Outcomes of different revascularization strategies among patients presenting with acute coronary syndromes without ST elevation

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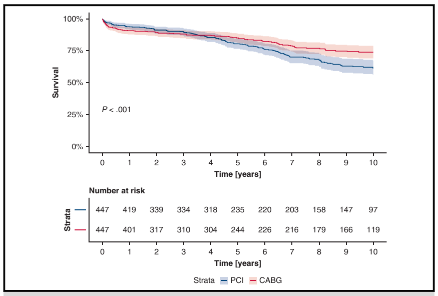
ABSTRACT

Objective: To compare short- and long-term outcomes of patients hospitalized with non–ST-segment myocardial infarction (NSTEMI) or unstable angina (UA) who were referred for revascularization by either coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) in a real-world national cohort.

Methods: This observational study included 5112 patients, who underwent either CABG or PCI, admitted for NSTEMI or UA and were enrolled in the Acute Coronary Syndrome Israeli Survey between 2000 and 2016. Propensity score-matching analysis compared early outcomes and all-cause mortality in patients who underwent revascularization by PCI with revascularization by CABG.

Results: Of the 5112 patients, 4327 (85%) underwent PCI and 785 (15%) CABG. Following propensity score analysis, 447 pairs were chosen (1:1). Independent predictors for CABG referral included 3-vessel CAD (odds ratio [OR], 5.5; 95% confidence interval [CI], 4.5-6.7, $P < .001$), absence of on-site cardiac surgery (OR, 1.3; 95% CI, 1.1-1.6, $P = .004$), no previous PCI (OR, 1.5; 95% CI, 1.2-1.9, $P = .002$) and no previous myocardial infarction (OR, 1.3; 95% CI, 1-1.7, $P = .022$). The 10-year mortality risk was significantly lower among those who underwent CABG compared with PCI (20.4% vs 28.4%, $P = .006$). Consistent with these findings, multivariable analysis showed that referral to CABG was independently associated with a significant 65% reduction in the risk of 10-year mortality ($P < .001$). This long-term advantage was seen among male patients ($P < .001$) and not female patients ($P = .910$).

Conclusions: In a real-life setting, revascularization by CABG provides excellent long-term outcomes in patients with NSTEMI or UA. The advantage of CABG over PCI was seen only in male patients. (J Thorac Cardiovasc Surg 2020;160:926-35)



Survival after propensity score matching.

Central Message

In a real-life setting, revascularization by CABG provides excellent long-term outcomes in patients with NSTEMI or UA.

Perspective

In a real-life setting, revascularization by CABG is associated with excellent long-term outcomes in patients with NSTEMI/UA acute coronary syndrome. Better survival of patient referral to CABG compared with PCI was seen only in male patients.

See Commentary on page 936.

Ischemic heart disease is the leading cause of death globally and accounts for about 7.4 million mortalities worldwide according to the World Health Organization's annual publication.[1] The numbers of patients presenting with non–ST-segment elevation myocardial infarction (NSTEMI) or unstable angina (UA) are increasing, and these patients have a poor prognosis due to multiple comorbidities.[2] Patients with acute coronary syndrome (ACS) without persistent ST-segment elevation undergo early

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Abbreviations and Acronyms

ACS	= acute coronary syndrome
ACSIS	= Acute Coronary Syndrome Israeli Survey
CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
CI	= confidence interval
HR	= hazard ratio
MACE	= major adverse cardiac events
MI	= myocardial infarction
NSTEMI	= non–ST-segment elevation myocardial infarction
OR	= odds ratio
PCI	= percutaneous coronary intervention
UA	= unstable angina

revascularization when compared with patients with stable coronary artery disease (CAD).[3]

Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are the options for revascularization in patients suffering from CAD. Choice of the most appropriate modality is affected by the clinical presentation, comorbidities, anatomical complexity of the CAD, and baseline characteristics of the patient.[4-7]

Although advances in PCI with drug-eluting stents have provided good outcomes, CABG remains an important revascularization strategy in patients with ACS. However, the current referral patterns and outcomes of patients admitted with NSTEMI/UA referred to either CABG or PCI are unknown. Furthermore, the comparison between CABG and PCI is based on cumulative data, which have revealed inconsistent results in various reports,[4,8,9] and therefore it is appropriate to study the real-world results of patients with ACS who are hemodynamically stable at admission and potential candidates for either one of the revascularization strategies.

Thus, in the present study, we sought to examine (1) the outcomes of matched patients with NSTEMI/UA referred to revascularization by PCI versus CABG in a real-world clinical practice, and (2) independent predictors for late all-cause mortality among patients with NSTEMI/UA who undergo revascularization by either PCI or CABG.

MATERIALS AND METHODS

Study Design

The Acute Coronary Syndrome Israeli Survey (ACSIS) is a voluntary biennial prospective national registry of all patients with ACS hospitalized in 25 coronary care units and cardiology departments in all public general hospitals in Israel over a 2-month period (March to April).[10] All 25 public cardiac departments that constitute the majority of cardiac practice in Israel participated in the survey. Site participation was stable during the study period, with no sites added or withdrawn during the study period.

ACSIS is managed by the Working Group on Acute Cardiovascular Care of the Israel Heart Society, in participation with the Israeli Center for Cardiovascular Research. Demographic, historical, and clinical data were recorded on prespecified forms for all patients. Patient management was at the discretion of the attending physicians. Admission and discharge diagnoses were recorded as determined by the attending physicians based on clinical, electrocardiographic, and biochemical criteria. Definitions of type of MI and UA were homogeneous, based on prespecified criteria according to accepted definitions during the specific survey period.[11-16] All patients signed an informed consent for participating in the ACSIS registry in each medical center, which also received approval from its institutional review board.[17]

Study Population

Between 2000 and 2016 (8 consecutive registries), 15,211 patients were hospitalized with ACS and were included in the ACSIS registry. Of them, 6993 patients were diagnosed with STEMI and were excluded from the current analysis, whereas 3033 patients with either NSTEMI or UA were treated conservatively. Of them, 63 were treated by both PCI and CABG, and were also excluded from the current analysis (Table E1). Accordingly, the current study population comprises 5112 patients who were categorized according to their chosen revascularization strategy: PCI versus CABG (Figure E1). Comparisons were made using data from each of the 8 registries.

Clinical Outcomes

Clinical outcomes included 30-day major adverse cardiac events (MACE, which included death, myocardial infarction [MI], stroke, and urgent revascularization), in-hospital complications, and long-term all-cause mortality.

Data Collection and Follow-up

All data from the participating hospitals were collected and pooled into a designated database. All centers used standardized definitions for data collection, including demographic parameters, medical history, chronic and periprocedural medical treatment, echocardiography measurements, procedure information, and outcome measures. All patients were prospectively followed up for clinical events at 30 days and for mortality at 36 months. Mortality data were ascertained from the Israeli Ministry of Interior Population Register through January 2018.

