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Long-term outcomes of myocardial revascularization in patients with multivessel coronary artery disease and comorbid pathology

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Abstract

Objective. To assess the long-term outcomes of myocardial revascularization in patients with multivessel coronary artery disease and varying degrees of comorbidity.

Materials and methods. 406 patients with low and moderate Syntax scores (SS) (<33) underwent primary percutaneous coronary intervention (PCI) (n=200) with a drug-eluting stent, and coronary artery bypass grafting (CABG) (n=206). Patients were stratified by the Charlson Comorbidity Index (CCI) into 2 groups: 1) CCI ≤ 3(n=108/26.6%); 2) CCI ≥ 4(n=298/73.4%). 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, decreased left ventricular ejection fraction, and high SS in dynamics.

Results. An increase in CCI of more than 4 points was significantly associated with the risk of developing a combination of MACCE (HR 1.3, 95% CI 1.2 – 1.4, p<0.001), all-cause mortality (HR 1.25, 95% CI 1.2 – 1.4, p<0.001), and cerebrovascular accidents (CVA) (HR 2.2, 95% CI 1.4 – 3.4, p=0.001). Patients with CCI ≥4 required repeat revascularization more frequently after PCI than after CABG (HR 2.6, 95% CI 1.8 – 3.7, p<0.001). Among patients with varying degrees of comorbidity, the risk of progression of coronary atherosclerosis (SS≥33) was higher after CABG compared with PCI.

Conclusion. A CCI score of more than 4 points was associated with an increased risk of developing of MACCE, all-cause mortality, and CVA. Among patients with varying degrees of comorbidity, PCI and CABG did not demonstrate significant advantages in terms of MACCE.

Keywords: Coronary Artery Disease, Percutaneous Coronary Intervention, Coronary Artery Bypass Grafting, Comorbidity.

Introduction

Despite the achievements in the diagnosis and treatment of coronary artery disease (CAD) in recent decades, it continues to occupy a prominent position in the morbidity and mortality statistics in most countries worldwide [1]. Coronary revascularization is undeniably the most important treatment strategy for CAD, and the choice of the optimal revascularization method, whether it be coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI), remains a current challenge [2, 3]. In recent years, patients are more frequently presenting with complex multivessel CAD and a wide range of comorbidities [4]. In these conditions, clinicians face a growing population of patients with unique clinical profiles and challenges in both interventional and surgical treatment. In cases of more complex multivessel coronary lesions, CABG achieves more complete revascularization than PCI [5]. As a consequence, the majority of prior studies comparing the long-term outcomes of surgical and interventional treatment in patients with multivessel disease have demonstrated the superiority of CABG over PCI in several aspects, including survival [2,6,7]. However, it is worth noting that, despite advances in surgical techniques, CABG remains a more invasive revascularization method compared to PCI.

Consequently, it is evident that surgery for comorbid patients is associated with additional risks of adverse events.

In recent years, interventional procedures have become the most frequently performed treatments for CAD. The introduction of advanced drug-eluting stents (DES) questions the relevance of earlier research in today's context. Some more recent long-term randomized clinical trials (RCTs) fail to find a significant difference in outcomes between PCI and CABG [8-10]. In modern conditions, when selecting the optimal revascularization method, it is necessary to consider not only the anatomical characteristics of coronary arteries but also to understand the impact of comorbidities on clinical outcomes [11]. Over the past decades, various long-term and short-term studies have been conducted to compare the outcomes of CABG and PCI in different patient groups while assessing the influence of comorbid pathologies [12-19]. Mostly, the impact of individual pathologies was evaluated, such as diabetes mellitus (DM) [12-14], renal pathology [15,16], prior cerebrovascular accidents (CVA) [17], Chronic Obstructive Pulmonary Disease (COPD) [18], infections [19]. However, the impact of the general burden of comorbid diseases on revascularization outcomes has been relatively understudied in recent decades and has been separately analyzed for each strategy [11, 20, 21]. Therefore, analyzing the results of both revascularization methods in comorbid patients is believed to be of significant interest. The Charlson Comorbidity Index (CCI) is a widely recognized and convenient tool for assessing the prognostic impact of comorbid conditions on survival [22, 23]. In our study, we used CCI to analyze the impact of comorbidity on long-term revascularization outcomes in general and in relation to the each strategy.

