

# How to predict the risk of postoperative complications after coronary artery bypass grafting in patients under 50 and over 80 years old. A retrospective cross-sectional study

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## Abstract

**Background:** Coronary artery disease (CAD) remains the leading cause of death in developed countries, and there is an increasing number of both young and elderly patients requiring surgical treatment. Despite improvement of conventional risk stratification scores (EuroSCORE II, STS risk score), all of the calculations are estimated based on the typical population and the studies emphasise that the scales may need further investigation and modernisation because demographic changes of the population suffering from CAD are unavoidable.

**Aim:** To characterise two increasing and challenging cohorts of patients undergoing coronary artery bypass grafting (CABG) and to identify preoperative risk factors for postoperative complications.

**Methods:** In the retrospective cross-sectional study, we analysed 388 patients  $\geq 80$  years old and 190 patients  $\leq 50$  years old, who underwent CABG consecutively at our Institution. Data were obtained from medical records.

**Results:** The vast majority of studied patients had commonly described risk factors for cardiovascular diseases, regardless of the age group. Diabetes was present in almost twice as many individuals in the older cohort, when compared to the EuroSCORE population. A similar observation was made for hypertension, which was more frequent in both age groups. Summarising all of the postoperative complications, at least one occurred significantly more frequently among the older group (10% vs. 20.9%,  $p = 0.001$ ). The vast majority of major adverse cardiac and cerebrovascular events (MACCE) in the older group led to death (79.4%). Among patients  $\geq 80$  years old, higher New York Heart Association (NYHA) class ( $p = 0.001$ , OR 2.05 [1.34–3.12] for every next class) and renal failure ( $p = 0.02$ , OR 2.47 [1.16–5.25]) increased the MACCE rate, whereas higher left ventricular ejection fraction (LVEF) ( $p = 0.002$ , OR 0.81 [0.7–0.93] for every 5%) decreased the risk. Emergent admission was the only factor increasing the occurrence of any postoperative complications among patients  $\leq 50$  years old ( $p = 0.007$ , OR 3.63, 95% CI 1.37–9.62). On the other hand, among patients  $\geq 80$  years old, emergent admission was not associated with any postoperative complications.

**Conclusions:** Young and old patients requiring CABG differ from the standard EuroSCORE population. Postoperative complications are more common among older patients, and MACCE is usually fatal in this age group. Individuals with risk factors for MACCE (higher NYHA class, renal failure, lower LVEF) should be carefully evaluated and qualified, and closely monitored post-surgery.

**Key words:** coronary artery disease, coronary artery bypass grafting, risk stratification, postoperative complications, major adverse cardiac and cerebrovascular events

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## INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of death in developed countries. Although the mortality has decreased over the last decade, CAD is still responsible for around 20% of deaths in the European population [1]. According to Polish Central Statistical Office data, cardiovascular diseases are the most common cause of death in males over 45 years old (yo) and females over 65 yo. Moreover, there are an increasing number of both young and elderly patients requiring surgical treatment. At present, individuals  $\leq 50$  yo and  $\geq 80$  yo account for 3.6% and 7.3%, respectively, of all coronary artery bypass grafting (CABG) procedures at our Institution.

Conventional risk stratification scores (i.e. EuroSCORE II, STS risk score) were developed to allow institutional quality control and epidemiological analysis. In addition, these allow physicians to establish the risk of perioperative mortality and properly inform the patient. Despite improvement of risk stratification scores over the last decades, recent studies question their applicability because they tend to overestimate the mortality rate in the general population and underestimate the mortality in a high-risk population [2–4]. The biggest available meta-analysis, however, evaluated the overestimation of EuroSCORE II and proved it to be statistically irrelevant. Nevertheless, the authors of the study emphasised that the scale may need further investigation and modernisation because demographic changes of the population suffering from CAD are unavoidable [5]. Moreover, all of the calculations are estimated based on the typical population undergoing CABG and should be used with caution in specific age groups [6]. The average age of patients in the two largest datasets used to create the risk scores was  $62.2 \pm 10.7$  years in EuroSCORE and  $65.2 \pm 9.7$  years in SYNTAX. Among the 19,030 patients in the EuroSCORE database, there were only 10%  $> 75$  yo [7, 8]. As the number of young and elderly patients requiring surgical revascularisation increases, studies investigating the outcome in these age groups are well founded.