Statistical Analysis

Data are presented as mean $\pm$ standard deviation for normal, or median for abnormal distribution. Continuous variables were tested with the Kolmogorov–Smirnov test for normal distribution. Categorical variables are given as frequencies and percentages. A χ^2 test was used for comparison of categorical variables between revascularization strategies (CABG and PCI), a Student t test was performed for comparison of normally distributed continuous variables, and Mann–Whitney U test was performed for non-normal distribution.

To reduce treatment selection bias and potential confounding factors, and to adjust for significant differences in patient characteristics, propensity score-matching was performed. Propensity scores were estimated using a multivariate logistic regression model for treatment with PCI versus CABG. All variables presented in Table 1 were entered to calculate the propensity score. A local optimal algorithm with the caliper method was used for the development of propensity score-matched pairs without replacement (1:1 match), (area under the curve of 0.78). A matching caliper of 0.2 standard deviations of the logit of the estimated propensity score was enforced to ensure that matches of poor fit were excluded. The matching procedure was performed by using the R Matching package (R Development Core Team, R Foundation for Statistical Computing, Vienna,

TABLE 1. Baseline characteristics

Characteristic	Before matching PCI N = 4327 (%)	Before matching CABG N = 785 (%)	Before matching P value	After matching PCI N = 447 (%)	After matching CABG N = 447 (%)	After matching P value	Standardized difference of mean
Age, y, mean (SD)	64 (12)	66 (11)	<.001	64 (12)	65 (11)	.184	0.089
Sex (male)	3385 (78)	612 (78)	.904	335 (75)	350 (78)	.269	0.079
Hypertension	2798 (65)	506 (64)	.909	299 (67)	299 (67)	1.000	<0.001
Current smoker	1456 (34)	233 (30)	.033	159 (36)	144 (32)	.323	0.071
Hyperlipidemia	3185 (74)	561 (72)	.257	331 (74)	329 (74)	.939	0.010
Diabetes mellitus	1652 (38)	335 (43)	.022	197 (44)	202 (45)	.788	0.023
Previous PCI	1594 (37)	213 (27)	<.001	126 (28)	127 (28)	1.000	0.005
Previous MI	1515 (35)	237 (30)	.011	134 (30)	140 (31)	.717	0.029
EF (%)			<.001			.229	
>50	1763 (57)	318 (49)		255 (57)	232 (52)		0.093
40-50	777 (25)	175 (27)		90 (20)	109 (24)		0.084
30-40	383 (13)	107 (16)		74 (17)	69 (16)		0.031
<30	144 (5)	55 (8)		28 (6)	37 (8)		0.078
Renal impairment	471 (11)	72 (9)	.165	50 (11)	48 (11)	.915	0.014
COPD	189 (6)	30 (5)	.462	19 (6)	18 (6)	1.000	0.011
History of CVA/TIA	325 (7)	75 (10)	.058	32 (7)	40 (9)	.390	0.066
Congestive heart failure	310 (7)	70 (9)	.098	37 (8)	43 (10)	.558	0.047
Vessels involved			<.001			.637	
1-vessel CAD	1115 (32)	33 (6)		30 (7)	24 (5)		0.056
2-vessel CAD	1273 (36)	138 (24)		114 (25)	110 (25)		0.021
3-vessel CAD	1101 (32)	400 (70)		303 (68)	313 (70)		0.048
Indication for angiography			.524			1.000	
NSTEMI	3018 (70)	538 (68)		332 (74)	332 (74)		<0.001
Unstable angina	1309 (30)	247 (32)		115 (26)	115 (26)		<0.001
On-site cardiac surgery	2476 (57)	410 (52)	.011	228 (51)	224 (50)	.927	0.011
Time period: after year 2008	2492 (58)	393 (50)	<.001	283 (63)	279 (62)	.835	0.019

PCI, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *SD*, standard deviation; *MI*, myocardial infarction; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *CAD*, coronary artery disease; *NSTEMI*, non–ST-segment elevation myocardial infarction.

Austria). After propensity score-matching, covariates were compared as described previously.

Multivariable logistic regression analysis was used to identify factors relating to CABG. All statistically different variables ($P < .1$) in Table 1 were entered into the model. The variables that were included by this indication were age, smoking, diabetes, previous PCI, previous MI, congestive heart failure, previous stroke, the number of vessels with CAD, on-site cardiac surgery, and the time of enrollment into the registry. Sex (prespecified) was also included in the model due to its clinical importance. Survival analysis was done using the Kaplan–Meier method, and comparison by the revascularization strategy (CABG vs PCI) was tested using the log-rank test. Landmark analysis was performed following the detection of risk reversal in the univariate analysis as a result of the non-proportional hazard function of the survival curves between PCI and CABG. Furthermore, mortality was evaluated by an additional model for the overall study period based on weighted Cox regression, to estimate the average hazard ratio (HR) in the event of non-proportional hazard. Statistically significant variables by univariable analysis and prespecified variables were used in the multivariable model to identify independent predictors of 10-year mortality. The variables included in the final model were age, revascularization strategy, sex, hypertension, smoking, diabetes, 3-vessel CAD, previous MI, renal impairment, previous stroke, congestive heart failure, and an on-site cardiac surgery unit. In a secondary analysis, consistency of the findings in the primary model was assessed using a model with a site as a random-effect to adjust for differences between centers and within-center variations. In addition, a subgroup analysis was carried out comparing outcomes by gender (Tables E2 and E3).

Statistical significance was assumed when the null hypothesis could be rejected at $P < .05$. All P values reflect results of 2-sided tests. Statistical analyses were conducted using R (version 3.4.1).[18]

RESULTS

Baseline Clinical Characteristics

Of the 5112 patients included in the study, 4327 (85%) underwent PCI and 785 (15%) CABG. Mean age of study patients was 65 ± 13 years, of whom 25% were women. Patients treated by PCI were somewhat younger, with less incidence of diabetes, peripheral vascular disease, previous stroke, and 3-vessel CAD. In contrast, the proportion of previous PCI, previous MI, and current smokers was greater in patients treated by PCI versus CABG (Table 1). After propensity score matching, baseline clinical characteristics of study patients by the revascularization strategy presented no statistically significant differences (Table 1).

Indications for the index coronary angiography in all study patients were as follows: NSTEMI in 70%, and UA pectoris in 30%; and among the matched groups: NSTEMI in 74%, and UA in 26%, without statistically significant differences between those who underwent PCI and CABG (Table 1).

Factors Associated With Referral for PCI Versus CABG

Multivariable logistic regression analysis showed that 3-vessel CAD versus 1 or 2- vessel CAD was the most powerful predictor for CABG referral. This analysis showed that patients with 3-vessel CAD were 5.5 times more likely to be referred to CABG, compared with patients who had only 1- or 2-vessel CAD (odds ratio [OR], 5.5; 95% confidence interval [CI], 4.5-6.7, $P < .001$). Additional independent predictors for PCI versus CABG included the absence of an on-site cardiac surgery unit, previous PCI, and previous MI. Older age, sex, smoking, diabetes mellitus, history of stroke, congestive heart failure, or era of revascularization were not associated with any revascularization strategy referral (Figure 1).

