	63 ± 12	73 ± 9	0.0003
Mean BMI [kg/m <sup>2</sup> ]	28.1 ± 3.9	25.7 ± 3.5	0.0129
Weight:			0.0349
Normal weight	73 (22.9%)	9 (40.9%)	
Overweight	149 (46.7%)	11 (50%)	
Obese	97 (30.4%)	2 (9.1%)	
ACS complicated with SCA	10 (3.2%)	4 (18.2%)	0.0042
Arterial hypertension	228 (71.9%)	14 (63.6%)	0.40
Diabetes mellitus	74 (23.3%)	7 (31.8%)	0.52
History of neoplasm	16 (5.02%)	4 (18.2%)	0.0382
Heart failure	19 (6.1%)	3 (13.6%)	0.08
Mean LVEF at presentation	49 ± 10	38 ± 10	< 0.0001
ACS in the past	110 (34.7%)	11 (50%)	0.15
ACS type:			0.42
STEMI	157 (49.7%)	13 (59.1%)	
NSTEMI	98 (31%)	7 (31.8%)	
Unstable angina	61 (19.3%)	2 (9.1%)	
Treatment:			0.35
Conservative	40 (12.5%)	5 (22.7%)	
PCI	260 (81.5%)	15 (68.2%)	
CABG	19 (6%)	2 (9.1%)	
Mean Hb at presentation [mmol/L]	9 ± 1	8.2 ± 1.3	0.0014
Mean hs-CRP at presentation [mL/min/1.73 m <sup>2</sup> ]	31.8 ± 41.3	60.9 ± 65.3	0.06
Mean glycaemia at presentation [mmol/L]	8.1 ± 3.9	8 ± 2.4	0.32
Mean eGFR at presentation [mg/L]	76 ± 22	63 ± 26	0.0239

Hb — haemoglobin concentration [mmol/L]; hsCRP — high sensitivity C-reactive protein; STEMI — ST-elevation myocardial infarction; NSTEMI — non-ST-elevation myocardial infarction; SCA — sudden cardiac arrest; rest abbreviation as in Table 1

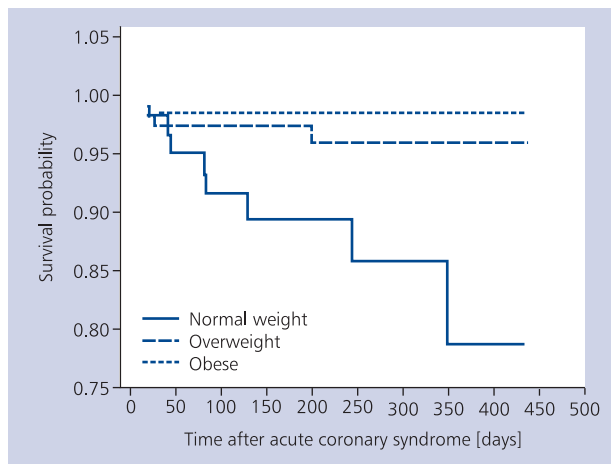
Many authors attribute the existence of obesity paradox to the younger age of the obese at presentation [9, 13, 14, 16, 17, 19–23] or their more aggressive or better guideline-recommended discharge treatment [13, 15, 18–20, 24]. There are also studies showing that BMI does not have an independent predictive value and that the obesity paradox is caused by other factors to which obesity is only co-factor. Kosuge et al. [19] reported a relationship between age and prognosis in patients after ACS, because age had an independent prognostic value in their study, whereas BMI showed none. However, only 4% of the patients included in this Japanese study were obese,



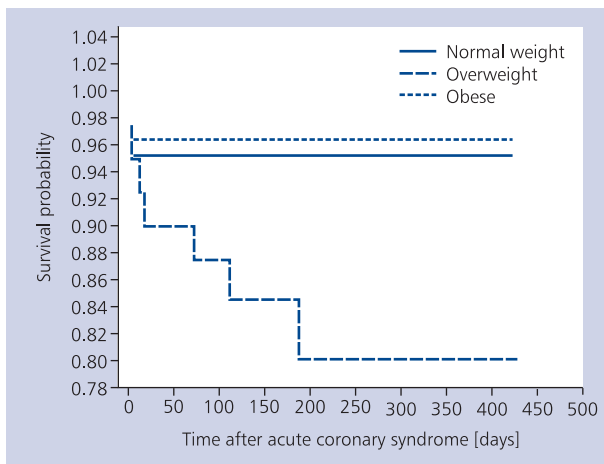
**Figure 1.** Mortality rates in patients with acute coronary syndrome (Kruskal-Wallis ANOVA test)



**Figure 2.** Survival probability in patients with acute coronary syndrome (p = 0.11) (Log-rank test, Kaplan-Meier plot)



**Figure 3.** Survival probability in men with acute coronary syndrome (p = 0.018) (Log-rank test, Kaplan-Meier plot)



**Figure 4.** Survival probability in women with acute coronary syndrome (p = 0.20) (Log-rank test, Kaplan-Meier plot)

and Kang et al. [21] obtained similar results in their study of a Korean population, with only 12.6% obese patients. Aronson et al. [25] reported that underweight and obese patients with acute myocardial infarction had the highest all-cause mortality, which was attributed to concomitant anaemia. Anaemia was an independent predictor of mortality in their study, and they showed a strong relationship between blood haemoglobin concentration and BMI [25]. The present study showed that the overweight and obese had significantly higher mean blood haemoglobin concentrations, but haemoglobin did not demonstrate any prognostic value. Our study did not show any significant differences between the investigated groups as to age on presentation or discharge treatment, and yet the obesity paradox could be observed.

