

## CLINICAL STUDY

# Long-term results of myocardial revascularization in patients with multivessel disease

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**ABSTRACT**

**BACKGROUND:** Choosing the method of revascularization – coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) – remains debatable.

**METHODS:** We selected 406 patients with multivessel disease who underwent PCI with a drug-eluting stent (DES) (n = 200, 100 with a SYNTAX score (SS) ≤ 22 and 100 with a SS 23–32); and CABG (n = 206, 100 with a SS ≤ 22 and 106 with a SS 23–32). The mean follow-up period was 9±1.9 years. The endpoints of the study were as follows: major adverse cardiac and cerebrovascular events (MACCE), a repeat revascularization (RR), diminished left ventricular ejection fraction (LVEF), and high SS in dynamics.

**RESULTS:** Patients with an intermediate SS needed RR more often with PCI than after CABG (64 % vs 22.6 %; HR: 3.52; CI: 2.19–5.66; p < 0.001). We found no significant differences for other MACCE between the groups. The decrease in LVEF was greater in the low SS subgroup in operated patients than after PCI (39.5 % vs 27.7 %; HR: 0.57; CI: 0.34–0.98; p = 0.04). The difference between the initial and final SS, was greater after the CABG than after PCI (43.5 % vs 10.9 %; HR: 0.26; CI: 0.14–0.47; p < 0.001).

**CONCLUSIONS:** After 9 ± 1.9 years in intermediate SS group CABG exhibited an advantage over PCI with DES in terms of the MACCE indicators due to a smaller number of RR in the CABG group. The CABG group showed a more significant progression of atherosclerosis, and more heart failure cases (Tab. 2, Fig. 4, Ref. 29). Text in PDF [www.elis.sk](http://www.elis.sk)

**KEY WORDS:** coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, SYNTAX score.

**Abbreviations:** CHD – coronary heart disease, CABG – coronary artery bypass grafting, CHF – chronic heart failure, CI – confidence interval, CVD – cardiovascular diseases, DES – drug-eluting stent, GFR – glomerular filtration rate, HR – hazard ratio, LVEF – left ventricular ejection fraction, MACCE – major adverse cardiac and cerebrovascular events, MI – myocardial infarction, PCI – percutaneous coronary intervention, RR – repeat revascularization, RCT – randomized clinical trials, SS – SYNTAX score, TIA – transient ischemic attack

**Introduction**

Despite the development and improvement of highly effective methods of diagnosis and treatment, cardiovascular diseases

(CVD) continue to constitute the leading causes of death and disability (1, 2). According to the World Health Organization (WHO), 17.9 million people die from CVD annually, accounting for 32 % of all deaths worldwide; and 85 % of these deaths are caused by heart attack and stroke (1, 3). Although myocardial revascularization is considered to be the primary method of treatment of coronary heart disease (CHD), the matter of choosing a method of revascularization, i.e., coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) – remains debatable.

The issues of immediate and one-year results, which the effectiveness of surgical and interventional methods of treatment have been well analyzed and widely covered, but long-term results with a follow-up period of nine or more years are less well studied. Thus, the follow-up periods in previously conducted randomized clinical trials (RCTs) in which the effectiveness of CABG and PCI in patients with multivessel disease was evaluated were 1, 3, 5, and 7 years (4–10); and an RCT with a 10-year follow-up period was reported in the SYNTAX study (11). Importantly, it should be noted that the authors of earlier studies used previous-generation stents (4–10). Considering the introduction of a new generation of stents into clinical practice and the improvement in stenting technologies that have proven to be more effective (12–14) than previous approaches, one can expect a significant improvement in long-term results with PCI. The authors of several studies have

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noted a significant progression in atherosclerosis after CABG in arteries located proximal to the distal anastomosis (15, 16), while other reports revealed occlusion of auto-venous bypasses after CABG of up to 45–50 % of cases by 8–10 years after the operation (15, 16). In this regard, the assessment of long-term results of CABG and PCI with a follow-up period of more than nine years would be of extreme practical and scientific interest. It should also be noted that most of the previously published studies were conducted in European countries and USA, while in Asian countries, their numbers are limited (10, 17, 18). For this reason, the present comparison of the long-term results of PCI and CABG in patients with multivessel coronary artery disease in whom the primary intervention was performed before the age of 65 years is relevant and timely. This was a two-center study that was conducted at the National Research Cardiac Surgery Center in Astana and at the Pavlodar Regional Cardiology Center.

**Methods:**

*Study design and patients:*

This work was a longitudinal, retrospective, clinical cohort study, and our study protocol was developed by the principal investigators (the first two authors) and approved by the local ethics committees of the participating centers. The researchers are solely responsible for the completeness and accuracy of the data and their analysis, as well as for the compliance of the study with respect to protocol.

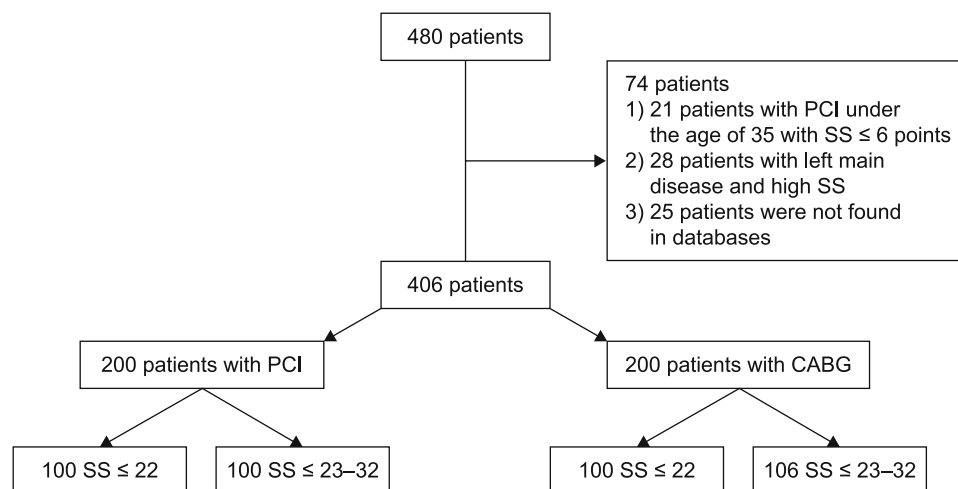
Based on the archives of case reports of the National Research Cardiac Surgery Center in Astana and the Regional Cardiology Center in Pavlodar, we selected 406 patients who had undergone primary PCI with the placement of a drug-eluting stent (DES) during the period 2010–2013 (n = 200), or who underwent primary CABG (n = 206) with or without cardiopulmonary bypass using

standard techniques. Patients with prior cardiac surgery or stenting were excluded from the study.