Early Outcomes Among the Matched Patients

Compared with patients who underwent PCI, patients who underwent CABG had a lower rate of recurrent MI at 30 days (0.9% vs 4.3%), with no difference in 30-day mortality (3.1% vs 2.2%) or MACE defined as mortality, recurrent MI or stroke at 30 days (5% vs 6.9%) (Table 2). Patients who underwent CABG had a non-statistically significant greater rate of 1-year mortality compared with patients who underwent PCI (9.5% vs 6.3%) (Figure E2). During the first year of follow-up, multivariable analysis showed no advantage for either one of the revascularization strategies ($P = .141$). Age >65 years ($P < .001$) and female sex ($P = .042$) were independently associated with 1-year mortality (Table 3).

Long-Term Survival in the Overall Study Cohort

Unadjusted comparison between the 2 revascularization strategies in the entire unmatched study cohort showed a long-term advantage toward CABG (Figure 2), with a statistically significant treatment-by-time interaction effect. Thus, 3-year cumulative survival rates were similar in patients who underwent CABG and PCI (89.3% vs 89.9%, $P = .669$), whereas landmark analysis showed that beginning with the third year following intervention, subsequent cumulative survival rates were significantly lower among

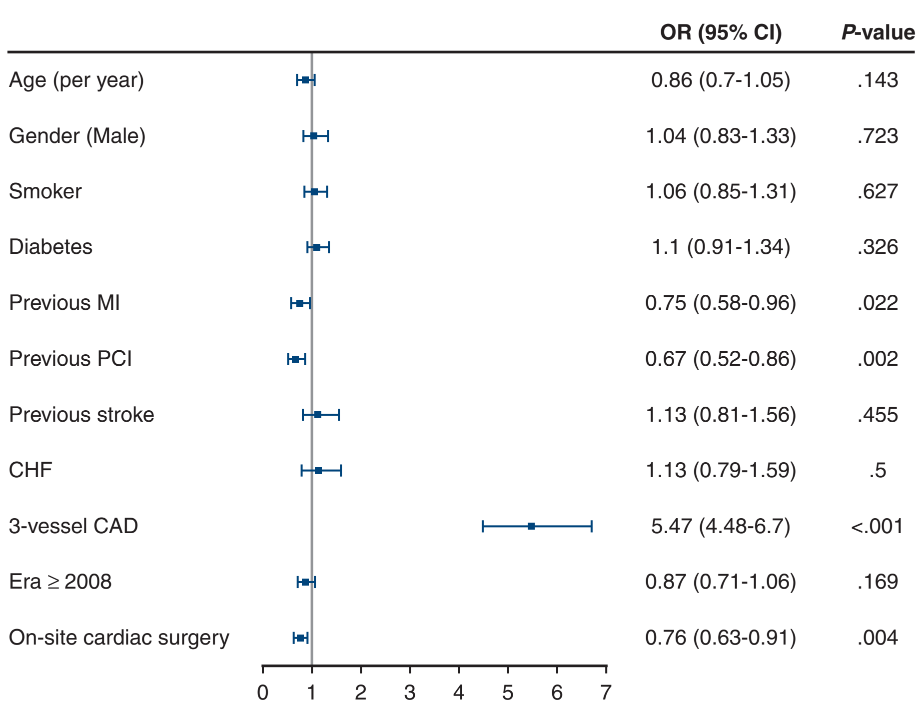

FIGURE 1. Multivariable logistic regression: OR for CABG treatment (vs PCI) with 95% CI. *OR*, Odds ratio; *CI*, confidence interval; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *CHF*, congestive heart failure; *CAD*, coronary artery disease.

TABLE 2. Early and late results of the unmatched and matched cohort

Outcome	Before matching PCI N = 4327 (%)	Before matching CABG N = 785 (%)	Before matching P value	After matching PCI N = 447 (%)	After matching CABG N = 447 (%)	After matching P value
30-d Outcomes						
Mortality	66 (1.5)	24 (3.1)	.004	10 (2.2)	14 (3.1)	.527
Recurrent MI	95 (2.3)	6 (0.9)	.018	19 (4.3)	4 (0.9)	.003
Stent thrombosis	15 (0.5)	–	–	1 (0.3)	–	–
CVA	16 (0.4)	2 (0.3)	.868	3 (0.7)	0 (0)	.247
MACE*	107 (3.4)	17 (3.5)	1.000	26 (6.9)	18 (5)	.342
1-y mortality	213 (5)	64 (8.2)	<.001	28 (6.3)	42 (9.5)	.097
10-y mortality	1110 (25.7)	158 (20.1)	.001	127 (28.4)	91 (20.4)	.006

PCI, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *MI*, myocardial infarction; *CVA*, cerebrovascular accident; *MACE*, major adverse cardiac events. *MACE is defined as mortality, recurrent MI or stroke at 30 days.

those who underwent PCI compared with CABG ($P < .001$ [Figure 2, Figure E3]).

Long-Term Survival Among the Matched Patients

Adjusted comparison between the 2 revascularization strategies by the propensity matching analysis showed a long-term advantage toward CABG (Figure 3). The 10-year mortality hazard was significantly lower in those who underwent CABG compared with PCI (20.4% vs 28.4%, $P = .006$). Consistent with these findings, nonproportional multivariable analysis showed that CABG was independently associated with a significant 65% reduction in the risk of 2- to 10-year mortality compared with PCI ($P < .001$). Additional predictors of 2- to 10-year mortality included the absence of an on-site cardiac surgery unit ($P = .026$), age >65 years ($P < .001$), history of congestive heart failure ($P = .001$), and diabetes mellitus ($P < .001$) (Table 4). These results were also consistent after adjustment for hospital site as a random effect thereby adjusting for the level of care effect of the different hospitals (HR, 0.46 for CABG; CI, 0.3-0.69, $P < .001$).

TABLE 3. Cox regression analysis: predictors for 0- to 1-year all-cause mortality

Variable	HR (95% CI)	P value
Age >65 y	2.96 (1.54-5.66)	.001
PCI vs CABG	0.68 (0.42-1.14)	.141
Sex (male)	0.59 (0.35-0.98)	.042
Hypertension	1.31 (0.7-2.48)	.400
Current smoker	0.57 (0.28-1.17)	.125
Diabetes mellitus	0.81 (0.5-1.33)	.414
3-vessel CAD	0.96 (0.57-1.62)	.872
Previous MI	1.3 (0.78-2.17)	.307
Renal impairment	1.67 (0.91-3.08)	.098
Previous stroke	1.57 (0.81-3.04)	.178
History of CHF	1.37 (0.71-2.67)	.349
On-site cardiac surgery	0.96 (0.57-1.6)	.862

HR, Hazard ratio; *CI*, confidence interval; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *CAD*, coronary artery disease; *MI*, myocardial infarction; *CHF*, congestive heart failure.

