Coronary Artery Bypass Grafting Versus Percutaneous Coronary Intervention in Patients With Non−ST-Elevation Myocardial Infarction and Left Main or Multivessel Coronary Disease

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Current recommendations on the optimal revascularization strategy in Non−ST-elevation myocardial infarction (NSTEMI) with left main (LM) or multivessel coronary disease (MVD) are based upon randomized clinical trials conducted in stable coronary artery disease. In a real-world contemporary observational registry, we compared the long-term outcome of NSTEMI patients with LM/MVD (n = 1,104) submitted to coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), or optimized medical therapy (OMT). The primary end point was 5-year all-cause mortality. Results were assessed in the entire population (CABG 289, PCI 399, and OMT 416) and in a propensity score-matched cohort of CABG (n = 159) and PCI (n = 159). Crude 5-year mortality rates in CABG and PCI were 25.3% versus 29.6%, respectively (unadjusted hazard ratio [HR] 1.2; 95% confidence intervals [CI] 0.9 to 1.6; p = 0.212); OMT, however, was associated with a twofold higher risk of mortality when compared with any revascularization strategy (unadjusted HR 2.0; 95% CI 1.7 to 2.5; p < 0.001). After propensity score-matching and multivariate analysis, there was a trend toward a higher incidence of the primary end point in patients who underwent PCI versus CABG (31% vs 21%; adjusted HR 1.52; 95% CI 0.93 to 2.50; p = 0.094). This was a consistent finding over subgroups deemed clinically relevant, such as in patients with LM or proximal left anterior descending disease, SYNergy between percutaneous coronary intervention with TAXus ≥23 and left ventricle ejection fraction <40%. In conclusion, in a real-world cohort of NSTEMI patients with LM/MVD, those selected for OMT had a dire outcome. Although adjusted 5-year mortality was statistically similar between revascularization strategies, there was a trend favoring CABG, which might be the preferred option in LM, proximal LAD, SYNergy between percutaneous coronary intervention with TAXus ≥23, and left ventricle ejection fraction <40% subgroups. **(Am J Cardiol 2019;123:717−724)**

Current recommendations[1,2] for selecting the best revascularization strategy in patients with left main (LM) or multivessel disease (MVD) sustaining non−ST-elevation myocardial infarction (NSTEMI) are based on the results of several randomized clinical trials,[3,4] which compared coronary artery bypass grafting (CABG) against percutaneous coronary intervention (PCI), mostly in patients with stable coronary disease. No contemporary randomized clinical trial comparing CABG with PCI in this important population subset has been performed so far and previous studies of LM or MVD have included a negligible fraction of NSTEMI patients (<10%).[5−7] Similarly, data regarding patients with NSTEMI and LM or MVD who are not amenable to revascularization due to severe/diffuse coronary artery disease or severe co-morbidity is sparse. We sought to evaluate the mid-to-long-term (5-year) all-cause mortality in a real-world single-center prospective registry of patients with NSTEMI and LM or MVD, according to baseline treatment strategy (CABG, PCI, or optimized medical therapy [OMT]). In addition, a propensity score (PS)-matched cohort of CABG and PCI patients was derived to investigate further the potential impact of different revascularization options on hard clinical outcomes.

Methods

All patients presenting with an acute coronary syndrome (ACS) at our institution and who underwent invasive coronary angiography from January 2009 to December 2014

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(n = 5,379) were prospectively included in a dedicated registry. From these, the population included in our analysis (n = 1,104) was identified and selected considering the following exclusion criteria: (1) ST-elevation myocardial infarction or unstable angina; (2) 1 vessel disease; (3) at least moderate valvular disease; (4) patients submitted to hybrid revascularization (CABG plus PCI); (5) patients lost to follow-up (Figure 1). Patients in whom coronary angiography was not performed are not represented in the present study.

According to local practice and guidelines—and after diagnostic coronarography—the attending Invasive Cardiologist would opt for angioplasty or Heart Team discussion, in case of anatomically complex coronary artery disease or when other clinical features are deemed relevant for the decision. Subsequently, the team would decide for PCI, CABG, or OMT alone, if patients were considered not amenable to revascularization. There were no protocol-mandated recommendations for decision-making.

Clinical and anatomical variables were collected at the time of diagnostic coronary angiography in a dedicated cath lab-based electronic database (Cardiobase, Infortucano, Lisbon, Portugal). Chronic renal disease was classified as follows: dialysis (regardless of serum creatinine level); moderately impaired renal function (30 to 60 ml/min/1.73 m^2); and severely impaired renal function (<30 ml/min/1.73 m^2). Severe pulmonary disease was considered present if long-term bronchodilators or steroids were being used for lung disease. The ischemic risk was assessed by the GRACE ACS risk score.[8] Left ventricle ejection fraction (LVEF) was stratified according to the latest recommendation[9] into preserved EF (LVEF ≥50%), mid-range EF (LVEF 40% to 49%) and reduced ejection fraction (LVEF <40%).