Material and methods

Study Design and Patients

The process of selecting patients for the study was described in detail earlier [24]. However, let's clarify key points. Our study is a retrospective, two-center clinical cohort study. Based on the archives of the medical records from two clinics, we selected 406 patients who underwent primary PCI with DES (n = 200) or primary CABG (n = 206) between 2010 and 2013. The study included patients with stable forms of CAD and stabilized patients with non-ST-segment elevation acute coronary syndrome, featuring multivessel disease and low or intermediate SYNTAX scores (SS) (i.e., ≤ 32). Patients with prior cardiac surgery or stenting were excluded from the study. Additional exclusion criteria from the study were: an acute coronary syndrome with an ST-elevation, left main disease, an SS ≥ 33, age over 65, single-vessel coronary disease, an aneurysm of the left ventricle, severe valvular dysfunction due to 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^2).

The severity of atherosclerotic coronary artery damage was assessed using the SYNTAX score [25, 26]. The SYNTAX score was not initially utilized during the period 2010–2013 when selecting a revascularization method. We retrospectively conducted the SYNTAX score assessment based on archival angiograms (https://syntaxscore2020.com) [25, 26]. Thus, 200 patients with a low SS and 206 patients with an intermediate SS (i.e., ≤ 32) were selected.

The search for patients and the collection of necessary clinical information occurred from 2020 to 2022 through the clinical electronic databases of participating centers, the Clinical Medical Information System (CMIS, Outpatient National Register; https://pvd.dmed.kz), the electronic register of inpatient (ERIP, National Inpatient Register; www.eisz.kz), as well as the current contact information of patients and their relatives. The mean follow-up period was 9±1.9 years, with a maximum follow-up period of 12 years.

Endpoints and definitions

The clinical endpoints of the study included the following: a combination of major adverse cardiac and cerebrovascular events (MACCE) and their components: all-cause mortality, CVA (transient ischemic attack [TIA] or stroke), myocardial infarction (MI), repeated revascularization, the development of chronic heart failure (CHF) (based on clinical status, decreased LVEF, heart chamber dilation with valvular dysfunction), and a high-degree atherosclerotic lesion of coronary arteries according to the SS (≥33) in dynamics.

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. Diagnoses of CVA and MI were recorded when confirming medical documentation. Heart failure development was clinically assessed, considering LVEF and heart chamber dilation, compared with initial echocardiographic parameters. A decrease in LVEF below 50% was considered significant for patients with an initial LVEF above 50%. For patients with primary LVEF in the range of 40-50%, a decrease of 5 points from the baseline was considered significant. Dilation of heart chambers with valve dysfunction was additionally recorded when echocardiography showed dilation of all heart chambers with the development of mitral and/or tricuspid valve insufficiency. Out of the 334 surviving patients, 238 patients (71.3%) underwent repeat angiography at participating centers and other hospitals in Kazakhstan and foreign clinics. Protocols and electronic media of angiograms were obtained from electronic databases of participating hospitals and from patients. The SYNTAX score was recalculated for patients who underwent repeat angiography (https://syntaxscore2020.com). If a patient had multiple angiography during the follow-up period, the SS was assessed on the last angiogram.

Patient comorbidity was assessed using the Charlson Comorbidity Index (CCI) [22, 23]. The CCI is a scoring system evaluating age and the presence of 16 comorbidities. Each condition is assigned 1, 2, 3, or 6 points based on the associated mortality risk. An additional point is added for each decade of life after the patient reaches the age of fifty (i.e., 50-59 years – 1 point, 60-69 years – 2 points, etc.) (Table 1, see the next page). The CCI was calculated for all patients (https://www.mdcalc.com/calc/3917/charlson-comorbidity-index-cci). The study population was divided into two groups: the first group comprised patients with mild/moderate comorbidity (CCI≤3), and the second group included patients with severe comorbidity (CCI≥4). The maximum CCI value was 12 points.

Our retrospective cohort study was conducted in accordance with the principles of the Declaration of Helsinki, and approval was obtained from the Local Ethical Commission of NJSC "Semey Medical University" (minutes no. 2, dated October 28, 2020) and the Committees of the participating centers.