Subgroup Analysis: Long-Term Survival Among Male and Female Patients

Adjusted comparison between the 2 revascularization strategies showed a long-term advantage toward CABG, with a statistically significant treatment-by-sex interaction effect ($P < .001$). A subanalysis of the matched population by sex (Tables E2 and E3) showed that the association between CABG and improved outcome was significant in male patients: a mortality rate of 17.4% compared with 27.8% in patients who underwent PCI (HR, 0.64; 95% CI, 0.46-0.89; $P = .010$) (Figure 4, *A*). However, among female patients there was no difference in 10-year mortality rates between CABG and PCI (30.9% vs 30.4%, respectively; HR, 0.97; 95% CI, 0.59-1.59, $P = .910$) (Figure 4, *B*).

Additional analysis demonstrated that CABG provides a greater survival advantage in younger patients, patients with diabetes, patients with no history of renal impairment, patients with hypertension, those with previous MI, and patients with 3-vessel CAD. While all these subgroups were statistically significant, the complementary subgroups showed a trend toward survival advantage for CABG, but this did not reach statistical significance (Figure E4). The only patients who showed no trend toward any revascularization strategy advantage were female patients and those without 3-vessel CAD.

DISCUSSION

Our findings, derived from a real-life prospective cohort of patients who were enrolled in a biennial national registry, provide several important implications regarding the outcomes of patients with NSTEMI/UA. We have shown that: (1) patients with multivessel disease were more likely to be referred to CABG whereas those with previous PCI or

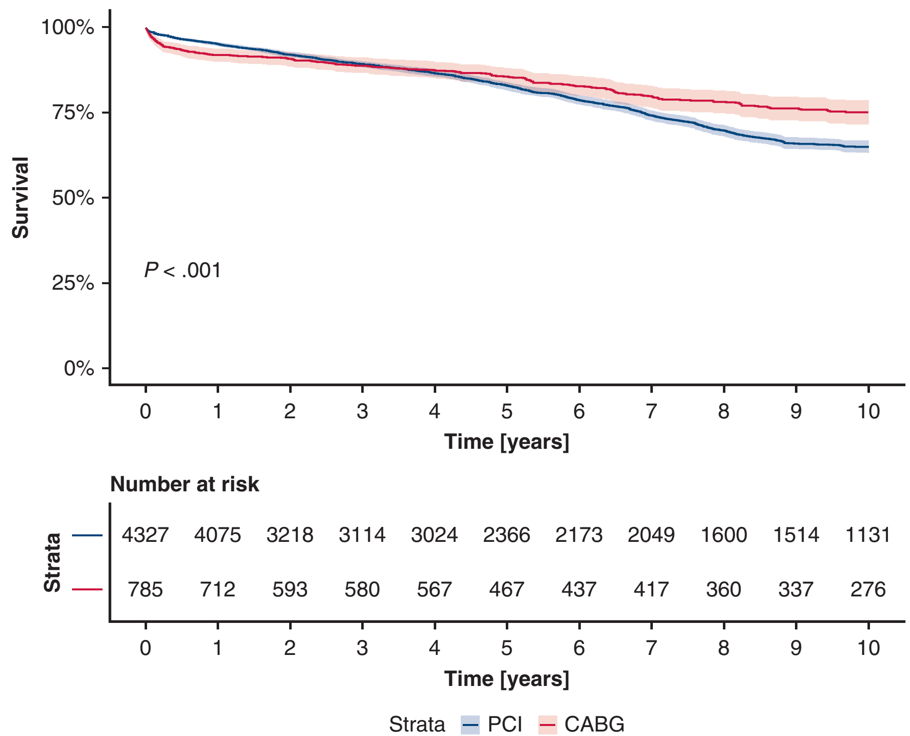

FIGURE 2. Overall 10-year survival curves by revascularization strategy (unmatched population). *P* value is for the landmark analysis from 3 years and thereafter. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft.

previous MI were more likely to have been referred to PCI; (2) patients' age, sex, diabetes mellitus, and congestive heart failure status were not associated with any particular revascularization strategy referral pattern; (3) in a real-life setting, revascularization by CABG provides excellent long-term outcomes; and (4) the advantage of CABG over PCI was statistically significant in the male patients (Video 1).

The current clinical decisions on choice of revascularization strategy is based on a combination of several factors: the anatomical severity and distribution of the CAD (such as left-main stenosis, number of vessels involved, SYNTAX score), comorbidities (such as diabetes mellitus, previous ischemic heart disease), baseline characteristics (such as the age of the patient), and on the clinical scenario (such as STEMI, NSTEMI, UA). Although these factors are recommended by current guidelines for the choice between CABG and PCI, there are no randomized clinical trials to compare CABG with PCI for patients with ACS without ST-segmental elevation.

In their study from the Milestone Registry, Buszman and colleagues[9] reported that PCI versus CABG was associated with a greater 3-year survival rate among 929 ACS without ST-segmental elevation–matched patients (86% vs 82%, $P = .01$). Another report by Ben-Gal and colleagues[19] on 528 matched pairs of ACS without ST-segment elevation patients, based on the post hoc analysis of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial, showed a similar all-cause mortality rate between PCI and CABG (95.6% vs 94.3%, $P = .58$) at 1 year. Although the early- and mid-term outcomes were comparable between the 2 different revascularization strategies in those studies, long-term follow-up was lacking. The present study demonstrated similar 1- and 3-year outcomes; however, for a longer follow-up period, CABG was associated with lower mortality rates compared with PCI before and after propensity matching. We have shown that during the first 3 years of follow-up, there were no differences in mortality between PCI and CABG. Thereafter, however, CABG provided more favorable results. Furthermore, since the late follow-up in our study included mortality as the only outcome, we speculated that had other outcomes (eg, MACE) been evaluated, CABG would have demonstrated additional advantages.

The last decade has shown a decline in the rate of isolated CABG.[20] In clinical practice, physicians tend to underuse surgical coronary revascularization in patients with CAD despite their being considered appropriate candidates. Hemingway and colleagues[21] showed that 26% of patients who demonstrated appropriate indications for CABG were eventually treated medically, an approach that resulted in adverse clinical outcomes. Our current report strengthens the use of CABG in eligible patients. Furthermore, in the ACSIS registry between 2000 and 2008, there was an increasing