A diseased epicardial vessel was defined as a major vessel (LM, left anterior descending [LAD], left circumflex, or right coronary artery, including its branches) containing 1 or more lesions with a visually estimated diameter stenosis >50%. MVD was defined as at least 2 diseased epicardial coronary arteries. The anatomical coronary complexity was evaluated according to the SYNergy between percutaneous coronary intervention with TAXus (SYNTAX) score[10] with subsequent categorization into low, intermediate, and high complexity (SYNTAX ≤22; 23 to 32; and ≥33 points, respectively). The surgical risk was estimated by the EuroSCORE II.[11] High, intermediate, and low surgical risk were defined according to the following cutoffs: <2%, 2 to 5%, and >5%, respectively.

Patients treated with PCI or OMT were discharged with dual antiplatelet therapy except when atrial fibrillation was present, in which case the antiplatelet regimen as well as its duration were decided on an individual basis. The antiplatelet strategy in patients treated with CABG was left at the discretion of the Cardiac Surgeon. The use of β blockers and angiotensin enzyme convertor inhibitors or angiotensin II receptor blockers were tailored to the patients' co-morbidities and heart failure status.

The study primary end point was all-cause mortality. Vital status and date of death was assessed by consulting the Portuguese National Patient Registry. Patients were censored at the time of the last known follow-up.

Normally and non-normally distributed variables were expressed as mean ± standard deviation and median (interquartile range [IQR]), respectively. Differences between groups were assessed using independent samples *t* test and chi-square test for continuous and categorical variables, respectively.

Given significant differences in preprocedural variables between the CABG and PCI groups we performed a PS-matching. The PS is a conditional probability of receiving a treatment given a set of baseline-measured covariates.[12] To make the 2 groups comparable, a PS was estimated by multivariable logistic regression with PCI as dependent variable and the following baseline characteristics as covariates/independent variables: age, gender, body mass index,

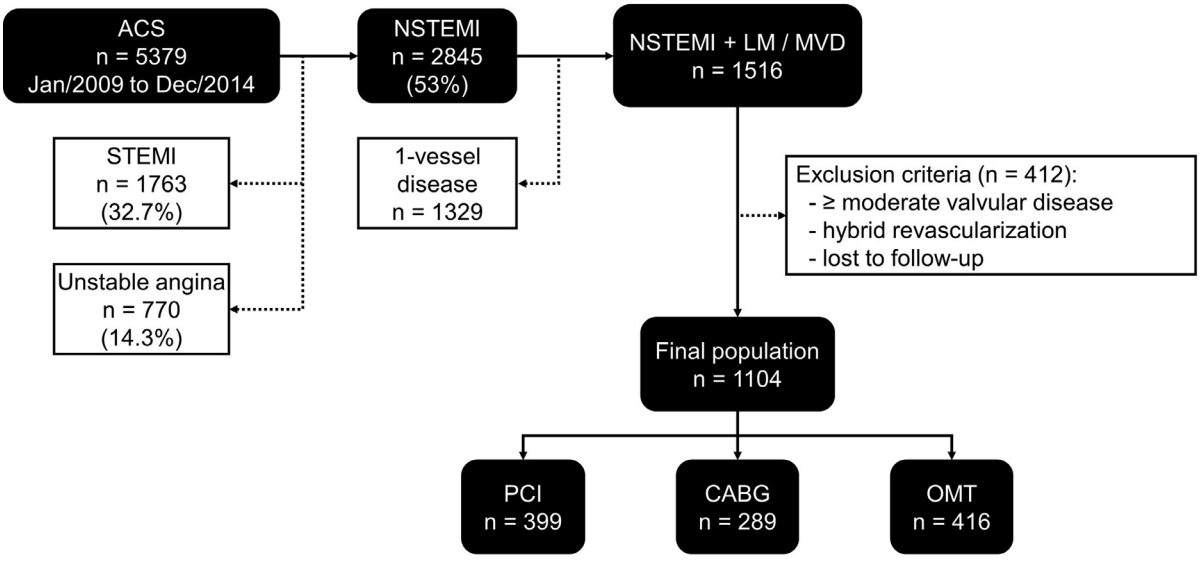

Figure 1. Study flowchart. ACS = acute coronary syndrome; CABG = coronary artery bypass graft; LM = left main; MVD = multivessel coronary disease; NSTEMI = non−ST-elevation myocardial infarction; OMT = optimized medical therapy; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

hypertension, smoking, diabetes mellitus, dyslipidemia, severe pulmonary disease, peripheral vascular disease, previous history of stroke/transient ischemic attack, previous history of myocardial infarction, previous history of PCI, previous history of CABG, LVEF strata, creatinine clearance, GRACE score and strata, SYNTAX score and strata, number of disease vessels, LM, proximal LAD, 3-vessel disease, and EuroSCORE II and strata. Matching was performed with the use of a 1:1 matching protocol without replacement, with a caliper width equal to 0.01 of the standard deviation of the logit of the PS. Standardized differences were estimated for all the baseline covariates before and after matching to assess prematch imbalance and postmatch balance. Standardized differences of less than 10% for a given covariate indicate a relatively small imbalance.