All of the above prompted us to characterise two increasing and challenging cohorts of patients undergoing CABG and to analyse the prevalence of risk factors for postoperative complications in individuals  $\leq 50$  yo or  $\geq 80$  yo.

## METHODS

In the retrospective cross-sectional study 578 consecutive patients were analysed, who underwent CABG procedure between 2010 and 2014. The enrolled patients consisted of two subgroups: 388 patients  $\geq 80$  yo and 190 patients  $\leq 50$  yo. All patients were qualified for surgical revascularisation based on European Society of Cardiology (ESC) guidelines [9, 10]. Data was obtained from the patients' medical records.

Postoperative complications were divided into two groups:

- major adverse cardiac and cerebrovascular events (MACCE), defined as any postoperative myocardial infarction (MI),

death from cardiac causes, or newly discovered postoperative neurological deficits;

- non-MACCE, including multiple organ dysfunction syndrome (MODS), acute kidney injury, prolonged mechanical ventilation (more than 72 h), low cardiac output syndrome (LCOS) without elevated cardiac enzymes (requiring intra-aortic balloon pump or bypass angiography), sternal dehiscence, and bleeding requiring re-exploration.

Preoperative data were analysed regarding the differences between the two age subgroups and the standard EuroSCORE population. Preoperative data were tested to search for the association with incidence of postoperative complications.

## Statistical analysis

Statistical analysis of the data was performed using STATISTICA software, version 10.0. In order to confirm a normal distribution of continuous variables, the Shapiro-Wilk test was used. The project results were presented based on the parameters of descriptive statistics, including the mean values and standard deviations and medians and quartiles, as appropriate. Categorical variables were presented as percentages. Comparisons between groups were performed using the t-test for independent variables (continuous variables) and the  $\chi^2$  test (proportions). Univariate logistic regression as well as stepwise multiple logistic regression analyses were performed to determine the factors affecting the risk of postoperative complications. The level of statistical significance was set to p-values lower than 0.05.

## RESULTS

### Baseline characteristic and comparison

The investigated group comprised of 144 females and 434 males (Table 1). Age groups significantly differed in the percentage content of sex (11.5% females among the younger vs. 32% among the older group,  $p < 0.001$ ). Mean body mass index (BMI) was higher among the younger group ( $28.2 \text{ kg/m}^2$  vs.  $27.1 \text{ kg/m}^2$ ,  $p = 0.03$ ) due to a greater number of obese individuals (31.6% vs. 21.9%,  $p = 0.01$ ). The prevalence of diabetes and hypertension was higher among the older group, but hyperlipidaemia occurred more frequently in younger patients (49 patients, 25.8% vs. 54 patients, 13.9%,  $p < 0.001$ ). Nevertheless, the median number of typical CAD risk factors (overweight/obesity, diabetes, hypertension, hyperlipidaemia) was two in both age groups. Other comorbidities, i.e. chronic kidney disease (CKD), chronic obstructive pulmonary disease, and atrial fibrillation occurred substantially more frequently in the older group. On admission, older patients had more expressed symptoms of both heart failure (24% of patients with New York Heart Association [NYHA] III–IV from older group vs. 6.9% of patients among from younger groups,  $p < 0.0001$ ) and angina (63.4% of patients from older group with Canadian Cardiovascular Society [CCS] III–IV vs. 46.9%