Statistical Analysis

All calculations were performed using IBM SPSS Statistics 23.0 (IBM Corporation, Armonk, New York, USA), and a p-value <0.05 was considered statistically significant. Continuous variables were compared using the Student's t-test or Mann-Whitney U test. Categorical variables were presented as percentages and numbers and compared using the χ 2 test, Fisher's exact test, or Kendall-Stewart test. The survival function of patients was assessed using Kaplan-Meier method, and the

Table 1 Clinical variables and definitions used to calculate Charlson co-morbidity index [22, 23]

Clinical Variables	Points
Age <50 years 50–59 years 60–69 years 70–79 years ≥80 years	 0 +1 +2 +3 +4
CHF Exertional or paroxysmal nocturnal dyspnea and has responded to digitalis, diuretics, or afterload reducing agents	+1
Peripheral vascular disease Intermittent claudication or past bypass for chronic arterial insufficiency, history of gangrene or acute arterial insufficiency, or untreated thoracic or abdominal aneurysm (≥6 cm)	+1
CVA or TIA History of a cerebrovascular accident with minor or no residua and transient ischemic attacks	+1
Dementia Chronic cognitive deficit	+1
COPD	+1
Connective tissue disease	+1
Peptic ulcer disease Any history of treatment for ulcer disease or history of ulcer bleeding	+1
Liver disease Severe = cirrhosis and portal hypertension with variceal bleeding history, moderate = cirrhosis and portal hypertension but no variceal bleeding history, mild = chronic hepatitis (or cirrhosis without portal hypertension)	None 0 Mild +1 Moderate to severe +3
Diabetes mellitus	None or diet-controlled 0 Uncomplicated +1 End-organ damage +2
Hemiplegia	+2
Moderate to severe CKD Severe = on dialysis, status post kidney transplant, uremia, moderate = creatinine >3 mg/dL (0.265 mmol/L)	+2
Solid tumor	None 0 Localized +2 Metastatic +6
Leukemia	+2
Lymphoma	+2
AIDS	+6

CHF = Congestive heart failure, COPD= Chronic obstructive pulmonary disease, CKD = Chronic kidney disease, CVA = cerebrovascular accident, TIA= Transient ischemic attack.

Cox proportional regression method with the determination of the Hazart ratio (HR) and 95% confidence interval (CI). Multivariate analysis was fulfilled to assess whether CCI is an independent predictor of adverse events. The Cox regression model included the following covariates: CCI, gender, age, smoking status, body mass index (BMI), dyslipidemia, arterial hypertension, diabetes, previous MI, previous CVA, peripheral vascular disease, atrial fibrillation (AF), COPD, primary LVEF, type of revascularization (PCI/CABG), initial SYNTAX score. Receiver-operating characteristic (ROC) curves were used to assess the diagnostic significance of CCI.

Results

Baseline characteristics

The baseline characteristics of the groups are presented in Table 2. In terms of their baseline characteristics, patients with severe comorbidity were, on average, 5 years older compared to patients with mild/moderate comorbidity (58 [53-61] years and 53 [48-57] years, respectively, p<0.001). There was no significant difference in the gender composition of the two groups; both groups were predominantly composed of males, over 80% in each group. Patients with severe comorbidity compared with the group patients with mild/moderate comorbidity, respectively, had a higher prevalence of the following conditions: a high degree of hypertension (66% vs. 49%, p=0.046), diabetes (41.3% vs. 10.2%, p<0.0001), and more often suffered from previous MI (71.8% vs. 37%, p<0.001), previous CVA (9.4% vs. 1.9%, p=0.012), were more likely to have peripheral vascular disease (19.8% vs. 8%, p=0.006), and more often had an abnormal lipid