Some authors did not report any evidence for the existence of the obesity paradox in patients with CAD and ACS. Li et al. [20] did not observe such a phenomenon in their study of

a Chinese population. However, this Chinese study included fewer obese patients (only 13.4%) than the other studies of European or United States populations. Also Akin et al. [22] in their study of the German Drug-eluting Stent Registry did not report any evidence for the obesity paradox. However, only 30% of the included patients were diagnosed with ACS and the rest with other types of CAD [22].

Our study did not demonstrate any influence of sex on prognosis, in spite of significant differences in baseline characteristics between both sexes. The adjusted analysis of influence of BMI and obesity on prognosis in both sexes separately suggests that BMI and obesity are independent risk factors only in men. In the present study obese men demonstrated the best outcomes, and the worst were observed in overweight women. A bimodal relationship was observed in a review of the British Columbia Cardiac Registry [26], with the worst outcomes of the underweight and morbidly obese

men and women. Kosuge et al. [19] reported a reverse relationship between in-hospital mortality rates and BMI, with the greatest influence of BMI on mortality in women. However, they used slightly different cut-off points for the BMI groups, i.e. low weight: < 20, normal weight: 20–24.9, overweight: 25–29.9, and obese: > 30; the patients with BMI < 20 were older, had more risk factors, and there were more women in this group. BMI appeared to be an independent predictor of mortality for the whole group, and the authors did not analyse both sexes separately [19].

### Limitations of the study

The limitations of this study are a relatively small group of patients and number of events (deaths), and an imbalance in numbers of men and women, which however is not surprising because ACS are more common in men. The women were significantly older, which again seems in accordance with previous studies of ACS, and age did not significantly influence mortality in our study. Another limitation is that BMI does not take distribution of body fat into account, and we did not use other markers of obesity, such as waist-to-hip ratio. This study also did not consider shifts of patients' body weight before the procedure and during follow-up. This was a retrospective study and had all the natural limitations of such studies.

### CONCLUSIONS

Our study confirms the existence of the obesity paradox in patients with ACS, and it shows that BMI is an independent prognostic factor of intermediate-term all-cause mortality in male patients.

Overweight and obesity are related to lower mortality rates, in spite of a better baseline clinical profile of normal weight patients in comparison with the obese.

Only male patients seem to contribute to the obesity paradox observed in patients with ACS. Obesity paradox does not occur in female patients when considered separately.

Obesity seems to have a different influence on outcomes in women and men, and this might be worthy of further studies.

**Conflict of interest:** Maciej Lesiak — AstraZeneca, Boston Scientific, Abbott Vascular consultant.

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## Czy wpływ otyłości na rokowanie jest różny u kobiet i mężczyzn? Paradoks otyłości u pacjentów z ostrym zespołem wieńcowym

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### Streszczenie

**Wstęp:** W ostatnich latach pojawiły się prace sugerujące występowanie paradoksu otyłości u pacjentów z ostrym zespołem wieńcowym (OZW).

**Cel:** Kobiety i mężczyźni różnią się przebiegiem otyłości, dlatego celem niniejszej pracy było sprawdzenie, czy wpływ otyłości na wyniki pacjentów z OZW zależy od płci.

**Metody:** Retrospektywne badanie przeprowadzono na grupie 341 pacjentów przyjętych do szpitala w 2012 r. w celu leczenia OZW. Podzielono ich ze względu na wskaźnik masy ciała (BMI), zgodnie z wytycznymi Światowej Organizacji Zdrowia, na osoby z prawidłową wagą, nadwagą i otyłością. Wszyscy zostali poddani standardowej terapii. Oceniano śmiertelność z wszystkich przyczyn podczas obserwacji trwającej  $212 \pm 121$  dni.

**Wyniki:** Grupa badana liczyła 82 (24%) osób z prawidłową masą ciała, 160 (47%) z nadwagą i 99 (29%) osób otyłych; w tym 252 (73,9%) mężczyzn. Śmiertelność z wszystkich przyczyn była niższa u mężczyzn otyłych i z nadwagą w porównaniu z mężczyznami z prawidłową masą ciała (odpowiednio 1,4% vs. 3,3% vs. 13,1%;  $p = 0,009$ ). Zaobserwowano trend sprzyjający kobietom z prawidłową wagą i otyłym w porównaniu z kobietami z nadwagą (odpowiednio 4,8% vs. 3,6% vs. 17,5%;  $p = 0,103$ ). W całej grupie badanej, po uwzględnieniu innych istotnych czynników, wzrost BMI o 1 powodował obniżenie ryzyka o 15,6% ( $p = 0,015$ ), a u osób otyłych ryzyko było mniejsze o 50,8% ( $p = 0,056$ ). U mężczyzn otyłość zmniejszała ryzyko o 69,4% ( $p = 0,015$ ), a wzrost BMI o 1 redukowało ryzyko o 22% ( $p = 0,002$ ). Wartość BMI i otyłość miały istotne znaczenie prognostyczne u mężczyzn, podczas gdy u kobiet nie zaobserwowano tego zjawiska.

**Wnioski:** Wydaje się, że wśród pacjentów z OZW paradoks otyłości występuje tylko u mężczyzn. Otyłość wydaje się mieć różny wpływ na przeżycie zależnie od płci, co może stanowić interesującą przesłankę do dalszych badań tego zjawiska.

**Słowa kluczowe:** otyłość, ostry zespół wieńcowy, płeć, rokowanie

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