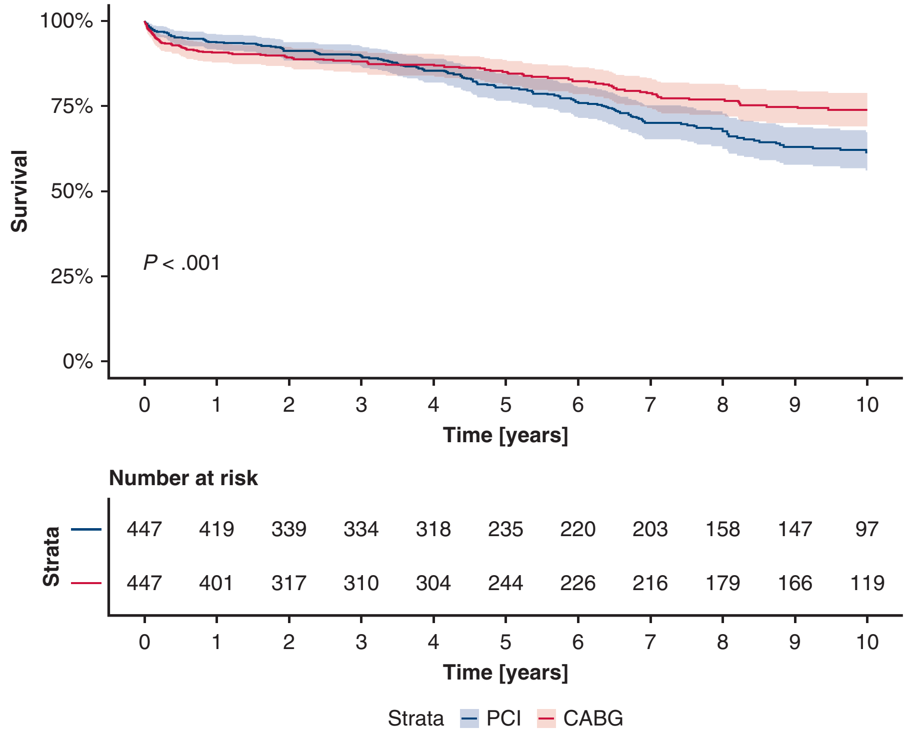

FIGURE 3. Kaplan–Meier curves for survival of the matched patients. *P* value is for the landmark analysis from 2 years and thereafter. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft.

use of PCI (from 37% in 2000 to 60% in 2008), whereas since 2008, there have been no significant changes in revascularization patterns. CABG rate did not change during these years despite the increasing use of PCI (Figure E1).

Current guidelines for the management of ACS without ST-segment elevation are predominantly based on the results of patients with stable CAD due to the lack of randomized studies in NSTEMI/UA patients.[22] The current guidelines recommend electing a revascularization strategy following a discussion by a multidisciplinary team comprising a cardiac surgeon, an interventional cardiologist, and a general cardiologist (Class I, Level of evidence C) stipulating no specific strategy recommendation. Appropriate patient selection via a local heart team approach is the key for successful patient management either by PCI or CABG. Although the current guidelines are based on the results of patients without ACS, it may not reflect real-life management and the results of NSTEMI/UA patients.

In certain circumstances, such as an emergency, performing PCI immediately after the diagnostic coronary angiogram is recommended and is preferable to delayed PCI. It is acceptable practice to perform culprit lesion PCI ad hoc after angiography. However, in nonemergency clinical situations, this approach is questionable. Hasty therapeutic decision-making may occur more frequently in centers without the routine use of a heart team. The present study included 25 hospitals in Israel that perform angiography and PCI. Of them, 16 did not have an on-site cardiac surgery department or unit, and thus no heart-team discussion occurred. In the 9 centers with on-site cardiac surgery services, a formal multidisciplinary heart-team discussion was conducted at the discretion of the treating physician, rather than routine

TABLE 4. Cox regression analysis: predictors for 2- to 10-year all-cause mortality

Variable	HR (95% CI)	*P* value
Age >65 y	2.83 (1.9-4.23)	<.001
PCI vs CABG	2.86 (1.92-4.17)	<.001
Sex (male)	1.11 (0.74-1.68)	.613
Hypertension	0.92 (0.61-1.38)	.677
Current smoker	1.01 (0.67-1.52)	.960
Diabetes mellitus	1.97 (1.38-2.82)	<.001
3-vessel CAD	1.2 (0.78-1.85)	.411
Previous MI	1.45 (0.99-2.14)	.058
Renal impairment	1.22 (0.73-2.03)	.454
Previous stroke	1.15 (0.65-2.03)	.633
History of CHF	2.32 (1.44-3.75)	.001
On-site cardiac surgery	0.65 (0.44-0.95)	.026

HR, Hazard ratio; *CI*, confidence interval; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *CAD*, coronary artery disease; *MI*, myocardial infarction; *CHF*, congestive heart failure.

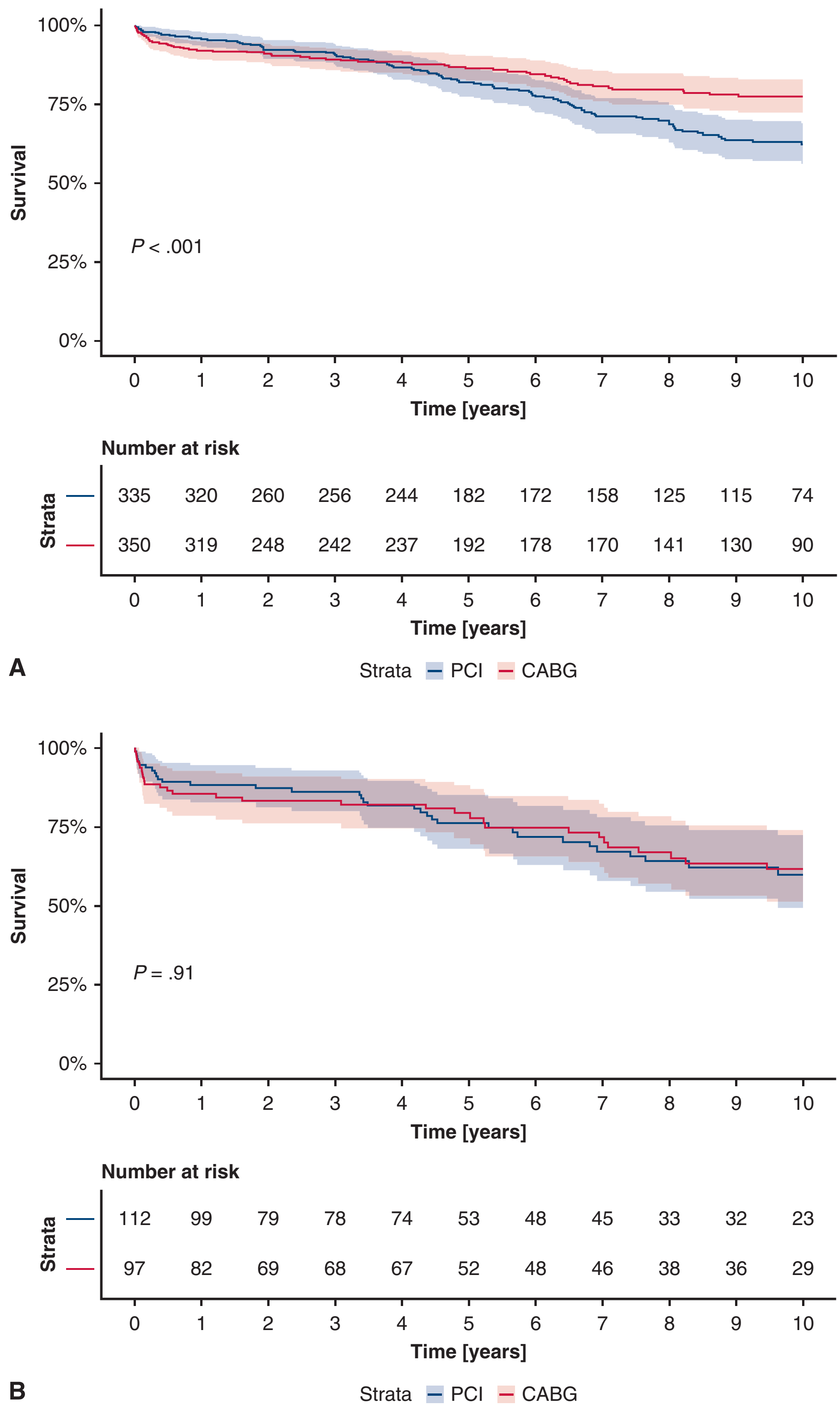

FIGURE 4. Ten-year survival curves for matched patients by sex. A, Subgroup of male sex. B, Subgroup of female sex. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft.