The study encompassed patients with stable forms of coronary artery disease who were admitted to our centers during the indicated period, and who showed multivessel disease and exhibited low or intermediate SYNTAX scores (SS) (i.e., ≤ 32). The exclusion criteria were patients with acute coronary syndrome with an ST elevation, left main coronary artery disease, an SS ≥ 33, age over 65, single-vessel coronary disease, an aneurysm of the left ventricle, severe valvular dysfunction in combination with CAD, rheumatic or congenital heart defects, a left ventricular ejection fraction (LVEF) of less than 40 %, severe chronic renal failure (i.e., a glomerular filtration rate(GFR) using the Cockcroft-Gault equation of less than 30 ml/min/1.73 m<sup>2</sup>).

Patients were followed up according to the clinical electronic databases of the centers, the clinical medical information system (CMIS, Polyclinic National Register; <https://pvd.dmed.kz>), electronic register of inpatient ERIP (National Inpatient Register; [www.eisz.kz](http://www.eisz.kz)), and via personal contacts with the patients. The strategy of percutaneous and surgical intervention and the tactics of drug therapy were conducted in accordance with the recommendations for myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) (19).

We initially selected 480 individuals, of which 250 patients had undergone PCI and 230 patients underwent CABG. Subsequently, 74 patients were excluded from the analysis for the following reasons: 1) 21 patients with PCI under the age of 35 with an SS ≤ 6 points were excluded from the study for the purpose of group comparability; 2) 28 patients who had left main disease and a high SS; and 3) 25 patients with no data in outpatient or inpatient registries and who provided no contact details. While we originally also planned to include patients with a high SS and



**Fig. 1.** Inclusion and randomization of patients with multivessel coronary disease. CABG = coronary artery bypass grafting, PCI= percutaneous coronary intervention, SS = SYNTAX score reflects the degree of damage to the coronary artery.

those with left main disease in the study, after analyzing the archival data for the specified time period, we found that CABG prevailed in this group of patients and that a very small number of patients with such characteristics underwent PCI. For this reason, we decided to exclude these patients from our study (Fig. 1), as well as the patients for whom the choice of revascularization method was obvious.

#### SYNTAX score

We herein included patients with low and intermediate scores (< 33) based on SYNTAX, which provides an anatomical assess-

ment of the degree of coronary artery damage. Since in the period 2010–2013 the SYNTAX score was not used when choosing a revascularization method, we performed the SS assessment retrospectively based on archival angiograms in accordance with the SYNTAX assessment algorithm (<https://syntaxscore2020.com>) (20, 21). Thus, 200 patients with a low SS and 206 patients with an intermediate SS were selected.

#### Endpoints and definitions

The clinical endpoints of the study were a combination of major adverse cardiac and cerebrovascular events (MACCE) and their