Table 2 Baseline patients characteristics by level of comorbidity

Parameter	Mild/Moderate, CCI≤3 (n=108/26.6%)	Severe, CCI≥4 (n=298/73.4%)	p-value
Age, years	53(48-57)	58(53-61)	<0.0001
Gender			0.095
Women	13(12%)	57(19%)	
Men	95(88%)	241(80.9%)	
Family history of heart disease	31(28.7%)	76(25.5%)	0.52
History of smoking	41(38%)	92(30.9%)	0.18
Body-mass index (BMI), kg/m^2	29.2(±5)	29.8(±4.7)	0.26
Dyslipidemia	74(68.5%)	250(83.9%)	0.001
GFR, ml/min/1.73m^2	97(82-108.75)	91(75-102)	0.003
Hypertension	105(97.2%)	294(98.7%)	0.39
Degrees of hypertension			0.046
Mild hypertension	13(12%)	7(2.3%)	
Moderate hypertension	39(36%)	90(30.2%)	
Severe hypertension	53(49%)	197(66%)	
Diabetes mellitus	11(10%)	123(41.3%)	<0.0001
Previous myocardial infarction	40(37%)	214(71.8%)	<0.0001
Previous CVA	2(1.9%)	28(9.4%)	0.02
Atrial fibrillation	17(15.7%)	63(21%)	0.23
Peripheral arterial disease	9(8.3%)	59(19.8%)	0.006
Chronic obstructive pulmonary disease	0	50(16.8%)	<0.0001
Left ventricular ejection fraction (%)	57(53.2-60)	55(49-59)	<0.0001
SYNTAX Score			
Mean	19.7(±7.1)	21.2(±6.65)	0.04
Conventional category			0.13
SYNTAX Score, ≤22	60(55.6%)	140(47%)	
SYNTAX Score, 23-32	48(44.4%)	158(53%)	
Disease extent			0.35
Two-vessel disease	59(54.6%)	147(49.3%)	
Three-vessel disease	49(45.4%)	151(50.7%)	
Type of revascularization			0.08
PCI	61(56.5%)	139(46.6%)	
CABG	47(43.5%)	159(53.4%)	

Values are shown as mean ± SD (n), Me (Q1-Q3) or % (n/N).
CCI= Charlson Comorbidity Index; CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention; SS = SYNTAX Score; CVA = cerebrovascular accident; GFR = glomerular filtration rate according to the Cockcroft-Gault formula.

Table 3 Clinical Outcomes According to level of comorbidity and Revascularization Treatment

Events	Mild/ Moderate, CCI≤3 (n = 108/26.6%)	Severe, CCI≥4 (n = 298/73,4%)	Hazard ratio (95% CI)	P value
MACCE	51 (47.2%)	206(69%)	0.57 (0.42 – 0.78)	<0.0001
Repeat revascularization	41(38%)	141(47.3%)	0.7 (0.5 – 0.99)	0.04
All-cause-Death / MI/Stroke/TIA	20(18.5%)	129(43.3%)	0.38 (0.24 – 0.6)	<0.0001
Death, all-cause	12(11%)	65(21.8%)	0.5 (0.27 – 0.9)	0.024
Cardiac death	10(9.3%)	40(13.4%)	0.67 (0.34 – 1.34)	0.26
Non-cardiac death	2(1.9%)	25(8.4%)	0.2 (0.05 – 0.9)	0.034
Myocardial infarction	7(6.5%)	49(16.4%)	0.37 (0.17 – 0.8)	0.01
Stroke/TIA	5(4.6%)	47(15.8%)	0.27 (0.1 – 0.7)	0.006
LVEF during follow-up (%)*	58(53-61)	51.9(44-58)		<0.0001
Decrease in LVEF	12(15.6%)	102(41.3%)	0.3 (0.18 – 0.6)	<0.0001
Heart chambers dilatation + valvular insufficiency	4(5.2%)	48(19.4%)	0.2 (0.08 – 0.65)	0.005
SYNTAX Score during follow-up*	20(8-27.5)	24.5(15.5-33.5)		0.005
SYNTAX Score, ≥33, during follow-up	11(18.6%)	51(28.5%)	0.56(0.3-1.08)	0.08

Values are number of events (%), unless otherwise indicated
*- Values are shown as mean ± SD (n), Me (Q1-Q3) or % (n/N). CCI= Charlson Comorbidity Index; CABG = coronary artery bypass grafting; CI = confidence interval; 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

profiles (83.9% vs. 68.5%, p=0.001). Notably, there were no reported cases of COPD among patients with mild/moderate comorbidity. The groups did not differ significantly in terms of BMI, with an average of 29.2 ± 5 for the first group and 29.8 ± 4.7 for the second (p=0.26). There were also no significant differences in the proportion of smoking patients (38% and 31%, p=0.18) or the prevalence of AF (15.7% vs. 21%, p=0.23) in the first and second groups, respectively.