procedure. To ensure better long-term results, we believe that all individual cases included in the current study should have been reviewed by a heart team before deciding on revascularization strategy. The heart team should consider the calculated SYNTAX score to evaluate the complexity of the coronary anatomy, along with each

VIDEO 1. Dr Eilon Ram explaining the importance and relevance of the paper. Video available at: https://www.jtcvs.org/article/S0022-5223(19)32010-0/fulltext.

individual patient's clinical factors and preference. We have shown in this observational study that a patient's age, sex, and presence of diabetes mellitus were not associated with any particular revascularization strategy referral pattern. Perhaps if all patients were reviewed by a heart team, more patient with diabetes, younger patients, and male patients would have been referred to surgical revascularization.

The mortality rate of coronary heart disease has decreased over the past decades, presumably as the result of better control of coronary risk factors and better clinical management, including revascularization procedures and cardiovascular drugs.[23-25] A wealth of evidence exists to support the efficacy of statins, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, and antiplatelet agents in patients with CAD.[26-29] Although the use of these medications for secondary prevention after discharge from revascularization therapy has been increasing,[30] it should be noted that different medical management strategies exist between patients who undergo PCI and CABG.[31] This study did not take into account the variety of postprocedure treatment plans available for the patient. In addition, the survival benefit attributed to CABG could be extended further to encompass postprocedure and follow-up care.

In the current cohort, we did not find any survival advantage for either one of the revascularization strategies in our female patients. Although female compared with male patients had more diabetes and more hypertension, they had less 3-vessel CAD, there were fewer smokers, and they had fewer previous PCIs and MIs (Table E2). These baseline differences between the sex groups may explain their different long-term results. Although CABG provides better complete revascularization in patients with diabetes compared with PCI, survival advantage was not seen in our female patients who had more diabetes but less 3-vessel CAD. A comparison between PCI and CABG in female compared with male patients demonstrated differences in the number of vessels with CAD and the number of patients with previous PCI. However, there were no differences in patient age, diabetes, previous MI, and ejection fraction, as was seen in the male patients. Following propensity matching analysis, all these differences were abolished (Table E3).

Study Limitations

The ACSIS registry primarily included patients admitted only to cardiology wards and intensive cardiac care units nationwide and in the main did not include patients who were hospitalized in internal medicine wards, thus introducing a selection bias. Data regarding the urgency of the procedure were unavailable. Lack of information on performance of emergency or elective procedures would have been helpful to reduce selection bias between revascularization strategies. There was insufficient anatomical information regarding the encumbrance of CAD and the specific artery involved, as well as the surgical techniques that were performed. Therefore, it is difficult to make assumptions regarding the association of specific interventions in native arteries or grafts with clinical outcomes. We had no information on the main cause of death or the rate of cardiac events, such as recurrent revascularization, during the follow-up period. Analysis of cardiac events could reinforce that CABG would have additional advantages. Since we had no information regarding the postprocedure medical treatment, we could not rule out the fact that the survival benefit attributed to CABG could be associated with postprocedure and follow-up care. Since the study includes data collected over 16 years, changes in PCI techniques, surgical techniques, and postprocedure care during that time period may have cofounded the results.

CONCLUSIONS

In a real-life setting, revascularization by CABG is associated with good long-term outcomes in patients with NSTEMI/UA ACS. Better survival of patient referral to CABG compared with PCI was seen only in male patients. Prospective randomized studies are required to provide stronger recommendations in future guidelines regarding the management of patients hospitalized with NSTEMI or UA deemed eligible for coronary revascularization therapy.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: acute coronary syndromes, revascularization, coronary artery bypass grafting, percutaneous coronary intervention, coronary artery disease

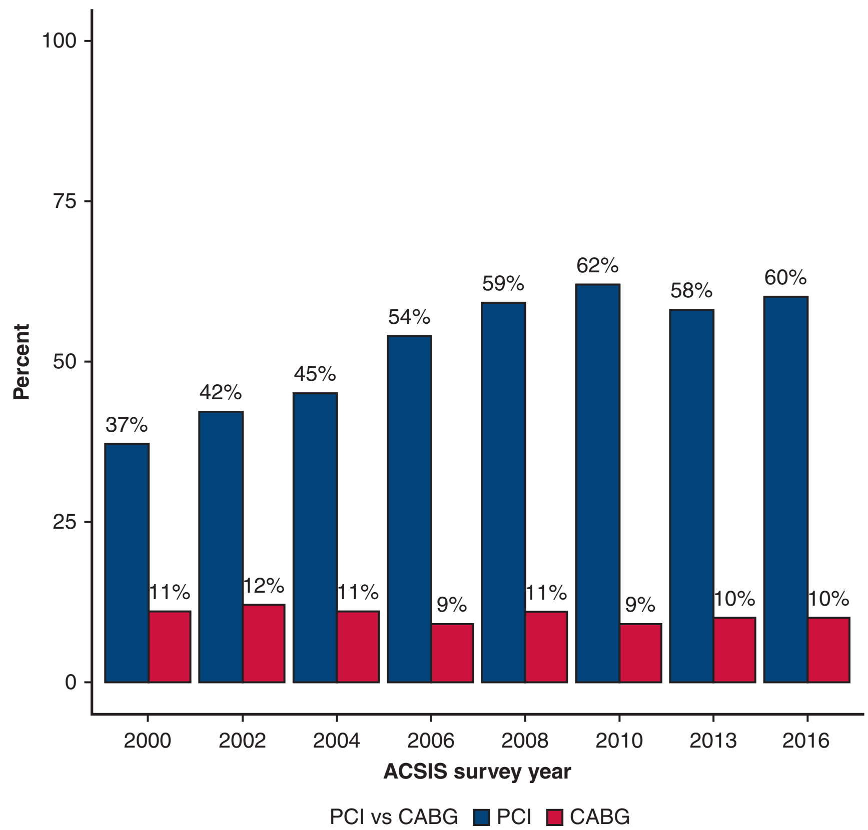

FIGURE E1. Revascularization pattern over the years. *ACSIS*, Acute Coronary Syndrome Israeli Survey; *CABG*, coronary artery bypass graft; *PCI*, percutaneous coronary intervention.