Table 1. Baseline characteristics

Variable	≥ 80 years old	≤ 50 years old	EuroSCORE dataset
Age [years]	82.4 ± 2.3	46 ± 4.1	62.5 ± 10.7
Male sex	264 (68%)	170 (89.5%)	(72)
Body mass index [kg/m <sup>2</sup> ]	27.12 ± 3.8	28.2 ± 4.2	26.3 ± 3.9
Normal weight	119 (30.7%)	53 (27.9%)	–
Underweight	5 (1.3%)	2 (1%)	–
Overweight	179 (46.1%)	75 (39.5%)	–
Obese	85 (21.9%)	60 (31.6%)	–
Diabetes	127 (32.7%)	34 (17.9%)	(16.7)
Hypertension	333 (85.8%)	142 (74.4%)	(43.6)
Hyperlipidaemia	54 (13.9%)	49 (25.8%)	–
Atrial fibrillation	54 (13.9%)	5 (2.6%)	(9)
COPD	23 (5.7%)	1 (0.5%)	(3.9)
Chronic kidney disease	76 (19.6%)	10 (5.3%)	(3.5)
CCS class 0	5 (1.3%)	2 (1%)	–
CCS class I	39 (10.1%)	20 (10.5%)	–
CCS class II	98 (25.26%)	79 (41.6%)	–
CCS class III	172 (44.3%)	67 (35.3%)	–
CCS class IV	74 (19.1%)	22 (11.6%)	(21)*
Single-vessel disease	72 (18.6%)	36 (19%)	(8)*
Two-vessel disease	69 (17.8%)	39 (20.5%)	(25)*
Three-vessel disease	243 (62.6%)	115 (60.5%)	(67)*
Left main disease	179 (62.6%)	62 (32.6%)	(22)*
LVEF [%]	48 ± 13	51.6 ± 11.1	–
Previous MI	246 (63.4%)	114 (60%)	–
Previous PCI	73 (18.8%)	56 (29.5%)	–
Emergent surgery	121 (31.2%)	43 (22.6%)	(21)*

COPD — chronic obstructive pulmonary disease; CCS — Canadian Cardiovascular Society; LVEF — left ventricular ejection fraction; MI — myocardial infarction; PCI — percutaneous coronary intervention

\*Data from a cohort undergoing isolated coronary artery bypass graft only.

Data from the EuroSCORE dataset obtained from Roques F, Nashef S, Thulin L, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. *Eur J Cardio-Thoracic Surg* [serial online]. n.d.; 15(6): 816–822.

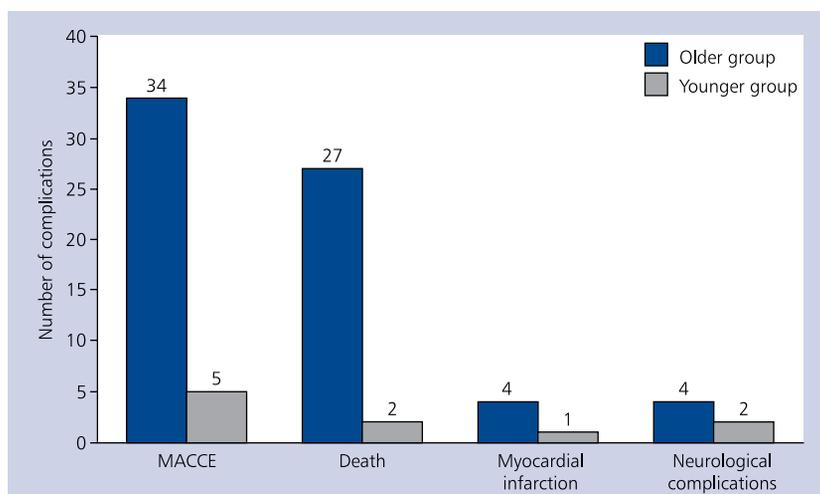
Data shown as mean ± standard deviation or as median (interquartile range) or number (percentage).

of patients from younger group,  $p = 0.004$ ). The number of previous MI did not differ in both groups; however, younger patients were more frequently previously treated with percutaneous coronary intervention (PCI) (29.5% vs. 18.5%,  $p = 0.004$ ). Older patients were more frequently admitted to the hospital in emergent mode, had lower left ventricular ejection fraction (LVEF) on admission, and suffered from left main disease.