On average, patients in both groups had a similar distribution of coronary artery lesions: two-vessel disease - 54.6% vs 49.3%; three-vessel disease - 45.4% vs 50.7% (p=0.35); low gradation of SS (≤22)- 55.6% vs 47%; intermediate SS category (23-32) - 44.4% vs 53% for the first and second groups, respectively. In addition, both groups had an even distribution of revascularization strategies: CABG or PCI (Table 2).

Outcomes

Patients with different degrees of comorbidity did not show significant differences in the risk of developing cardiac death and the likelihood of developing a high degree of atherosclerotic damage to the coronary arteries based on SS (≥33). However, for other endpoints, patients with severe comorbidity predictably had a higher risk of experiencing adverse events compared to patients with mild/moderate comorbidity (Table 3).

When analyzing revascularization outcomes with stratification by CCI, patients with severe comorbidity had a greater risk of requiring repeat revascularization after PCI compared to CABG (68% and 29%, HR 2.6, 95% CI 1.8 – 3.7, respectively; p<0.001). Among patients with different levels of comorbidity, undergoing CABG was associated with a higher likelihood of developing severe coronary artery lesions based on SS (≥33) compared to PCI (37.5% and 5.7%, HR 14.3, 95% CI 1.8-114, p=0.012; vs 45.9% and 12.8%, HR 3.1, 95% CI 1.6-5.9, respectively, for the first and second groups). Regarding other endpoints, no significant advantages were found between CABG and PCI (Table 4).

Table 4 Clinical Outcomes According to level of comorbidity and Revascularization Assignment

Events	Mild/Moderate, CCI≤3				Severe, CCI≥4 (n=298/73.4%)				
	(n=108/26.6%)	CABG (n=47)	Hazard ratio (95% CI)	P value	PCI (n=139)	CABG (n=159)	Hazard ratio (95% CI)	P value	P value interaction
MACCE	33(54%)	18(38.3%)	1.2 (0.66-2.2)	0.54	116(83.5%)	90(56.6%)	1.6 (1.2-2.1)	0.001	0.001
Repeat revascularization	29(47.5%)	12(25.5%)	1.5 (0.75 -3)	0.24	95(68.3%)	46(28.9%)	2.6 (1.8-3.7)	<0.0001	<0.0001
All-cause-Death /MI/ Stroke/TIA	10(16.4%)	10(21.3%)	0.8 (0.33-1.9)	0.6	63(45.3%)	66(41.5%)	1.2 (0.8 – 1.6)	0.39	0.55
Death, all-cause	4(6.6%)	8(17%)	0.4 (0.12-1.3)	0.14	31(22.3%)	34(21.4%)	1.1 (0.68-1.8)	0.69	0.8
Cardiac death	3(4.9%)	7(14.9%)	0.34 (0.09-1.3)	0.12	17(12.2%)	23(14.5%)	0.88 (0.47-1.6)	0.68	0.27
Non-cardiac death	1(1.6%)	1(2%)	0.8 (0.05-13.4)	0.9	14(10.1%)	11(6.9%)	1.6 (0.7 – 3.5)	0.25	0.28
Myocardial infarction	6(9.8%)	1(2%)	4.6 (0.55-38)	0.16	29(20.9%)	20(12.6%)	1.75 (0.99-3)	0.055	0.02
Stroke/TIA	3(4.9%)	2(4.3%)	1.2 (0.2-7.3)	0.8	21(15%)	26(16.4%)	0.94 (0.53-1.7)	0.8	0.9
LVEF during follow-up (%)*	56.5(±6.8)	56.7(±6.6)		0.87	50.9(±10.9)	48.2(±11)		0.049	
Decrease in LVEF	8(18.2%)	4(12%)	1.3 (0.37-4.4)	0.7	38(32.2%)	64(49.6%)	0.7 (0.47-1.01)	0.09	0.13
Heart chambers dilatation + valvular insufficiency	2(4.5%)	2(6%)	0.4 (0.04- 4.5)	0.47	18(15.3%)	30(23.3%)	0.74 (0.4 – 1.3)	0.3	0.2
SYNTAX Score during follow-up*	12(5-21.5)	26.5(20-39.5)		<0.0001	18.5(9.8-26)	31.5(24-35.8)		<0.0001	
SYNTAX Score, ≥33, during follow-up	2(5.7%)	9(37.5%)	0.07 (0.01-0.56)	0.012	12(12.8%)	39(45.9%)	0.33 (0.17-0.6)	0.001	<0.0001

Values are number of events (%), unless otherwise indicated
*- Values are shown as mean ± SD (n), Me(Q1-Q3) or % (n/N). CCI= Charlson Comorbidity Index; CABG = coronary artery bypass grafting; CI = confidence interval; 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.