**Tab. 1. Baseline characteristics of patients with multi-vessel disease.**

| Criteria                                      | SYNTAX Categories |              |        |                |              |        |
|---|-------------------|--------------|--------|----------------|--------------|--------|
|   | Low               |              | p      | Intermediate   |              | p      |
|   | PCI (n=100)       | CABG (n=100) |        | PCI (n=100)    | CABG (n=106) |        |
| Age, years                                    | 54.3±5.9          | 55.5±6.1     | 0.13   | 55.6±6.5       | 56.7±6.0     | 0.2    |
| Women   | 15 (15%)          | 16 (16%)     | 0.8    | 20 (20%)       | 19 (17.9%)   | 0.7    |
| Men   | 85 (85%)          | 84 (84%)     | 0.8    | 80 (80%)       | 87 (82.1%)   | 0.7    |
| Heredity                                      | 29 (29%)          | 25 (25%)     | 0.52   | 29 (29%)       | 24 (22.6%)   | 0.29   |
| Current smoker                                | 46 (46%)          | 33 (33%)     | 0.06   | 31 (31%)       | 23 (21.7%)   | 0.12   |
| Body mass index (BMI), kg/m <sup>2</sup>      | 29.3±4.2          | 28.9±4.5     | 0.5    | 30.8±5.5       | 29.4±4.7     | 0.047  |
| Weight categories                             |                   |              |        |                |              |        |
| Normal weight, BMI 18–24.9                    | 11 (11%)          | 17 (17%)     | 0.22   | 11 (11%)       | 9 (8.5%)     | 0.8    |
| Overweight, BMI 25–29.9 kg/m <sup>2</sup>     | 40 (40%)          | 38 (38%)     | 0.77   | 38 (38%)       | 53 (50%)     | 0.08   |
| Obesity 1 dg, BMI 30–34.9 kg/m <sup>2</sup>   | 36 (36%)          | 33 (33%)     | 0.65   | 27 (27%)       | 26 (24.5%)   | 0.6    |
| Obesity 2 dg, BMI 35–39.9 kg/m <sup>2</sup>   | 8 (8%)            | 10 (10%)     | 0.62   | 16 (16%)       | 17 (16%)     | 0.9    |
| Obesity 3 dg, BMI ≥40 kg/m <sup>2</sup>       | 5 (5%)            | 2 (2%)       | 0.24   | 8 (8%)         | 1 (0.9%)     | p>0.05 |
| Waist circumference, male                     | 102.3±10.1        | 102.8±13.8   | 0.84   | 105±11.3       | 103.7±10.4   | 0.53   |
| Waist circumference, female                   | 104±11.6          | 102.5±8.5    | 0.78   | 108.6±17.1     | 103±8.2      | 0.62   |
| Dyslipidemia                                  | 79 (79%)          | 79 (79%)     | 1.0    | 81 (81%)       | 85 (80.2%)   | 0.8    |
| Atherogenic index                             | 3.6±1.4           | 3.6±1.5      | 0.99   | 3.9±1.6        | 4.2±1.9      | 0.27   |
| Diabetes mellitus                             | 36 (36%)          | 25 (25%)     | 0.09   | 39 (39%)       | 34 (32.1%)   | 0.3    |
| GFR, ml/min/1.73m <sup>2</sup>                | 89.5±20.2         | 89.8±16.5    | 0.9    | 91.8±19.6      | 91.34±19.9   | 0.8    |
| Hypertension                                  | 98 (98%)          | 100 (100%)   | 0.15   | 97 (97%)       | 104 (98.1%)  | 0.6    |
| Degrees of hypertension                       |                   |              |        |                |              |        |
| Mild hypertension                             | 6 (6%)            | 5 (5%)       | 0.7    | 7 (7%)         | 2 (1.9%)     | 0.068  |
| Moderate hypertension                         | 36 (36%)          | 34 (34%)     | 0.07   | 24 (24%)       | 35 (33%)     | 0.15   |
| Severe hypertension                           | 56 (56%)          | 61 (61%)     | 0.07   | 65 (65%)       | 67 (63.2%)   | 0.78   |
| Previous myocardial infarction                | 65 (65%)          | 59 (59%)     | 0.38   | 61 (61%)       | 69 (65.1%)   | 0.54   |
| Previous stroke or transient ischaemic attack | 9 (9%)            | 6 (6%)       | 0.59   | 4 (4%)         | 11 (10.4%)   | 0.13   |
| Arrhythmia, atrial fibrillation               | 18 (18%)          | 16 (16%)     | 0.7    | 21 (21%)       | 21 (19.8%)   | 0.83   |
| Peripheral arterial disease                   | 11 (11%)          | 14 (14%)     | 0.52   | 22 (22%)       | 24 (22.6%)   | 0.91   |
| Chronic lung disease                          | 11 (11%)          | 12 (12%)     | 0.82   | 14 (14%)       | 13 (12.3%)   | 0.71   |
| Previous pulmonary embolism                   | 0                 | 0            |        | 1              | 0            |        |
| Charlson Comorbidity Index (21, 22)           | 4.2±1.8           | 4.8±1.7      | 0.03   | 4.8±2          | 5.1±2.1      | 0.21   |
| Left ventricular ejection fraction, %         | 56 (52–60)        | 55 (49–59)   | 0.02   | 54.4±7.0       | 54.9±6.8     | 0.6    |
| SYNTAX Score                                  | 14 (10–17.9)      | 16.7 (13–20) | 0.01   | 24.5 (23–27.5) | 27.5 (24–30) | 0.000  |
| Two-vessel disease                            | 76 (76%)          | 63 (63%)     | 0.046  | 36 (36%)       | 31 (29.2%)   | 0.3    |
| LAD+CF  | 36 (36%)          | 38 (38%)     | 0.77   | 13 (13%)       | 15 (14.2%)   | 0.8    |
| LAD+RSA                                       | 24 (24%)          | 24 (24%)     | 1.0    | 22 (22%)       | 16 (15.1%)   | 0.2    |
| CF+RSA  | 16 (16%)          | 1 (1%)       | <0.001 | 1 (1%)         | 0            |        |
| Three-vessel disease                          | 24 (24%)          | 37 (37%)     | 0.046  | 64 (64%)       | 75 (70.8%)   | 0.3    |

Values are shown as mean ± SD (n), Me (Q1–Q3) or % (n/N). CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention; Atherogenic index (AI) was calculated using the formula AI = (total cholesterol – density lipoproteins)/high-density lipoproteins; GFR = glomerular filtration rate according to the Cockcroft–Gault formula; LAD – left anterior descending artery, CF – left circumflex artery, RCA – right coronary artery; dg = degree

individual components: all-cause death, cerebrovascular accident (transient ischemic attack (TIA)/stroke), myocardial infarction (MI), repeated revascularization, development of chronic heart failure (CHF), and a high category of coronary artery lesion as characterized by an SS  $\geq$  33.

The cause of death was classified as definite cardiovascular, definite non-cardiovascular, and undetermined death. If it was not possible to establish the exact cause of death, then the cases were conservatively regarded as cardiovascular. The diagnoses of cerebrovascular events (TIA/stroke) and MI were entered into this study in the form they were established at the time of admission of patients to hospitals, and upon official registration of these events in outpatient and inpatient state registries in accordance with the definitions of these events based on accepted recommendations at the time of establishment.

Repeated revascularization – either by PCI or by surgical intervention – was registered based on information on the procedures conducted in our country’s hospitals and in clinics abroad. Repeated revascularization was established using our national outpatient and inpatient registries, as well as by obtaining information directly from patients or their relatives. The development of CHF was assessed clinically, with the determination of the left ventricular ejection fraction (LVEF) and dilatation of the heart

chambers; and these were compared with baseline data. We also recalculated SS for patients who underwent repeated coronary angiography over time.