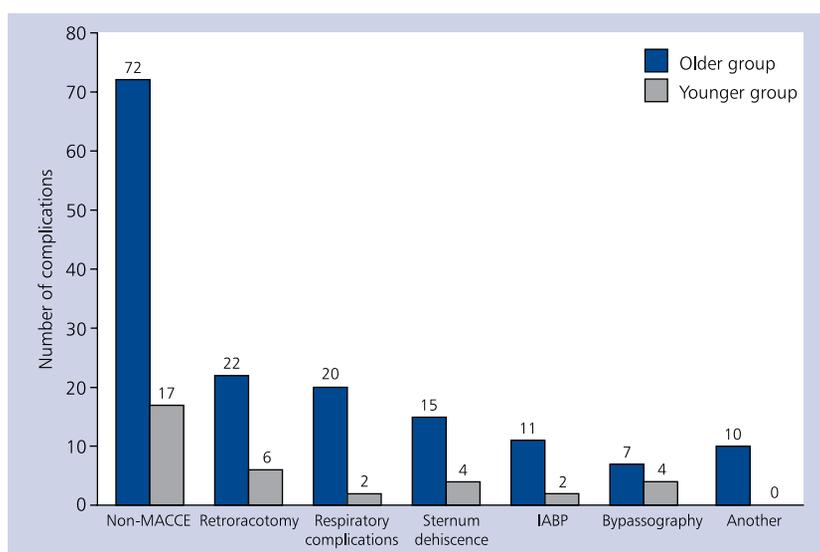
### **Postoperative complications — MACCE and non-MACCE**

Summarising all of the postoperative complications, at least one occurred significantly more frequently among the older group (10% vs. 20.9%,  $p = 0.0011$ ). Similar results were observed after the distinction of MACCE (2.6% vs. 8.8%,

$p = 0.006$ ) and non-MACCE (8.9% vs. 18.6%,  $p = 0.002$ ) complications. The vast majority of MACCE in the older group led to death (79.4%) whereas in younger group this percentage was lower (50%) (Fig. 1). The primary cause of death was cardiac in all of the cases, either as a result of MI, LCOS with subsequent MODS, or cardiac tamponade (Table 2). In both groups the most frequent non-MACCE complication was need for rethoracotomy. Other problems rarely occurred, such as prolonged mechanical ventilation and sternal dehiscence (Fig. 2). Univariate regression analysis allowed selection of preoperative factors that significantly influenced the rate of postoperative complications. Emergent admission was the only risk factor associated with higher incidence of any postoperative complication in the younger group ( $p = 0.007$ , odds ratio [OR] 3.63, 95% confidence interval [CI] 1.37–9.62), but it



**Figure 1.** Comparison between postoperative complications — major adverse cardiac and cerebrovascular events (MACCE). In one case among the older group, myocardial infarction and neurological complications occurred in the same patient



**Figure 2.** Comparison between postoperative complications — non-major adverse cardiac and cerebrovascular events (non-MACCE). Some patients had more than one complication; IABP — intra-aortic balloon pump

**Table 2.** Primary cause of death

Cause of death	≥ 80 years old	≤ 50 years old
	(n = 27)	(n = 2)
Fatal myocardial infarction	12 (44.4%)	1 (50%)
LCOS with subsequent MODS	14 (51.9%)	1 (50%)
Cardiac tamponade	3 (11.1%)	0 (0%)

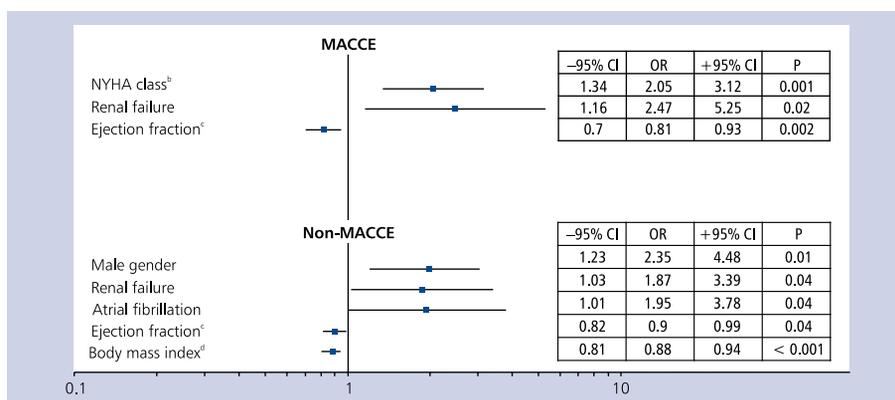
Data shown as number (percentage); LCOS — low cardiac output syndrome; MODS — multiple organ dysfunction syndrome

did not affect the incidence of postoperative complications in elderly patients. Higher NYHA class, renal failure, and LVEF influenced the MACCE rate in the older cohort. Male sex,