We conducted a multivariate Cox regression analysis for all study endpoints, including the following covariates: CCI, gender, age, smoking, BMI, dyslipidemia, hypertension, DM, previous MI, previous CVA, peripheral atherosclerotic vascular disease, AF, COPD, primary LVEF, type of revascularization (CABG/PCI), and initial SYNTAX Scores. As a result, CCI was significantly associated with the risk of developing MACCE (All-cause-Death/MI/CVA) (HR 1.3, 95% CI 1.2 – 1.4, p<0.001), all-cause mortality (HR 1.25, 95% CI 1.2 – 1.4, p<0.001), and CVA (HR 2.2, 95% CI 1.4 – 3.4, p=0.001). However, CCI did not have a significant impact on the other endpoints in our study (Table 5).

Table 5 Results of multivariate analysis for Charlson comorbidity index

Events	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI) *	P value
All-cause-Death /MI/Stroke/TIA	1.3 (1.2 – 1.4)	<0.0001	1.3 (1.2 – 1.4)	<0.001
Death, all-cause	1.3 (1.2 – 1.5)	<0,0001	1,25 (1,12-1,4)	<0.001
Cardiac death	1.2 (1.06 – 1.4)	0.004	1,1 (0,9 - 1,2)	0.42
Myocardial infarction	1.13 (1.002 – 1.28)	0.045	1.12 (0.98 – 1.3)	0.09
Stroke/TIA	1.4 (1.3-1.6)	<0,0001	2.2 (1.4 – 3.4)	0.001
Heart failure with decrease in LVEF	1.2 (1.14-1.35)	<0.0001	1.12(0.9 - 1.37)	0.27
Heart failure with heart chambers dilatation and valvular insufficiency	1.3 (1.1-1.4)	<0,0001	1.13 (0.98 – 1.3)	0.1
SYNTAX Score, ≥33, during follow-up	1.1 (0.95 -1.24)	0.25	-	
Repeat revascularization	1.05 (0.98 -1.14)	0.17	-	

* Adjusted for sex, age, smoking status, body mass index, dyslipidemia, arterial hypertension, diabetes mellitus, myocardial infarction, peripheral vascular disease, atrial fibrillation, COPD, CVA, primary LVEF, type of revascularization (PCI/CABG), initial SYNTAX score
CABG = coronary artery bypass grafting; CI = confidence interval COPD = Chronic obstructive pulmonary disease; CVA = cerebrovascular accident; HR = Hazard ratio; MI = myocardial infarction; PCI = percutaneous coronary intervention; TIA = transient ischemic attack; LVEF = Left ventricular ejection fraction.

To assess the diagnostic significance, sensitivity, and specificity of CCI, a Receiver Operating Characteristic (ROC) analysis was conducted. The area under the ROC curve (AUC) showed good predictive capability for CCI in influencing the development of MACCE and CVA (AUC 0.73, 95% CI 0.68-0.78; and AUC 0.76, 95% CI 0.68-0.8; respectively, p<0.001). For all-cause mortality, the AUC was 0.69 (95% CI 0.62-0.76, p<0.001), indicating a moderate model quality. The cut-off value was determined to be 4.5 (Figure 1).

Discussion

The treatment of patients with comorbid conditions is always accompanied by difficulties. The higher frequency of adverse outcomes in patients with comorbidities is well recognized. Meanwhile, researchers have reported an increasing burden of comorbidities among patients undergoing CABG and PCI [11]. It is important to note that despite the increasing prevalence of comorbid conditions, many studies have shown improvements in outcomes, reflecting the progress in surgical and interventional treatments [11, 27, 28]. Determining the optimal revascularization strategy for patients with comorbidities is a challenging task. It is also important to note that high-risk patients were often excluded from revascularization studies [4, 11]. Therefore, the conclusions drawn from these studies may not be directly applicable to high-risk patients. This presents a challenging dilemma for practicing physicians when it comes to choosing the optimal revascularization method, especially considering the limited availability of reliable information to guide decision-making. Over the last decade, most research in the field of revascularization has focused on evaluating the impact of individual pathologies on revascularization outcomes [12-19], while the influence of general comorbidity burden has been separately studied for each revascularization strategy [11, 20, 21].