In the matched cohort, paired comparisons were performed with the use of McNemar's test for binary variables and a paired Student's *t* test or paired-sample test for continuous variables. The comparative risk of all-cause mortality was further adjusted for in the matched cohort with the use of a Cox proportional hazards regression model. Kaplan−Meier curves were used to report all-cause mortality over time. Differences in the survival curves of both PCI and CABG groups were assessed with the log-rank test.

Prespecified subgroup analyses were performed based on 2 types of characteristics. Anatomical subgroups were based

Table 1
Baseline clinical and angiographic characteristics of study cohort

Variable	CABG (n = 289)	PCI (n = 399)	OMT (n = 416)	p value (CABG vs PCI)	p value (OMT vs others)
Age (years)	69 (61−76)	69 (60−77)	74 (65−80)	0.514	**<0.001**
Men	221 (77%)	283 (71%)	279 (67%)	0.105	**0.028**
BMI (Kg/m^2)	27.3 (24.5−30.1)	27.3 (24.8−29.8)	26.7 (24.2−29.4)	0.770	**0.007**
Diabetes mellitus	117 (41%)	163 (41%)	209 (50%)	0.923	**0.002**
Insulin-requiring	24 (8.3%)	39 (9.8%)	45 (10.8%)	0.509	0.368
Hypertension	211 (73%)	321 (81%)	364 (88%)	**0.021**	**<0.001**
Dyslipidemia	166 (57%)	227 (57%)	266 (64%)	0.886	**0.025**
Smoker	56 (19%)	91 (23%)	59 (14%)	0.279	**0.003**
Previous MI	65 (23%)	119 (30%)	164 (39%)	**0.032**	**<0.001**
Previous PCI	37 (13%)	100 (25%)	100 (24%)	**<0.001**	0.106
Previous CABG	5 (1.7%)	59 (15%)	108 (26%)	**<0.001**	**<0.001**
Previous stroke/TIA	25 (8.7%)	43 (11%)	51 (12%)	0.356	0.217
Peripheral vascular disease	44 (15%)	62 (15%)	99 (24%)	0.910	**0.001**
Severe pulmonary disease	42 (15%)	68 (17%)	88 (21%)	0.375	**0.030**
SYNTAX score	22 (17−28)	16 (10−24)	19 (12−28)	**<0.001**	0.805
Low (0−22)	156 (54%)	289 (72%)	258 (62%)	**<0.001**	0.373
Intermediate (23−32)	89 (31%)	67 (17%)	89 (21%)	**<0.001**	0.620
High (≥ 33)	44 (15%)	43 (11%)	69 (17%)	0.083	0.068
GFR MDRD (mL/min/1.73 m^2)	73.7 ± 30.8	76.1 ± 32.9	64.5 ± 30.9	0.334	**<0.001**
>60	194 (67%)	279 (70%)	238 (57%)	0.435	**<0.001**
30−60	75 (26%)	93 (23%)	117 (28%)	0.426	0.173
<30	11 (3.8%)	13 (3.3%)	31 (7.5%)	0.699	**0.003**
Dialysis	9 (3.1%)	14 (3.5%)	30 (7.2%)	0.776	**0.004**
LVEF					
≥50%	197 (68%)	280 (70%)	270 (65%)	0.573	0.128
40−50%	36 (13%)	55 (14%)	70 (17%)	0.612	0.101
<40%	56 (19%)	64 (16%)	76 (18%)	0.255	0.727
Critical status	6 (2.1%)	13 (3.3%)	8 (1.9%)	0.350	0.382
GRACE score	149 (126−170)	143 (122−170)	153 (132−177)	0.151	**0.001**
EuroSCORE II (%)	1.87 (1.17−2.98)	2.12 (1.14−4.35)	3.69 (1.95−6.02)	0.056	**<0.001**
Low risk	153 (53%)	192 (48%)	110 (26%)	0.212	**<0.001**
Intermediate risk	101 (35%)	119 (30%)	168 (40%)	0.155	**0.005**
High risk	35 (12%)	88 (22%)	138 (33%)	**0.001**	**<0.001**
Number diseased vessels	3 (3−3)	3 (2−3)	3 (2−3)	**<0.001**	0.055
LM	107 (37%)	52 (13%)	64 (15%)	**<0.001**	**0.002**
Proximal LAD	96 (53%)	119 (34%)	135 (38%)	**<0.001**	0.496
Three-vessel disease	137 (47%)	196 (49%)	202 (49%)	0.656	0.960
Medication at discharge					
Beta blockers	154 (53%)	194 (49%)	208 (50%)	0.227	0.851
ACEi/ARB	154 (53%)	209 (52%)	211 (51%)	0.814	0.511

Continuous values are presented as median (interquartile range) or mean ± standard deviation.