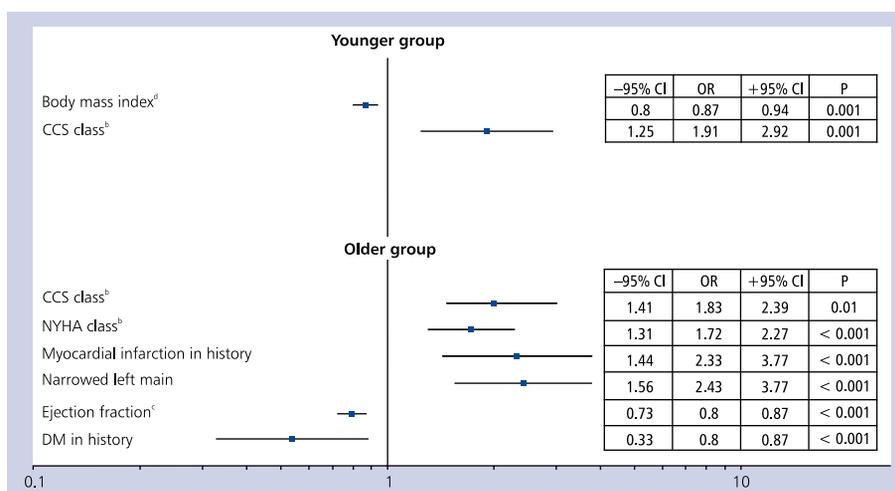
renal failure, and atrial fibrillation increased the non-MACCE rate in the older group. Higher LVEF and BMI in the range 17–31 kg/m<sup>2</sup> decreased the incidence of non-MACCE complications in the older group (Fig. 3).

**Factors influencing admission in emergent mode**

Severity of angina, expressed as CCS class, in both groups was related with emergent admission. Exacerbated symptoms of heart failure (NYHA class) increased the risk of emergent procedure only among the older group. BMI in the range 17–31 kg/m<sup>2</sup> in younger patients, and diabetes and higher LVEF in the older age group, decreased the risk of emergent admission (Fig. 4).



**Figure 3.** Risk factors for major adverse cardiac and cerebrovascular events (MACCE) and non-MACCE complications in the older cohort; <sup>b</sup>for every next higher class; <sup>c</sup>for every 5% increase in left ventricular ejection fraction; <sup>d</sup>for every next 1 kg/m<sup>2</sup> but only in the range 17–31 kg/m<sup>2</sup>; NYHA — New York Heart Association



**Figure 4.** Risk factors for emergent admission; <sup>b</sup>for every next higher class; <sup>c</sup>for every 5% increase in left ventricular ejection fraction; <sup>d</sup>for every next 1 kg/m<sup>2</sup> but only in the range 17–31 kg/m<sup>2</sup>; CCS — Canadian Cardiovascular Society; DM — diabetes mellitus; NYHA — New York Heart Association

### DISCUSSION

The vast majority of studied patients had commonly-described risk factors for cardiovascular diseases, regardless of the age group. Moreover, diabetes was present in almost twice as many individuals in the older cohort, when compared to the EuroSCORE population. A similar observation was made for hypertension, which was more frequent in both age groups (Table 1). According to the literature, all of the described comorbidities tend to worsen the outcome after CABG. However, it is also reported that optimal medical therapy (OMT), resulting in normalisation of the parameters, can diminish the risk of surgery [11, 12]. It is therefore crucial to introduce extensive screening for coronary lesions that may require surgical intervention because, undoubtedly, in both of the studied cohorts, avoiding the surgery or delaying the necessity of one until OMT is introduced would be beneficial.