Statistical analysis

Continuous variables following a normal distribution are presented as means  $\pm$  standard deviation and were compared using Student’s *t*-test. Variables with a non-normal distribution were described using median values (Me) and lower and upper quartiles (Q1–Q3), and the Mann-Whitney U-test was used for comparisons. Categorical data are presented as frequencies (absolute numbers and percentages) and compared using the  $\chi^2$  or Fisher’s exact-probability test. We recorded events for the specified observation period (from 2010 to 2022) and coded them as binary indicators. The frequency of distant events was estimated using Kaplan-Meier curves with statistical comparisons performed using the log-rank test. Endpoint risk was assessed using the Cox regression method, where PCI was considered as an independent predictor compared to the CABG group. We executed subgroup analysis according to Syntax score II (21), and a two-tailed p value  $<$  0.05 was an indication of statistical significance. All the statistical analyses were conducted using IBM SPSS Statistics 23.0 (IBM Corporation, Armonk, NY, USA).

Tab. 2. Clinical Outcomes According to SYNTAX Score Categories and Revascularization Treatment.

|  | SYNTAX Categories |                 |                          |         |                   |                    |                          |        |
|--|-------------------|-----------------|--------------------------|---------|-------------------|--------------------|--------------------------|--------|
|  | Low               |                 |                          |         | Intermediate      |                    |                          |        |
|  | PCI<br>(n=100)    | CABG<br>(n=100) | Hazard ratio<br>(95% CI) | P       | PCI<br>(n=100)    | CABG<br>(n=106)    | Hazard ratio<br>(95% CI) | P      |
| MACCE  | 68 (68%)          | 55 (55%)        | 1.02 (0.71–1.46)         | 0.95    | 81 (81%)          | 53 (50%)           | 2.01 (1.41–2.85)         | <0.001 |
| Repeat revascularization                                       | 60 (60%)          | 34 (34%)        | 1.44 (0.94–2.19)         | 0.09    | 64 (64%)          | 24 (22.6%)         | 3.52 (2.19–5.66)         | <0.001 |
| All-cause death /MI/Stroke/TIA                                 | 38 (38%)          | 33 (33%)        | 0.99 (0.62–1.59)         | 0.98    | 35 (35%)          | 43 (40.6%)         | 1.08 (0.69–1.69)         | 0.74   |
| Cardiac death/ MI/ Stroke /TIA                                 | 36 (36%)          | 27 (27%)        | 1.14 (0.69–1.89)         | 0.6     | 28 (28%)          | 39 (36.8%)         | 0.95 (0.58–1.55)         | 0.84   |
| Death, all-cause   | 10 (10%)          | 19 (19%)        | 0.48 (0.22–1.03)         | 0.06    | 22 (22%)          | 21 (19.8%)         | 1.24 (0.68–2.27)         | 0.48   |
| Cardiac death  | 5 (5%)            | 12 (12%)        | 0.38 (0.13–1.07)         | 0.07    | 13 (13%)          | 16 (15.1%)         | 0.93 (0.45–1.94)         | 0.85   |
| Non-cardiac death  | 5 (5%)            | 7 (7%)          | 0.66 (0.21–2.08)         | 0.48    | 9 (9%)            | 5 (4.7%)           | 2.29 (0.77–6.87)         | 0.14   |
| Average age of death*  | 60.8 $\pm$ 7.58   | 62.8 $\pm$ 5.26 |                          | 0.41    | 62.64 $\pm$ 6.48  | 63.62 $\pm$ 6.29   |                          | 0.62   |
| Mean number of years after intervention/operation until death* | 8.1 $\pm$ 2.64    | 6.9 $\pm$ 3.25  |                          | 0.33    | 5.11 $\pm$ 2.01   | 6.17 $\pm$ 2.37    |                          | 0.12   |
| Myocardial infarction  | 22 (22%)          | 11 (11%)        | 1.69 (0.82–3.51)         | 0.16    | 14 (14%)          | 11 (10.4%)         | 1.69 (0.76–3.75)         | 0.19   |
| Stroke/TIA   | 15 (15%)          | 10 (10%)        | 1.21 (0.54–2.71)         | 0.64    | 10 (10%)          | 19 (17.9%)         | 0.75 (0.35–1.63)         | 0.47   |
| Pulmonary embolism during follow-up                            | 2 (2%)            | 1 (1%)          |                          | >0.05   | 0                 | 0                  |                          |        |
| LVEF during follow-up (%)*                                     | 55 (50–59)        | 51.9 (44–58)    |                          | 0.02    | 51.3 $\pm$ 11.7   | 50.9 $\pm$ 10.7    |                          | 0.85   |
| Diminution in LVEF   | 23 (27.7%)        | 34 (39.5%)      | 0.57 (0.34–0.98)         | 0.04    | 23 (29.1%)        | 32 (42.7%)         | 0.84 (0.49–1.45)         | 0.53   |
| Heart chambers dilatation+valvular insufficiency               | 8 (9.6%)          | 17 (19.8%)      | 0.42 (0.18–0.98)         | 0.046   | 12 (15.2%)        | 15 (20%)           | 0.98 (0.46–2.1)          | 0.95   |
| SYNTAX Score during follow-up*                                 | 14.5 (8–22.3)     | 26 (20.5–33.5)  |                          | < 0.001 | 19.5 (10.5–26.88) | 34.5 (27.75–41.75) |                          | <0.001 |
| SYNTAX Score =0  | 3 (4.2%)          | 0               |                          | 0.1     | 3 (5.4%)          | 0                  |                          | 0.1    |
| SYNTAX Score, $\leq$ 22  | 53 (73.6%)        | 24 (35.8%)      | 1.86 (1.15–3.01)         | 0.01    | 30 (53.6%)        | 4 (9.8%)           | 7.52 (2.64–21.42)        | <0.001 |
| SYNTAX Score, 23–32  | 11 (15.3%)        | 23 (34.3%)      | 0.38 (0.19–0.79)         | 0.01    | 14 (25%)          | 10 (24.4%)         | 1.31 (0.57–2.97)         | 0.52   |
| SYNTAX Score, $\geq$ 33  | 5 (6.9%)          | 20 (29.9%)      | 0.19 (0.07–0.51)         | 0.001   | 9 (16.1%)         | 27 (65.9%)         | 0.36 (0.17–0.76)         | 0.008  |
| Left main disease during follow-up                             | 1 (1.4%)          | 3 (4.5%)        | 4.29 (0.44–41.4)         | 0.2     | 5 (8.9%)          | 5 (12.2%)          | 1.04 (0.29–3.64)         | 0.95   |
| Stent restenosis/bypass graft occlusion                        | 42 (56%)          | 35 (52.2%)      |                          | 0.65    | 32 (48.5%)        | 27 (69.2%)         |                          | 0.78   |