Bold represent statistically significant p values.

Abbreviations: ACEi/ARB = angiotensin enzyme convertor inhibitors or angiotensin II receptor blockers; BMI = body mass index; CABG = coronary artery bypass grafting; Cr = creatinine; GFR = glomerular filtration rate; LAD = left anterior descending; LM = left main; LVEF = left ventricular ejection fraction; MDRD = Modification of Diet in Renal Disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

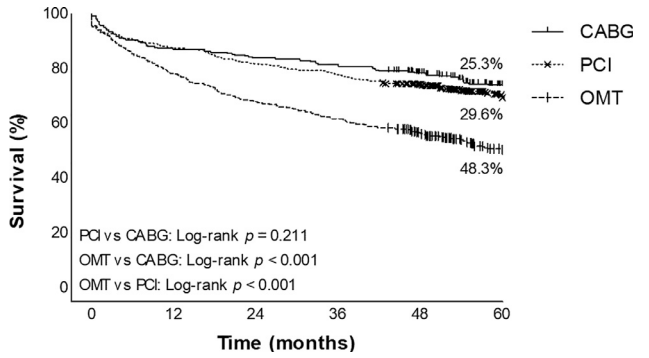

Figure 2. Survival analysis before propensity score matching according to the treatment strategy. CABG = coronary artery bypass graft; OMT = optimized medical treatment; PCI = percutaneous coronary intervention.

on LM disease, proximal LAD disease, and SYNTAX strata (low vs intermediate/high anatomic complexity). Clinical subgroups were based on gender, diabetes status, and LVEF strata (≥50% vs 40% to 49% vs <40%). Tests for interaction were performed to assess for heterogeneity of treatment effect among subgroups. p Values for interaction where corrected with the formula $1 - (1 - P)^6$ to account for multiple testing.[13]

All tests were 2-sided and statistical significance was accepted if p value <0.05. Analyses were performed using SPSS 25.0 and Stata 13.0.

Results

Among the 5,379 patients with ACS included in the registry during the selected period, 1,516 had NSTEMI with LM or MVD. After applying the study-defined exclusion criteria, we identified 289 patients treated with CABG, 399 patients treated with PCI, and 416 patients managed with OMT alone (final study population of n = 1,104; Figure 1). Baseline population characteristics are depicted in Table 1, where the imbalance between CABG and PCI subgroups can be observed. As expected, patients selected to OMT alone were older, had more co-morbidities and were more severely ill.

Before PS-matching and among PCI-treated patients, stents were implanted in 93% (n = 371), mostly drug-eluting stents (73%). The mean number of stents was 1.60 ± 0.44 stents/patient and the mean number of treated vessels per patient was 1.17 ± 0.50. The rate of complete revascularization in the PCI group was 9.5% (n = 38). In the CABG group, the mean number of grafts/patient was 2.31 ± 0.79, with arterial graft used in 98% of the cases. Off-pump CABG was performed in 63% of the patients. The median time from admission to revascularization in the CABG group was 9 days (IQR: 4 to 16 days). The proportion of complete revascularization was 47% (n = 136).

The overall median of the follow-up was 58 months (IQR 30 to 60 months); although it was shorter in the OMT group (49 months, p < 0.001), it did not differ significantly between revascularization groups (CABG 64 months vs PCI 61 months, p = 0.616). The primary outcome of all-cause mortality occurred in 118 patients (29.6%) in the PCI group, in 73 patients (25.3%) in the CABG group and in 201 patients (48.3%) in the OMT group (Figure 2). There was no statistically meaningful difference in long-term all-cause mortality between PCI and CABG (unadjusted HR 1.2; 95% CI 0.9 to 1.6; p = 0.212). However, OMT was associated with a twofold increase in the mortality risk over the study period, when compared with percutaneous or surgical revascularization (unadjusted HR 2.0; 95% CI 1.7 to 2.5; p < 0.001).

Using a PS-matching methodology, 159 patients who underwent PCI where matched with 159 patients who underwent CABG. After matching, the standardized differences were ≤10% for all variables, indicating only small