On the other hand, age is a significant risk factor for poor outcome after cardiac procedures and is included in all risk stratification scores [13]. The elderly tend to suffer from more comorbidities, also non cardiac, and the same results were determined from our study. For example, CKD, which occurred over five times more frequently than in the EuroSCORE population (Table 1), was associated with higher incidence of MACCE (Fig. 3). Similar correlation was previously reported in the analysis of the influence of CKD and anaemia in a younger population (median age 71.1 years), but the association was observed only when both parameters coexisted [14]. The issue of CKD is also well described in the literature regarding the impact on in-hospital mortality [13], and the individuals are at high risk of cardiovascular events even when not undergoing interventional treatment or despite the revascularisation method applied [15]. However, our study

results show that CKD may influence the early mortality also as a result of the increase in non-MACCE occurrence (Fig. 3). Therefore, patients  $\geq 80$  yo suffering from both CAD and CKD are at very high risk of postoperative complications, and should be carefully investigated before qualifying for surgical revascularisation, properly informed, and closely monitored postoperatively.

Another risk factor increasing the MACCE rate among older patients was high NYHA class (Fig. 3). Conversely, CCS class, which was usually lower than observed in the EuroSCORE population (Table 1), was not associated with the postoperative course. This suggests that in the case of older individuals it is warranted to assess heart failure symptoms other than angina.

Males comprised the majority of individuals in both age groups, although females were more frequent in older population. This result is consistent with the literature, and parameters defining this issue are well described. However, sex distribution was observed to be similar to the EuroSCORE population only in the older cohort (Table 1). On the other hand, male gender was associated with higher non-MACCE incidence in the older population, probably due to the fact that more males were evaluated as higher NYHA class in this cohort.

In the studied population, mean BMI was in the range for overweight for both age groups. A similar observation can be made for the EuroSCORE population (Table 1). The analysis of the data showed that BMI in the range of 17–31 kg/m<sup>2</sup> was associated with lower risk of non-MACCE complications among the elderly (Fig. 3). In contrast to the previously reported relationship between higher BMI and postoperative complications after cardiac surgery, recent studies underline that only underweight and obesity have poor prognostic value. A similar observation was also described for all patients with cardiovascular diseases [16].

The prevalence of previous medical history of MI did not significantly differ between groups. Young patients were more frequently treated with PCI, presumably due to the development of interventional cardiology that has been observed over the last decade. Nevertheless, this observation concludes that at least some individuals  $\leq 50$  yo had a diagnosis of CAD prior to qualifying for CABG. Because 22.6% of young patients were operated in an emergent mode, we can assume that nearly 40% of the cohort qualified for secondary prevention prior to surgery. However, a recent study analysing a Polish population of individuals  $\leq 80$  yo, who were hospitalised due to acute coronary syndrome or myocardial revascularisation, showed that only 30.5% participated in a rehabilitation or a secondary prevention programme and only 28.2% took part in at least half of the planned sessions [17].

On the other hand, lower incidence of emergent CABG was observed in patients  $\geq 80$  yo suffering from diabetes (Fig. 4). This may result from the fact that for individuals suffering from hyperlipidaemia or diabetes, assessing the risk of CAD

is always recommended when over 45 yo [18]. However, actuarial studies show that the screening is still not at a satisfactory level and tests detecting CAD are not performed in 26% of individuals with diabetes [19].

Nevertheless, young patients with at least one risk factor for CAD should be closely monitored, and the prognostic value of non-cardiac conditions and gene polymorphism of the early onset and exacerbation of CAD is currently an active area of research [20, 21].

Patients with CKD should be considered at high risk of complications when in need for surgical revascularisation. However, further analysis to establish the actuarial glomerular filtration rate that increase the risk of surgery above the acceptable level in elderly patients is required.

## CONCLUSIONS

We demonstrated that typical risk factors of CAD (such as obesity, hypertension, diabetes, and hyperlipidaemia) have also high prevalence in CABG patients  $\leq 50$  yo and  $\geq 80$  yo. Nevertheless, these increasing cohorts of young and old patients requiring CABG differ from the standard EuroSCORE population. Therefore, proper risk adjustment remains challenging in these groups, and general risk stratification models should be applied with caution. Patient age-specific risk adjustment can allow adequate qualification for surgical treatment and optimisation of health care costs.