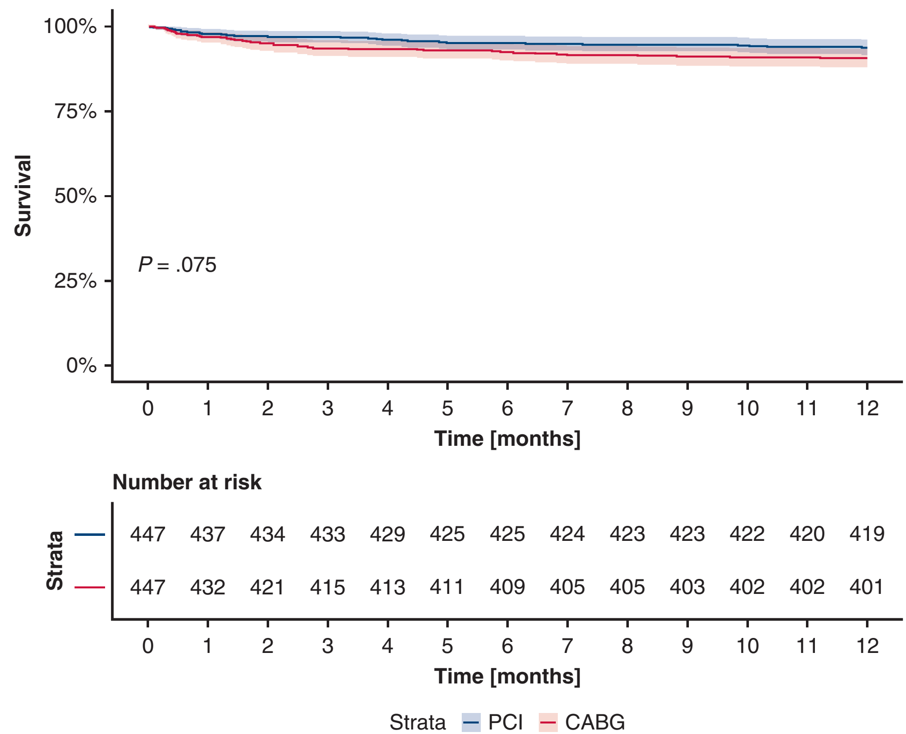

FIGURE E2. Overall 1-year survival curves by revascularization strategy (matched population). *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft.

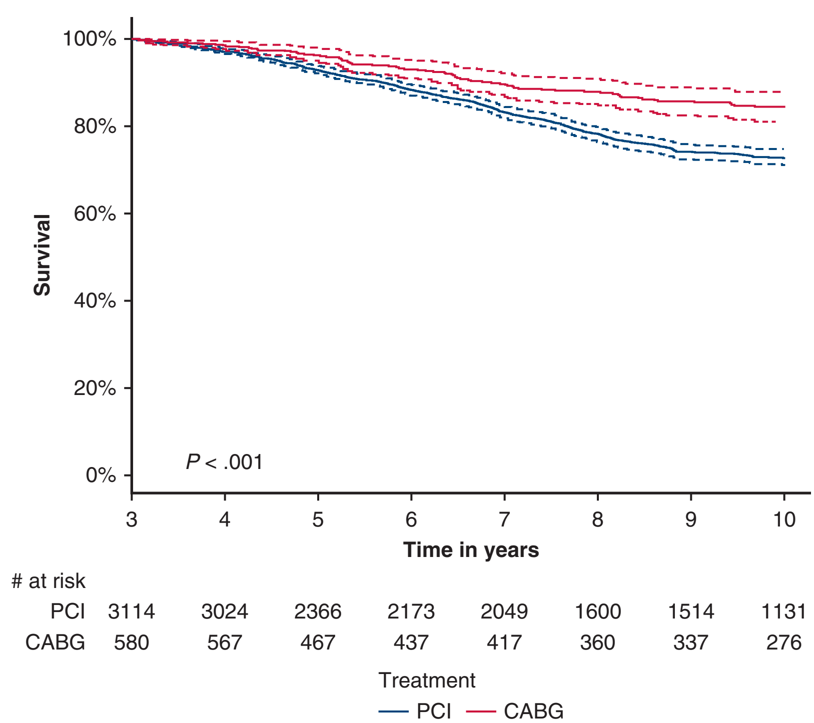

FIGURE E3. Landmark analysis: Survival from 3 to 10 years after revascularization. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft.

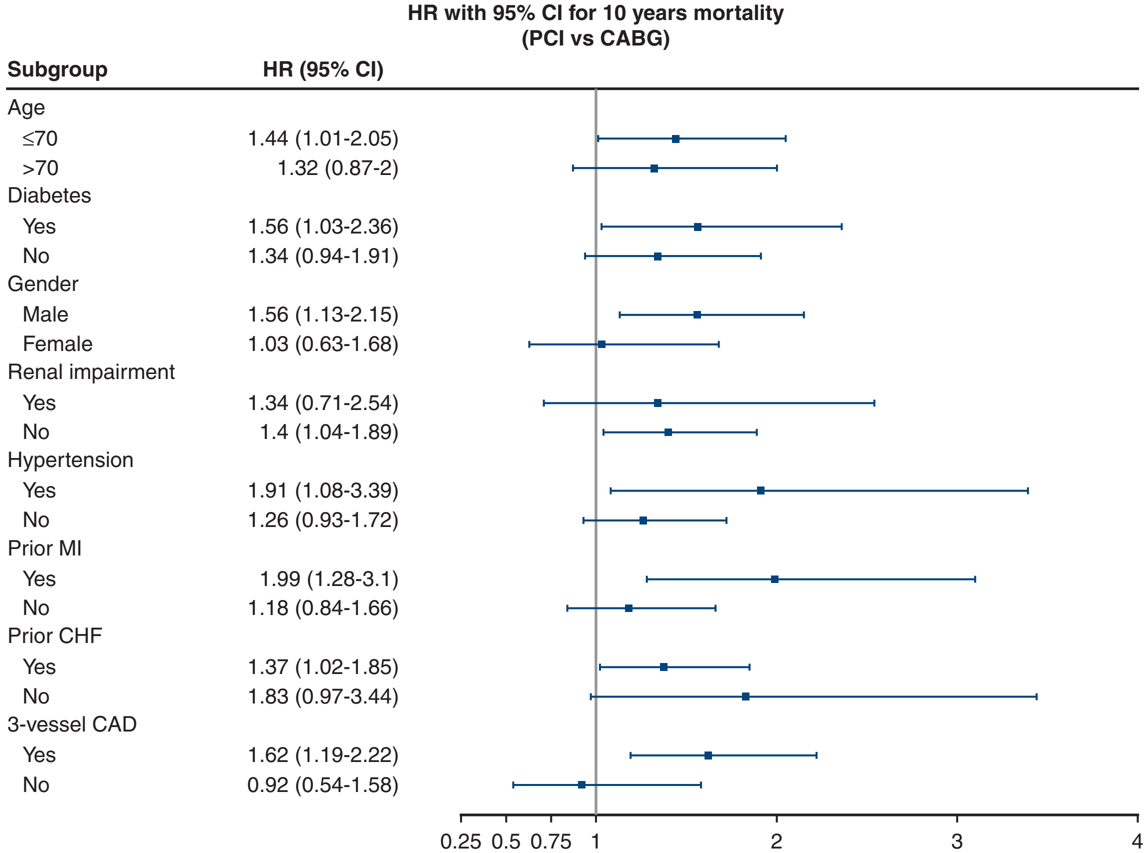

FIGURE E4. Subgroup analysis: HR with 95% CI for 10 years mortality (PCI vs CABG). *HR*, Hazard ratio; *CI*, confidence interval; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *MI*, myocardial infarction; *CHF*, congestive heart failure; *CAD*, coronary artery disease.