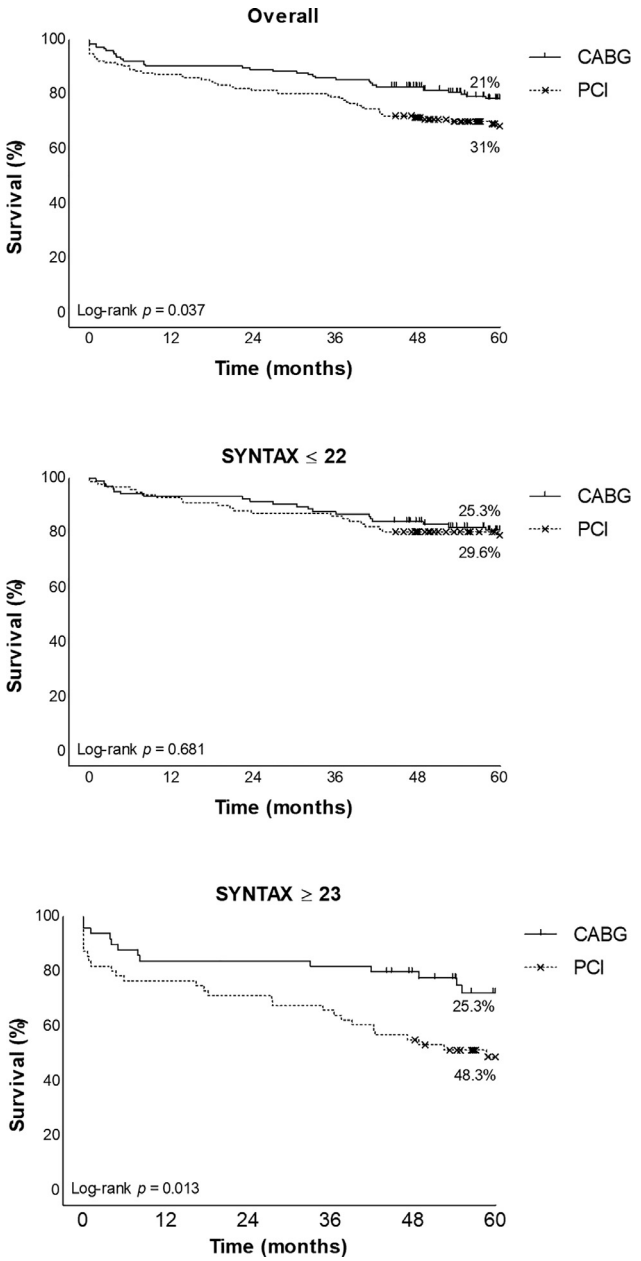

Figure 3. Survival analysis after propensity score matching comparing CABG with PCI in the overall population and according to the anatomical complexity. CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.

Table 2
Baseline clinical and angiographic characteristics of study cohort after propensity score matching

Variable	CABG (n = 159)	PCI (n = 159)	Std mean diff
Age (years)	68 (58−76)	66 (58−76)	0.1%
Men	116 (73%)	111 (70%)	6.6%
BMI (Kg/m^2)	27.7 (25.0−31.2)	27.3 (24.6−29.8)	6.9%
Diabetes mellitus	91 (57%)	93 (59%)	2.0%
Insulin-requiring	12 (7.5%)	17 (10.7%)	10.0%
Hypertension	121 (76%)	115 (72%)	9.1%
Dyslipidemia	90 (57%)	88 (55%)	4.0%
Smoker	33 (21%)	40 (25%)	9.5%
Previous MI	38 (24%)	28 (24%)	0.0%
Previous PCI	27 (17%)	22 (14%)	8.3%
Previous CABG	5 (3.1%)	6 (3.8%)	5.4%
Previous stroke/TIA	19 (11.9%)	14 (8.8%)	9.8%
Peripheral vascular disease	29 (18%)	23 (15%)	10.0%
Severe pulmonary disease	25 (16%)	26 (16%)	1.7%
SYNTAX score	19 (14.5−24.0)	18 (13−25.5)	8.8%
Low (0−22)	109 (69%)	103 (65%)	8.0%
Intermediate (23−32)	38 (24%)	39 (25%)	1.5%
High (≥ 33)	12 (7.5%)	17 (10.7%)	10.0%
GFR MDRD (mL/min/1.73 m^2)	75.0 ± 29.3	73.7 ± 30.6	4.3%
> 60	112 (70%)	111 (70%)	1.4%
30−60	37 (23%)	36 (23%)	1.5%
<30	7 (4.4%)	8 (5.0%)	3.0%
Dialysis	3 (1.9%)	4 (2.5%)	4.3%
LVEF			
>50%	110 (69%)	111 (70%)	1.5%
40−50%	20 (13%)	22 (14%)	3.6%
< 40%	29 (18%)	26 (16%)	5.0%
Critical status	3 (1.9%)	4 (2.5%)	4.3%
GRACE score	146 (125−170)	144 (119−176)	4.6%
Low risk	20 (13%)	20 (13%)	0.0%
Intermediate risk	48 (30%)	52 (32%)	5.4%
High risk	91 (57%)	87 (55%)	5.1%
EuroSCORE II (%)	1.83 (1.11−3.09)	1.86 (1.07−3.24)	3.4%
Low risk	86 (54%)	83 (52%)	3.8%
Intermediate risk	50 (31%)	54 (34%)	5.4%
High risk	23 (15%)	22 (14%)	1.8%
Number diseased vessels	3 (2−3)	3 (2−3)	1.1%
LM	22 (14%)	24 (15%)	3.6%
Proximal LAD	61 (45%)	60 (44%)	0.2%
Three-vessel disease	100 (63%)	94 (59%)	7.8%
Medication at discharge			
Beta blockers	81 (51%)	75 (47%)	7.6%
ACEi/ARB	86 (54%)	81 (51%)	6.3%

Continuous values are presented as median (interquartile range) or mean ± standard deviation.