Values are number of events (%), unless otherwise indicated. \* – Values are shown as mean  $\pm$  SD (n), Me (Q1–Q3) or % (n/N). CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; MACCE= major adverse cardiac and cerebrovascular events = All-cause death +MI+Stroke/TIA+ Repeat revascularization; MI = myocardial infarction; TIA = transient ischemic attack; LVEF = Left ventricular ejection fraction

## Results

### Baseline characteristics

A total of 406 patients with multivessel disease who underwent primary interventions in 2010–2013 were retrospectively sampled. Of these, 200 patients underwent primary PCI with DES placement ( $n = 200$ , 100 patients with an SS  $\leq 22$ ; and 100 patients with an SS of 23–32). Two hundred six patients also underwent CABG ( $n = 206$ , 100 patients with SS  $\leq 22$ ; and 106 patients with an SS of 23–32).

Baseline clinical and angiographic characteristics of the patients included in the study are shown in Table 1. The groups did not differ with respect to age or sex, but the mean body mass index (BMI) in the intermediate SS group was 1.4 % higher in patients with PCI than in operated patients ( $30.8 \pm 5.5$  vs  $29.4 \pm 4.7$ , respectively,  $p = 0.04$ ). In the low-Syntax score groups, patients did not differ significantly with respect to BMI, the distribution of body weight, or average waist circumference for both men and women. Blood lipid levels did not reach the target values in 79 % of patients with low SS or in 80 % of patients with intermediate SS. Atherogenic index ((total cholesterol – density lipoproteins)/high-density lipoproteins) was also similar between groups. As for heredity (the presence of first-line relatives with cardiovascular diseases or diabetes), we noted no statistical differences between the groups. Although the number of smokers showed a tendency to be higher in the PCI group relative to the CABG group (46 % vs 33 % for low SS,  $p = 0.06$ ; and 31 % vs 21.7 % for intermediate SS,  $p = 0.12$ ), this apparent difference was not statistically significant. The average GFRs estimated using the Cockcroft–Gault formula in the groups were the same, and mean LVEF values were comparable (56 (52–60) vs 55 (49–59) for low SS PCI and CABG groups,  $p = 0.02$ ; and  $54.4 \pm 7.0$  vs  $54.9 \pm 6.8$ ,  $p = 0.6$  in the intermediate SS groups). More than 97 % of patients in the groups reported arterial hypertension, but the groups did not differ in their degree of hypertension, and there were no statistical differences in the prevalence of diabetes mellitus (DM). The groups did not differ significantly in patient histories of cerebrovascular accident, myocardial infarction, arrhythmias, peripheral atherosclerotic vascular disease, or chronic obstructive pulmonary disease (COPD), and, therefore, the average value of the Charlson co-morbidity index (22, 23) for stented and operated patients did not differ. According to the Syntax score, the PCI and CABG groups differed in the range of up to three points (respectively, 14 (10–17.8) vs 16.7 (13–20),  $p = 0.01$ , for low SS; and 24.5 (23–27.5) vs 27.5 (24–30),  $p < 0.001$  in the intermediate SS group), while in the intermediate SS group, the ratios of patients with two- or three-vessel disease were comparable. However, patients with three-vessel disease in the low SS group were more likely to undergo CABG than stenting (37 % and 24 %,  $p = 0.04$ ) (Tab. 1).

### Outcomes

Data collection and analysis were carried out from the time of the initial intervention (2010–2013) until 2022, and the follow-up period averaged  $9 \pm 1.9$  years. The frequency of MACCE during the follow-up period was generally significantly higher in

patients who underwent PCI (74.5 %) compared with the CABG group (52.4 %) (hazard ratio, (HR) 1.4; confidence interval (CI), 1.09–1.8);  $p = 0.008$ ). When we analyzed the low and moderate SS groups, MACCE were more frequently recorded after PCI than after CABG, and this difference was statistically significant for the intermediate SS group, but not for the low SS group (Tab. 2).