Our findings regarding the impact of comorbid conditions on the development of adverse events partially coincide with previous studies. Earlier studies indicated a connection between the CCI and the development of MACCE (All-cause Death/MI/CVA) in patients after PCI and those with acute coronary syndrome [21, 29, 30]. In our study, for each additional point increase in CCI, the risk of developing MACCE in the general cohort and in the PCI group increased by 1.3 times (HR 1.3, 95% CI 1.2 – 1.4, p<0.0001), and in the surgical group, it increased by 1.36 times (HR 1.36, 95% CI 1.2-1.5, p<0.0001). In a multifactorial analysis in the general cohort, other covariates

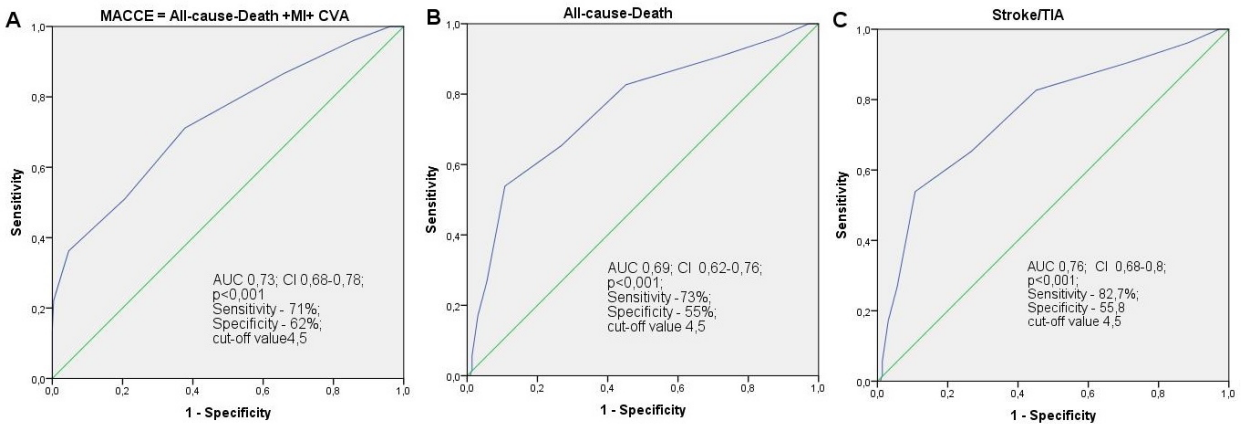

Figure 1 – Receiver operator characteristic (ROC) curve of the Charlson comorbidity index to predict MACCE.

Receiver-operating characteristic (ROC) curves for (A) MACCE (All-cause-Death/MI/CVA); (B) death from any cause; and (C) stroke/TIA based on the Charlson comorbidity index are shown. AUC = area under the ROC curve; MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; CVA = cerebrovascular accident; TIA = transient ischemic attack.