Abbreviations: ACEi/ARB = angiotensin enzyme convertor inhibitors or angiotensin II receptor blockers; BMI = body mass index; CABG = coronary artery bypass grafting; Cr = creatinine; diff = differences; GFR = glomerular filtration rate; LAD = left anterior descending; LM = left main; LVEF = left ventricular ejection fraction; MDRD = Modification of Diet in Renal Disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; Std = standardized; TIA = transient ischemic attack.

differences between the 2 groups. Baseline and postmatching baseline characteristics of the population are depicted in Table 2 and in Supplementary Table 1.

In the PS-matched cohort, the median follow-up was 60 months (IQR 47 to 60 months) in the overall population, 60 months (IQR 49 to 60 months) in the CABG group, and 60 months (IQR 41 to 60 months) in the PCI group (p = 0.06). Procedural characteristics were similar before and after PS-matching. Among PS-matched PCI-treated patients, stents were implanted in 94% (n = 149) of all patients, with drug-eluting stents used in 70% of stented patients. Mean number of stents was 1.61 ± 0.47 stents/patient. Mean number of vessels treated in the PCI group was 1.13 ± 0.55 per patient. In the CABG group, the mean number of grafts/patient was 2.30 ± 0.78, with arterial bypass used in 98% of the patients. There were 72% of the patients submitted to off-pump surgery. The median time from admission to revascularization in the CABG group was 9 days (IQR 4 to 20 days). Notably, CABG was associated with a higher prevalence of complete revascularization when compared with PCI (48% vs 5%, p < 0.001).

Table 3
Univariate and multivariate (Cox regression) analysis after propensity score matching

	Univariate analysis			Multivariate analysis		
	Unadjusted HR	95% CI	p value	Adjusted HR	95% CI	p value
Diabetes mellitus	1.88	1.22−2.91	**0.005**	1.63	1.04 − 2.54	**0.033**
EuroSCORE II (per unit)	1.08	1.06−1.11	**<0.001**	1.07	1.04 − 1.10	**< 0.001**
SYNTAX intermediate/high	2.31	1.50−3.56	**<0.001**	1.93	1.23 − 3.02	**0.004**
Incomplete revascularization	1.89	1.06−3.35	**0.031**	1.25	0.66 − 2.38	0.493
PCI	1.59	1.02−2.48	**0.039**	1.52	0.93 − 2.50	0.094
Age* (per unit)	1.07	1.04−1.09	**<0.001**	–	–	–
Creatinine clearance* (per unit)	0.98	0.98−0.99	**<0.001**	–	–	–
GRACE score* (per unit)	1.02	1.02−1.03	**< 0.001**	–	–	–
LVEF ≥50%*	0.34	0.22−0.52	**<0.001**	–	–	–
LVEF 40−50%*	2.16	1.28−3.64	**0.004**	–	–	–
LVEF <40%*	2.39	1.50−3.84	**<0.001**	–	–	–
Critical status*	8.79	3.79−20.4	**<0.001**	–	–	–
Left main disease*	1.91	1.13−3.22	**0.015**	–	–	–

Bold represent statistically significant p values.
Abbreviations: CI = confidence interval; HR = hazard ratio; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.
* not included in multivariate analysis given the presence of multicollinearity.

In the matched population, the primary outcome of all-cause mortality occurred in 49 patients (31%) in the PCI group and in 33 patients (21%) in the CABG group (unadjusted HR 1.59; 95% CI 1.02 to 2.48; p = 0.039). After further adjustment for variables considered prognostically relevant this difference was no longer statistically significant, although a trend could be detected favoring CABG (adjusted HR 1.52; 95% CI 0.93 to 2.50; p = 0.094; taking CABG as reference; Table 3). Furthermore, diabetes mellitus, EuroSCORE II and SYNTAX score (intermediate/high anatomic complexity) remained independent predictors of all-cause mortality. Survival analyses of the overall comparison and according to the SYNTAX score are depicted in Figure 3.

Subgroup analysis showed a trend for better long-term outcomes favoring CABG in patients with LM disease, proximal LAD disease, intermediate/high SYNTAX, and LVEF <40% (Figure 4). Of note, among patients with LVEF <40% those who achieved complete revascularization had a lower 5-year mortality rate than those who did not (24.0% vs 54.2%, p < 0.001).