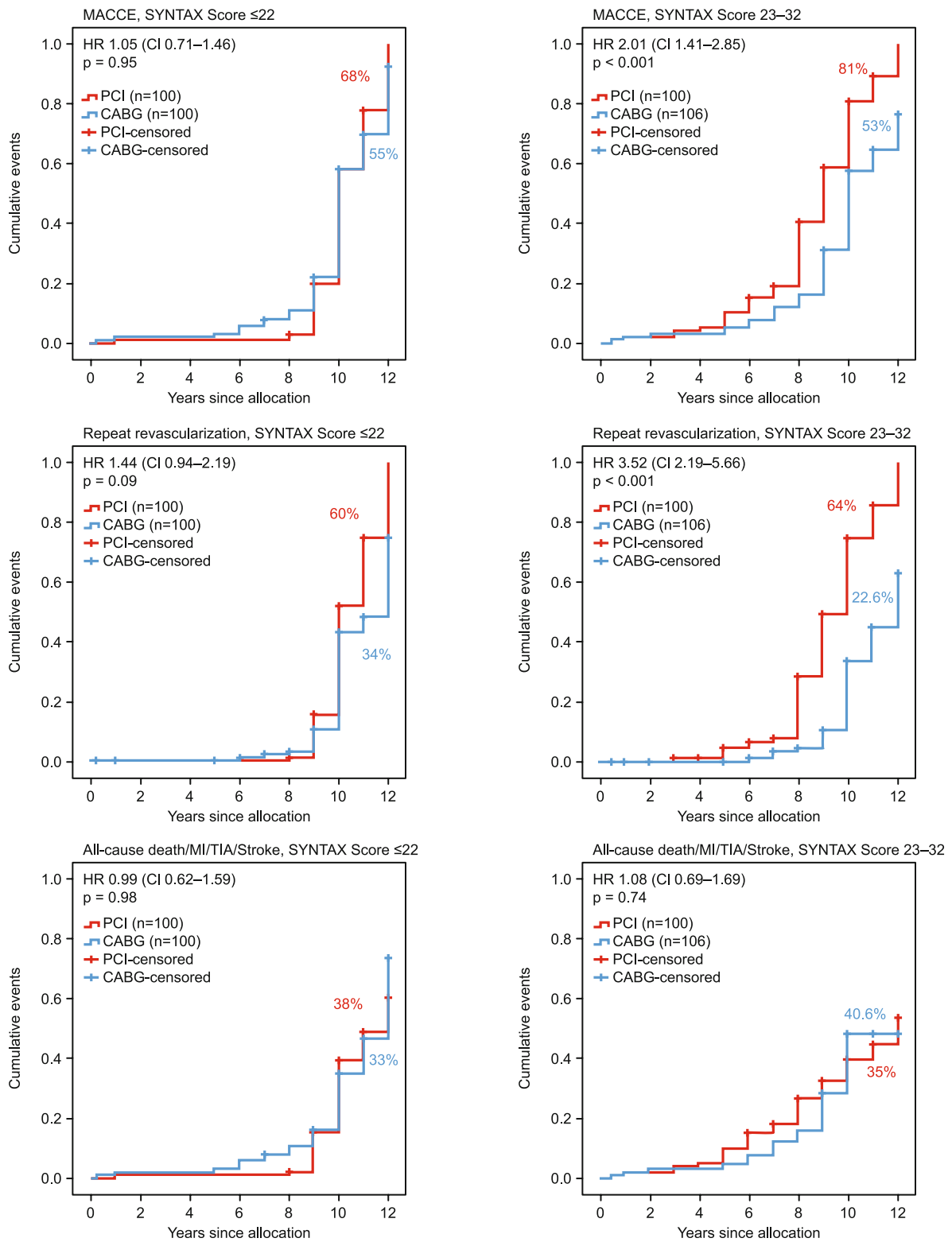
It was noteworthy that this difference was due to repeated revascularization. Thus, stented patients with intermediate SS needed repeated revascularization significantly more often than operated patients (64 % vs 22.6 %; HR, 3.52 (CI, 2.19–5.66),  $p < 0.001$ ). However, although patients with low SS also had a predominance of repeated revascularization in the PCI group compared to the CABG group, this was not statistically significant (60 % vs 34 %, respectively; HR, 1.44 (CI, 0.94–2.19);  $p = 0.09$ ) (Fig. 2).

We observed that the groups did not exhibit significant differences in terms of the other MACCE combinations or in their individual components (i.e., all-cause-death/MI/stroke/TIA, cardiac death/MI/stroke/TIA, all-cause-deaths, separate cardiac and non-cardiac deaths, or the development of MI/stroke/TIA) (Tab. 2). We ascertained that in the low SS subgroup of the CABG group, the number of cases of cardiac death in absolute terms was recorded more often than in the PCI group, although this difference was not significant (12 % and 5 %, respectively;  $p = 0.07$ ) (Tab. 2). The mean age of the deceased patients did not manifest statistically significant differences, neither between groups nor in subgroups of intermediate or low SS. Lethal cases were observed on average at a similar time interval both after stenting and after CABG ( $8.1 \pm 2.64/6.9 \pm 3.25$ ,  $p = 0.33$  for low SS; and  $5.11 \pm 2.01/6.17 \pm 2.37$ , respectively;  $p = 0.12$  for intermediate SS). However, deaths among patients with low SS were detected two years later than in patients with intermediate SS (8 (5–11) years and 6 (4–8) years, respectively;  $p = 0.002$ ). Although there were no statistical differences between the groups in terms of the incidence of MI or cerebrovascular disorders, it was notable that there was a non-significant quantitative preponderance of cases of MI in the low SS group in stented patients compared to operated patients (22 % and 11 %, respectively;  $p = 0.16$ ), and also a non-significant quantitative difference between cases of TIA/stroke in the intermediate risk group after CABG vs after PCI (17.9 % and 10 %, respectively;  $p = 0.47$ ) (Tab. 2).