**Conflict of interest:** none declared

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# Jak ocenić ryzyko wystąpienia powikłań pooperacyjnych po pomostowaniu aortalno-wieńcowym u chorych poniżej 50. i powyżej 80. roku życia? Retrospektywne badanie przekrojowe

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## Streszczenie

**Wstęp:** Choroba wieńcowa pozostaje jedną z głównych przyczyn zgonów w krajach rozwiniętych. Zwiększa się również liczba zarówno młodych, jak i starszych pacjentów, którzy wymagają chirurgicznej rewaskularyzacji. Powszechnie stosowane skale do oceny ryzyka zabiegu operacyjnego (EuroSCORE II, STS risk score) powstały, aby przeprowadzić analizę epidemiologiczną oraz umożliwić instytucjonalną kontrolę jakości. Ponadto pozwalają one na przedoperacyjną ocenę ryzyka oraz właściwie poinformowanie pacjenta. Mimo ich ciągłego rozwoju i udoskonalania, obliczenia są prowadzone na podstawie danych zebranych od typowej populacji chorych, poddawanych zabiegom kardiologicznym. Badacze podkreślają obecnie, że skale te będą wymagały dalszych modernizacji, ponieważ zmiany demograficzne w populacji pacjentów cierpiących z powodu chorób układu sercowo-naczyniowego są nieuniknione.

**Cel:** Celem pracy była analiza epidemiologiczna dwóch rosnących i nietypowych grup chorych poddawanych pomostowaniu aortalno-wieńcowemu (CABG) oraz określenie przedoperacyjnych czynników ryzyka wystąpienia powikłań pooperacyjnych.

**Metody:** Przeprowadzona analiza jest retrospektywnym badaniem przekrojowym, do którego włączono 388 kolejnych chorych powyżej 80. rż. oraz 190 kolejnych pacjentów poniżej 50. rż., u których przeprowadzono CABG w latach 2010–2014. Analizowane dane pochodzą z dokumentacji medycznej chorych.

**Wyniki:** U większości włączonych do analizy osób zaobserwowano typowe czynniki ryzyka chorób układu sercowo-naczyniowego, bez względu na grupę wiekową. Wśród starszych pacjentów cukrzyca występowała 2-krotnie częściej niż w populacji z badania EuroSCORE. Podobną zależność zaobserwowano w przypadku nadciśnienia tętniczego, które występowało częściej niż w populacji EuroSCORE w obu grupach wiekowych. Podsumowując wszystkie powikłania pooperacyjne, przynajmniej jedno wystąpiło zdecydowanie częściej w grupie starszych chorych niż u młodszych pacjentów (10% vs. 20,9%;  $p = 0,001$ ). Zdecydowana większość pooperacyjnych niepożądanych zdarzeń sercowych i mózgowo-naczyniowych (MACCE) prowadziła do zgonu w grupie starszych chorych (79,4%). Wśród osób powyżej 80. rż. wyższa klasa wg *New York Heart Association* (NYHA) ( $p = 0,001$ ; OR 2,05 [1,34–3,12] na każdą kolejną klasę) i niewydolność nerek ( $p = 0,02$ ; OR 2,47 [1,16–5,25]) zwiększały ryzyko wystąpienia MACCE, podczas gdy wyższa przedoperacyjna frakcja wyrzutowa lewej komory (LVEF) zmniejszała to ryzyko ( $p = 0,002$ ; OR 0,81 [0,7–0,93] na każde kolejne 5%). Przyjęcie w trybie pilnym zwiększało ryzyko wystąpienia jakiegokolwiek powikłania wśród młodszych chorych ( $p = 0,007$ ; OR 3,63; 95% CI 1,37–9,62). Z kolei wśród osób powyżej 80. rż. tryb przyjęcia nie wiązał się z wystąpieniem powikłań pooperacyjnych.

**Wnioski:** Zarówno młodzi, jak i starsi pacjenci wymagający CABG różnią się od typowej populacji EuroSCORE. Powikłania pooperacyjne są częstsze u starszych chorych i wystąpienie MACCE wiąże się w tej grupie z dużą śmiertelnością. Pacjenci z czynnikami ryzyka wystąpienia tego powikłania (wysoka klasa NYHA, niewydolność nerek, niska LVEF) powinni być ostrożnie ocenieni i rozważnie zakwalifikowani oraz dokładnie monitorowani po zabiegu operacyjnym.

**Słowa kluczowe:** choroba wieńcowa, pomostowanie aortalno-wieńcove, ocena ryzyka, powikłania pooperacyjne, niepożądane zdarzenia sercowe i mózgowo-naczyniowe

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