Discussion

To our best knowledge, this is the first study that compared mid-to-long-term mortality in a population of NSTEMI patients with LM or MVD, treated with PCI, CABG, or OMT. Our results can be summarized as follows: (1) OMT is associated with a worse long-term prognosis when compared with any revascularization strategy; (2) long-term mortality seems to be equivalent in patients treated with PCI or CABG, however; (3) a trend for lower mortality with CABG was found, especially in the subgroups of patients with LM disease, proximal LAD disease, intermediate/high risk SYNTAX score, and LVEF <40%.

A substantial proportion (up to 50%) of patients with NSTEMI who underwent invasive management has LM or MVD on the index angiography.[2,14,15] In real-word practice, these patients are considered for ad hoc angioplasty or heart team discussion to decide whether CABG, PCI, or OMT is the best option and this decision is closely linked namely to the anatomical complexity of the disease, to patient-specific characteristics and the ischemic burden. Data regarding the role of OMT in this population is scarce. In a population with symptomatic stable coronary artery disease, it has been shown that those treated with OMT had a higher mortality at 3 years.[16] Similarly, we report a two-fold higher risk of 5-year mortality when NSTEMI patients with LM or MVD deemed not amenable to revascularization are medically treated. Whether or not high-risk revascularization approaches can significantly impact this dire scenario remains to be fully determined.

Until now, no randomized clinical trial in NSTEMI patients with LM or MVD has been conducted. Indeed, the current recommendations for revascularization in this setting derive from studies conducted in stable coronary artery disease. Although a post hoc analysis from the Acute Catheterization and Urgent Intervention Triage strategy trial showed no differences in 1-year mortality between these 2 revascularization strategies (4.4% for CABG vs 5.7% for PCI; p = 0.58), the more recent Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease (FREEDOM) and the SYNTAX trials showed a potential benefit of CABG specially in the subgroup of patients with more complex disease.[3−5] The 5-year results of the SYNTAX trial revealed that patients randomly treated with CABG had a lower rate of MACCE when compared with the PCI group (26.9% vs 37.3%, p < 0.001). Furthermore, in patients with the highest anatomical complexity (SYNTAX score ≥33), CABG was also associated with lower mortality (11.4% vs 19.2%, p = 0.005). Similar results were reported in the FREEDOM trial, where the rates of the composite end point of all-cause death, cerebrovascular accident, or myocardial infarction were lower in CABG when compared with PCI (18.7% vs 26.6%, p = 0.005). Yet, in the FREEDOM trial, the mortality benefit associated with CABG was found only in patients with intermediate anatomical complexity (SYNTAX score 23 to 32). Our findings are supported and parallel those of both the FREEDOM and SYNTAX