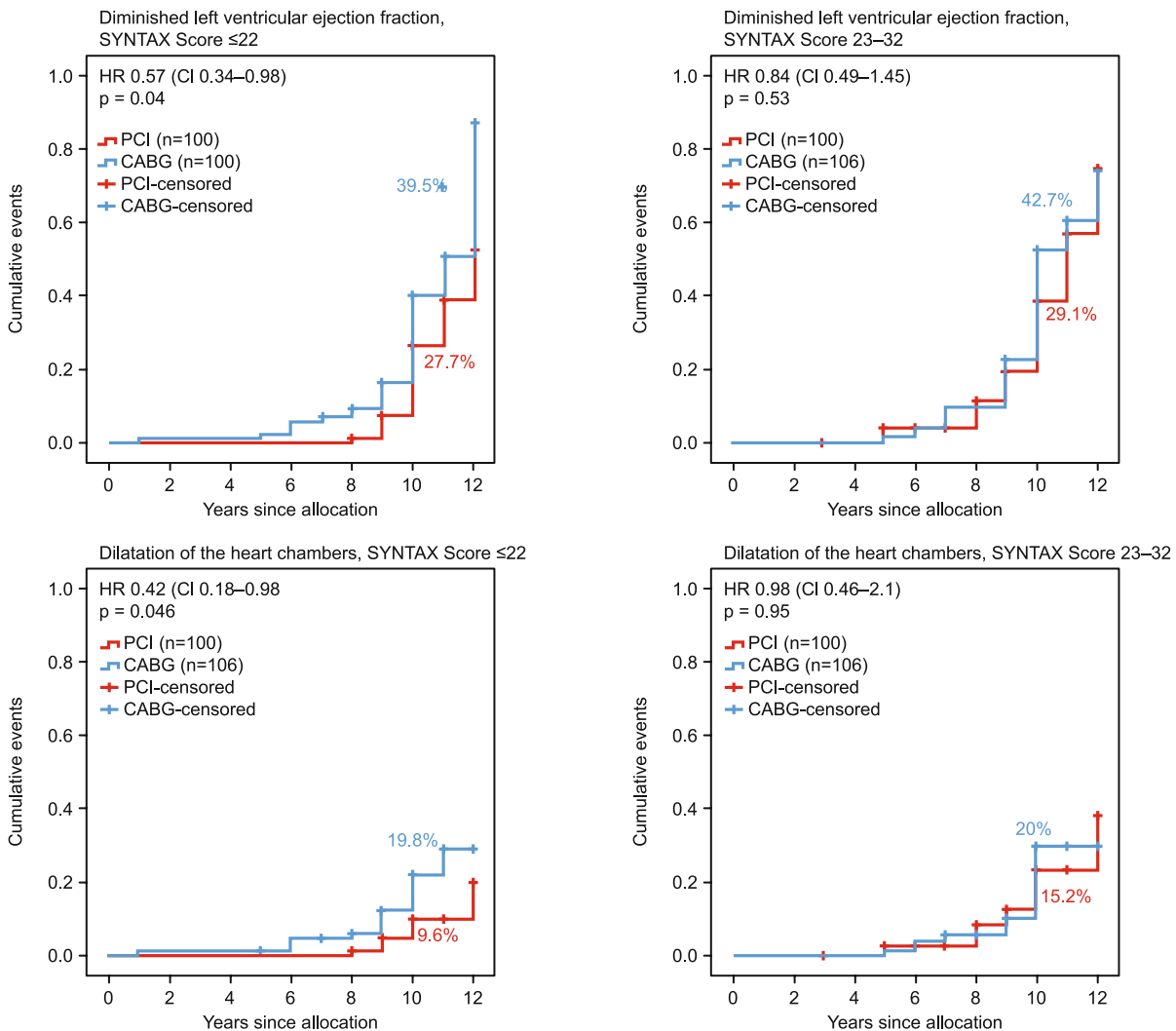
The duration without angina symptoms was two years longer in the intermediate SS group in operated patients than in stented patients (5 (0.38–6) vs 3 (1–5), respectively;  $p = 0.02$ ). In the low SS group, anginal complaints recurred on average after the same time interval post-initial intervention ( $4.62 \pm 2.93$  for PCI and  $4.62 \pm 3$  for CABG,  $p = 0.99$ ).

The development and progression of CHF with a diminution in LVEF was observed in the low-risk subgroup of the CABG group, with a median LVEF for this subgroup of 51.9 (44–58) vs the PCI group at 55 (50–59) ( $p = 0.02$ ). Subsequent analysis depicted a reduction in LVEF from baseline as significantly more common in the low-risk group after CABG compared with patients after PCI (39.5 % vs 27.7 %; HR, 0.57 (CI, 0.34–0.98);  $p = 0.04$ ). Dilatation of all heart chambers with valvular insufficiency also developed more often in the low-risk group in operated patients compared





**Fig. 2.** Kaplan-Meier cumulative event curves for low (A, C, E) and intermediate (B, D, F) SS categories at the nine-year follow-up. CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention; SS = SYNTAX score; MACCE= major adverse cardiac and cerebrovascular events = All-cause-death +MI + Stroke/TIA+ Repeat revascularization; MI = myocardial infarction; TIA = transient ischemic attack; HR = hazard ratio; CI = confidence interval.



**Fig. 3.** Kaplan–Meier cumulative event curves for low (A, C) and intermediate (B, D) SS categories at the nine-year follow-up. CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention; SS = SYNTAX score; HR = hazard ratio; CI = confidence interval.

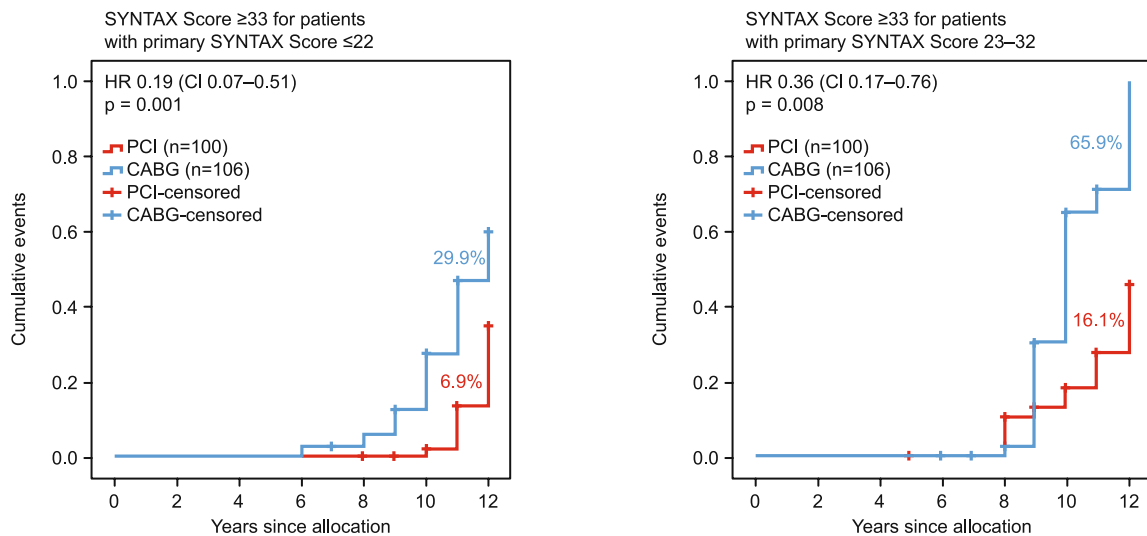
with stented patients (19.8 % vs 9.6 %; HR, 0.42 (CI, 0.18–0.98);  $p = 0.04$ ) (Fig. 3). The values for these indicators of CHF in the intermediate risk group, however, did not attain statistical significance.