TABLE E1. Baseline characteristics of the sample population (intervention patients) and the nonintervention patients (conservatively treated)

	Intervention (CABG or PCI) N = 5112	Nonintervention N = 3033	*P* value
Age, y, mean (SD)	64 (12)	68 (13)	<.001
Sex (male)	3997 (78)	2176 (72)	<.001
Hypertension	3304 (65)	2162 (71)	<.001
Current smoker	1689 (33)	756 (25)	<.001
Hyperlipidemia	2456 (73)	2105 (69)	<.001
Diabetes mellitus	1987 (39)	1312 (43)	.001
Previous PCI	1807 (35)	1120 (37)	.405
Previous MI	1752 (34)	1378 (45)	<.001
EF (%)			<.001
>50	2081 (56)	1044 (48)	
40-50	952 (26)	493 (22)	
30-40	490 (13)	364 (17)	
<30	199 (5)	281 (13)	
Renal impairment	543 (11)	644 (21)	<.001
COPD	219 (6)	209 (7)	<.001
History of CVA/TIA	400 (8)	341 (11)	<.001
Congestive heart failure	380 (7)	534 (18)	<.001
Vessels involved			<.001
1-vessel CAD	1148 (28)	247 (27)	
2-vessel CAD	1411 (35)	250 (28)	
3-vessel CAD	1501 (37)	403 (45)	
Indication for angiography			.199
NSTEMI	3556 (70)	2062 (68)	
Unstable angina	1556 (30)	971 (32)	
Era: after year 2008	2884 (56)	1292 (43)	<.001

CABG, Coronary artery bypass graft; *PCI*, percutaneous coronary intervention; *SD*, standard deviation; *MI*, myocardial infarction; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *CAD*, coronary artery disease; *NSTEMI*, non–ST-segment elevation myocardial infarction.

TABLE E2. Baseline characteristics of the subgroups of male and female patients

	Male patients			Female patients		
	PCI N = 3385 (%)	CABG N = 612 (%)	*P* value	PCI N = 942 (%)	CABG N = 173 (%)	*P* value
Age, y, mean (SD)	62 (12)	64 (11)	<.001	69 (11)	70 (10)	.200
Hypertension	2061 (61)	375 (61)	.921	737 (78)	131 (76)	.511
Current smoker	1304 (39)	212 (35)	.081	152 (16)	21 (12)	.213
Hyperlipidemia	2456 (73)	424 (70)	.110	729 (77)	137 (80)	.578
Diabetes mellitus	1185 (35)	247 (40)	.014	467 (50)	88 (51)	.828
Previous PCI	1302 (39)	178 (29)	<.001	292 (31)	35 (20)	.006
Previous MI	1243 (37)	195 (32)	.027	272 (29)	42 (24)	.253
EF (%)			<.001			.845
>50	1388 (58)	237 (47)		375 (55)	81 (54)	
40-50	602 (25)	138 (27)		175 (26)	37 (24)	
30-40	293 (12)	83 (16)		90 (13)	24 (16)	
<30	107 (5)	46 (9)		37 (6)	9 (6)	
Renal impairment	364 (11)	55 (9)	.212	107 (11)	17 (10)	.631
COPD	153 (6)	23 (5)	.350	36 (5)	7 (5)	1.000
History of CVA/TIA	227 (7)	55 (9)	.051	98 (10)	20 (12)	.749
Congestive heart failure	228 (7)	47 (8)	.441	82 (9)	23 (13)	.079
Vessels involved			<.001			<.001
1-vessel CAD	851 (31)	22 (5)		264 (35)	11 (9)	
2-vessel CAD	1020 (37)	98 (22)		253 (34)	40 (31)	
3-vessel CAD	865 (32)	323 (73)		236 (31)	77 (60)	
Indication for angiography			.438			.991
NSTEMI	2390 (71)	422 (69)		628 (67)	116 (67)	
Unstable angina	995 (29)	190 (31)		314 (33)	57 (33)	
Era: after year 2008	1951 (58)	311 (51)	.002	541 (57)	81 (47)	.012

PCI, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *SD*, standard deviation; *MI*, myocardial infarction; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *CAD*, coronary artery disease; *NSTEMI*, non–ST-segment elevation myocardial infarction.

TABLE E3. Baseline characteristics of the subgroups of male and female patients after propensity score matching

	Male patients			Female patients		
	PCI N = 335 (%)	CABG N = 350 (%)	*P* value	PCI N = 112 (%)	CABG N = 97 (%)	*P* value
Age, y, mean (SD)	63 (12)	64 (11)	.193	69 (12)	71 (10)	.291
Hypertension	208 (62)	223 (64)	.718	91 (81)	76 (78)	.727
Current smoker	130 (39)	132 (38)	.830	17 (15)	12 (12)	.216
Hyperlipidemia	243 (72)	250 (71)	.812	88 (79)	79 (81)	.731
Diabetes mellitus	134 (40)	149 (43)	.545	63 (56)	53 (55)	.925
Previous PCI	108 (32)	107 (31)	.698	18 (16)	20 (21)	.503
Previous MI	111 (33)	116 (33)	1.000	23 (21)	24 (25)	.575
EF (%)			.160			.933
>50	188 (56)	175 (50)		67 (60)	57 (59)	
40-50	66 (20)	90 (26)		24 (21)	19 (20)	
30-40	58 (17)	54 (15)		16 (14)	15 (15)	
<30	23 (7)	31 (9)		5 (5)	6 (6)	
Renal impairment	43 (13)	37 (10)	.422	7 (6)	11 (11)	.289
COPD	14 (7)	15 (7)	1.000	5 (6)	3 (5)	.929
History of CVA/TIA	23 (7)	29 (8)	.577	9 (8)	11 (11)	.566
Congestive heart failure	31 (9)	28 (8)	.654	10 (9)	13 (13)	.119
Vessels involved			.376			.113
1-vessel CAD	16 (5)	17 (5)		14 (13)	7 (7)	
2-vessel CAD	90 (27)	78 (22)		24 (21)	32 (33)	
3-vessel CAD	229 (68)	255 (73)		74 (66)	58 (60)	
Indication for angiography			.991			.975
NSTEMI	249 (74)	259 (74)		83 (74)	73 (75)	
Unstable angina	86 (26)	91 (26)		29 (26)	24 (25)	
Era: after year 2008	212 (63)	224 (64)	.908	71 (63)	55 (57)	.399

PCI, Percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *SD*, standard deviation; *MI*, myocardial infarction; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *CAD*, coronary artery disease; *NSTEMI*, non–ST-segment elevation myocardial infarction.