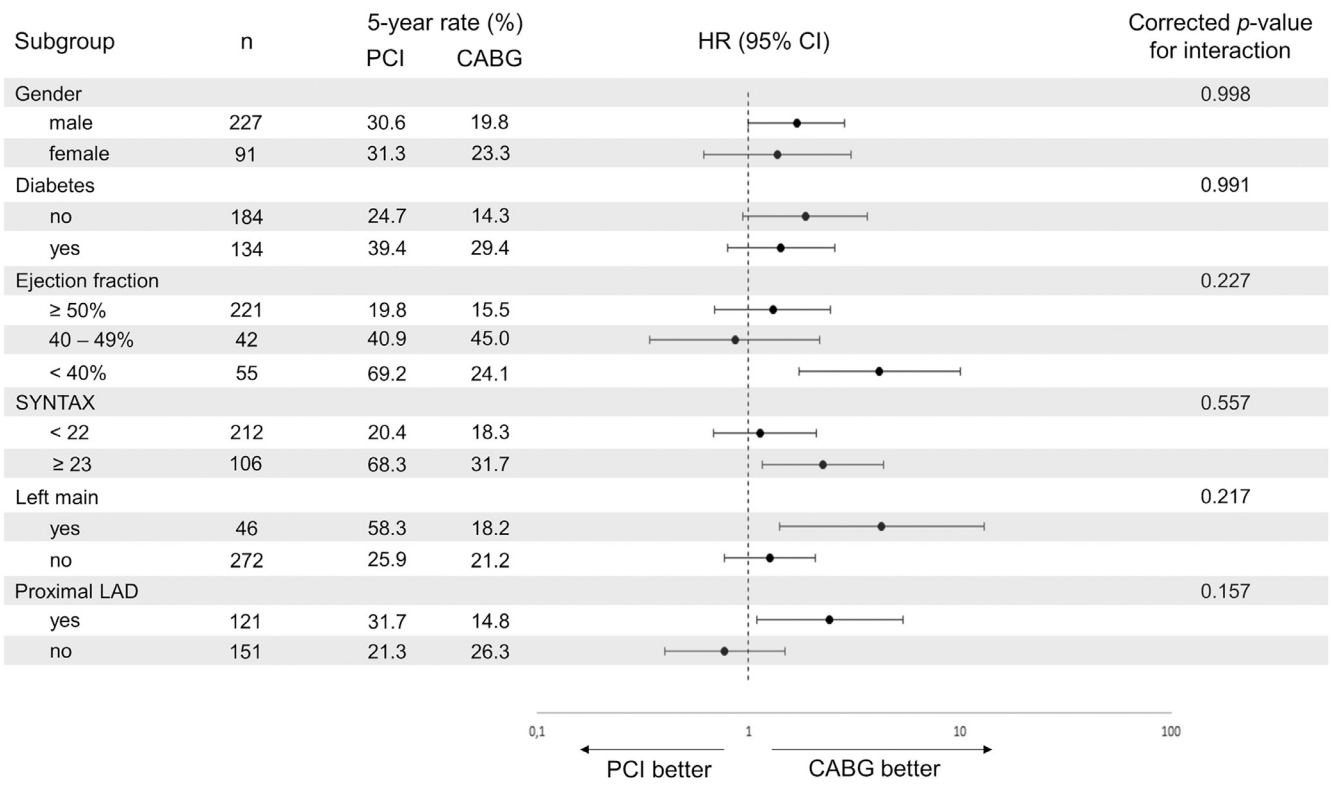

Figure 4. Subgroup analysis after propensity score matching. CABG = coronary artery bypass graft; CI = confidence interval; HR = hazard ratio; LAD = left anterior descending artery; PCI = percutaneous coronary intervention.

trials. The magnitude of the numerical difference in mortality between CABG and PCI that we found in our study is within the range reported by the aforementioned trials. After double adjustment by PS-matching and Cox multivariate analysis (to overcome residual bias), the difference was no longer statistically significant. However, a trend persisted favoring CABG and, moreover, the impact seemed to be more striking in patients with an intermediate/high anatomical complexity (SYNTAX ≥23), LM or proximal LAD disease or LVEF <40%. In a similar study[7] that pooled data from 3 randomized clinical trials performed in the setting of ACS with non−ST-elevation with LM or MVD (n = 1,246 patients), the 5-year rate of all-cause mortality, myocardial infarction, or stroke was significantly lower with CABG than with PCI (HR 0.74; 95% CI 0.56 to 0.98; p = 0.036). Nevertheless, in this study, only 6% of the patients were admitted with NSTEMI (n = 77), contrasting with our work where a total of 1,104 NSTEMI patients were included. Also, our analysis was conducted in a real-world population without the caveats of patient inclusion/selection from randomized clinical trials.

Some important aspects should be mentioned when interpreting our results. First, the CABG group had a higher degree of revascularization as showed by a higher mean of vessels treated and a lower rate of incomplete revascularization. Indeed, several studies support the concept that an incomplete revascularization strategy can be detrimental in the long-term, thus it could have conferred an advantage to the CABG group in our population.[17,18] Also, the presumed better results of CABG in the subgroup of patients with LVEF <40% could be explained by the higher rate of complete revascularization that was achieved when compared with PCI. Finally, the median time from admission to revascularization in the CABG group was 9 days, which could translate into a lower risk population when compared with patients treated by PCI that could not be mitigated by the PS-matching or multivariate analysis.

We recognize that the sample size is modest, hampering definitive conclusions for the comparison between groups due to type II error (lack of adequate statistical power). Secondly, due to its retrospective nature, potential confounding might persist even after adequate PS-matching and multivariate analysis, although standardized differences were ≤10% for all the variables in the model. As such, our results should be regarded as hypothesis generating especially the subgroup analysis where study underpower is almost a certainty. Even so, they are strongly supported by similar findings reported in the literature from the abovementioned randomized clinical trials and from a recent individual patient-data pooled analysis[19] performed in a broader patient population. Moreover, this is a single-center analysis and the decisions around revascularization strategies might not reflect the practice in other institutions. Third, we did not collect data regarding stroke, acute myocardial infarction and subsequent revascularization, which could have changed (and probably strengthen) our findings. Also, even though we have information about the medical therapy at discharge, we do not report changes in therapy during the follow-up, which could have influenced the outcome. Finally, epicardial coronary artery disease was anatomically defined as at least 50% stenosis and it remains uncertain if results would be the same whether a different threshold (e.g., 70% stenosis) or a functional definition had been used.

In conclusion, in a real-world NSTEMI patient population with LM or MVD, OMT alone was associated with a dire outcome. Although 5-year all-cause mortality was statistically similar between CABG and PCI, a signal toward a potential benefit of CABG over PCI was detected, which may be particularly important in patients with intermediate/high anatomical complexity (SYNTAX ≥23), LM disease, proximal LAD disease, and LVEF <40%. Dedicated randomized trials are needed to further elucidate the role of current revascularization options in this growing patient population.

Acknowledgment

None to declare.

Declarations of Interest

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.amjcard.2018.11.052.

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