The rate of atherosclerotic progression as calculated by initial Syntax score and after  $9 \pm 1.9$  years was higher in the CABG group than after PCI, both in the low-risk group (Me SS, 26 (20.5–33.5) vs 14.5 (8–22.3);  $p < 0.001$ ) and in the intermediate risk group (34.5 (27.85–41.85) vs 19.5 (10.5–26.9),  $p < 0.001$ ). Left main disease developed in a small number of patients with no significant difference between groups. High SS was achieved significantly more often by patients in the CABG groups compared to the PCI group (29.9 % vs 6.9 %; HR, 0.19 (CI, 0.07–0.51);  $p = 0.001$  for initially low SS; and 65.9 % and 16.1 %; HR, 0.36 (CI 0.17–0.76);  $p = 0.008$  for initially intermediate SS) (Fig. 4). We noted that the frequency of stent restenosis in the group of PCI patients and bypass graft restenosis in operated patients did not show a sig-

nificant difference with respect to either the low SS group (56 % and 52.2 %, respectively;  $p = 0.65$ ) or the intermediate category (48.5 % vs 69.2 %,  $p = 0.78$ ) (Tab. 2).

**Discussion**

Most authors who compared the long-term results of CABG and PCI in patients with multivessel disease demonstrated an advantage of CABG over PCI (4–6, 10–11, 24) in a number of parameters, including survival. At the same time, meta-analyses by Chew et al. and Brown et al. revealed the advantage of CABG over PCI in patients with multivessel disease and intermediate and high Syntax scores (25, 26), and comparable results for individuals with low SS (26). Our study revealed a predominance in the frequency of MACCE in patients with intermediate SS who underwent PCI compared with those who underwent CABG (81 % and 50 %, re-



**Fig. 4.** Kaplan-Meier curves for a high-gradation SYNTAX score ( $\geq 33$ ) in patients with primary low (A) and intermediate (B) SYNTAX scores ( $< 33$ ). CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention; HR = hazard ratio; CI = confidence interval.

spectively; HR, 2.01 (CI, 1.4–2.9);  $p < 0.01$ ). This difference was due solely to the augmented number of repeated revascularizations in the PCI group relative to the CABG group (64% and 22.6%, respectively; HR, 3.5 (CI, 2.2–5.7);  $p < 0.001$ ). We observed no statistical differences in the frequency of MACCE and in repeated revascularizations in the low SS group. The frequency of disparate combinations and individual components of MACCE (all-cause-deaths, or the development of MI or stroke) other than repeated revascularizations in our study did not differ significantly between the PCI and CABG groups, either in the intermediate or low SS group. Thus, the data obtained suggest that PCI with DES may have comparable long-term results with CABG in terms of survival, mortality, and the number of recurrent myocardial infarctions in patients with multivessel disease and an intermediate SS. This difference indicates that the study of long-term outcomes in the intermediate SS groups should continue to be of particular interest.

It should also be noted that most of the RCTs conducted reflected a shorter follow-up period, and 10-year monitoring of outcomes regarding patients with multivessel coronary disease was applied only in the SYNTAX study (11). The mean follow-up period of the present study was  $9 \pm 1.9$  years.

A particular difference between our study and other studies was that previously conducted prospective RCTs possessed certain inclusion criteria that did not allow extrapolation of the results to normal clinical practice (27). For example, in our study, we retrospectively selected patients who underwent CABG or PCI under actual clinical conditions. Meanwhile, in recent meta-analyses (24–26, 28) comprising RCTs in which the investigators compared the outcomes of PCI and CABG, disparate approaches were implemented to determine study endpoints, and a different composition of SS groups would have affected the authors' recommendations.

In this regard, it is intriguing that in our study the development of CHF with a drop in LVEF was more often detected in the low

SS subgroup after CABG than after PCI and in the intermediate SS groups, the incidence of CHF did not differ significantly between PCI and CABG methods. This difference was perhaps because in patients in the CABG group during the follow-up period, the progression of atherosclerosis (including the development of chronic occlusions) was significantly higher than in the PCI group. Only the LE MANS study included LVEF as a study endpoint, and 10-year follow-up showed improved outcomes after PCI relative to post-CABG groups (29). However, these authors unfortunately limited their study to patients with left main disease, and other RCTs in which stent and surgical data in patients with multivessel disease were compared did not report on LVEF.

It should also be stipulated that compared with earlier RCTs, our study was conducted in a setting that comprised more modern percutaneous and operative technologies, as well as new methods of drug therapy, and this may also constitute a reason for a variety of outcomes between studies. A limitation of the present study was the number of patients who failed to complete the study, and such data could also affect results.

Our study ultimately allowed us to assess the long-term results of PCI with DES and CABG in the low and moderate SS groups in patients with multivessel disease.

## Conclusions

In summary, after  $9 \pm 1.9$  years patients with ischemic heart disease patients and an intermediate SS needed repeated revascularizations more often with PCI than after CABG. There were no significant differences in the frequencies of all-cause-deaths, cardiac deaths, or the development of myocardial infarction or stroke during the follow-up period between the PCI and CABG groups. The decrease in LVEF was significantly higher in the low SS subgroup in operated patients than after PCI. Atherosclerotic



progression as calculated from the increase in SS values in the CABG group was significantly higher than in the PCI group, either in the intermediate or low SS category.

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