besides CCI did not significantly impact the development of MACCE. However, for stented patients, along with CCI, persistent and permanent AF and smoking became significant predictors of MACCE [HR 1.9, 95% CI 1.13 – 3.3, p=0.015 and HR 2.7, 95% CI 1.6 – 4.4, p<0.0001, respectively]. This aligns with previous research results. According to the largest-scale SYNTAX study comparing outcomes of PCI and CABG, 5-year results showed a significant influence of smoking on the development of the composite endpoint of death/MI/stroke [31]. The 10-year results indicated more than a twofold higher adjusted risk of all-cause mortality in current smokers compared to those who never smoked [32]. In our study, smoking was associated with MACCE but did not significantly impact on all-cause and cardiovascular mortality. Our analysis also assessed the impact of persistent/permanent AF on revascularization outcomes. It is reported correlation between AF and CAD [33]. Unfortunately, we did not find reliable information on the impact of persistent/permanent AF on myocardial revascularization outcomes in the last 10 years. However, based on the HORIZONS-AMI study, new-onset AF after PCI in patients with ST-segment elevation myocardial infarction was associated with higher 3-year rates of adverse events and mortality [34]. Rashid M et al., in their review, reported an increased risk of death with the presence and increasing number of comorbidities in patients with acute coronary syndrome, stable CAD, and patients who underwent PCI [35]. In our study, a multivariate analysis revealed that an increase in CCI raised the risk of all-cause death in the general cohort (HR 1.25, 95% CI 1.12-1.4, p<0.0001). However, there was no significant impact of CCI on the development of cardiac death in our observation. Besides CCI, for the development of all-cause mortality in our study, an increase in BMI (HR 1.05, 95% CI 1.002-1.1, p=0.04) and prior CVA (HR 2.3, 95% CI 1.2 – 4.2, p=0.008) had a significant influence. For cardiac mortality, only BMI and prior CVA were significant predictors (HR 1.1, 95% CI 1.02 – 1.15, p=0.01 and HR 2.9, 95% CI 1.4 – 5.9, p=0.004, respectively). In the SYNTAX study, prior cerebrovascular disease was associated with a significantly increased risk of all-cause death over 10 years for both PCI and CABG patients [17]. It is noteworthy that we did not find a significant link between prior CVA and subsequent development of stroke/TIA in our study. The increase in BMI predictably had a significant impact on the development of cardiac mortality in our analysis, aligning with recent findings on the influence of obesity on PCI outcomes [36], but not CABG outcomes [37].

Interestingly, COPD in our study was associated with the risk of developing MI in the general cohort (HR 2.2, 95% CI 1.2 – 4.2, p=0.014) and with a high degree of atherosclerotic coronary artery damage in stented patients (HR 3.9, 95% CI 1.15 – 13, p=0.03). In this regard, it is worth noting that according to Li Y et al., COPD was independently associated with adverse outcomes after PCI or CABG [38], and in the SYNTAX Extended Survival study, COPD was associated with a higher risk of 10-year all-cause death after revascularization for complex coronary artery disease [18].

The most closely associated comorbidity with CAD is diabetes mellitus, which is linked to worse outcomes of coronary revascularization [39]. Results of revascularization indicate that CABG surpasses PCI for this patient group [40]. In our study, DM did not have a significant impact on the development of MACCE, and neither revascularization method showed advantages in patients with diabetes.

Thus, myocardial revascularization in patients with CAD and comorbid conditions requires an individualized and detailed approach. The integration of interdisciplinary expertise, advancements in PCI and CABG technologies, and understanding the complex relationships between CAD and comorbidities are crucial in optimizing the choice of revascularization method for this patient population.

Often in clinical practice, many patients with severe comorbidity receive a justified refusal to undergo CABG. In our study, we excluded patients with severe coronary lesions and clear indications for surgery. We included patients with multivessel coronary artery disease and varying levels of comorbidity with low-to-intermediate SS, making both CABG and PCI feasible. Our analysis did not reveal any advantages for CABG or PCI in terms of the MACCE (All-cause Death/MI/CVA). Consequently, improvements in CABG and PCI techniques may lead to their consideration in broader population groups, including patients with severe comorbidity.

Limitation

Our findings should be interpreted in light of the following limitations:

Firstly, due to the modest sample size, this analysis may lack sufficient statistical power.

Secondly, despite the measures taken and corrections applied, due to the retrospective observational nature of the study, there was a possibility of systematic selection bias.

Thirdly, our study included stable patients with multivessel CAD without left main disease and with low to intermediate SS who underwent primary PCI or CABG before the age of 65. Therefore, these results cannot be extrapolated to other coronary heart disease patients.

Conclusion

An increase in the Charlson Comorbidity Index of more than 4 points was significantly associated with the risk of developing a combination of MACCE, all-cause mortality, and cerebrovascular accident. Patients with severe comorbidity significantly more frequently required repeat revascularization after PCI than after CABG. In patients with varying degrees of comorbidity, the risk of developing severe coronary atherosclerotic lesions (≥33) was higher after surgery than after stenting. In other aspects, PCI and CABG did not show significant advantages in patients with varying degrees of comorbidity.

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