Risk Profile and 10-Year Survival in the SYNTAX Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting Nested Registries

Mohanad Hamandi, Karim Al-Azizi, Daniel J.F.M. Thuijs, Jasjit K. Banwait, Patrick W. Serruys MD, Friedrich-Wilhelm Mohr, Piroze Davierwala, David R. Holmes Jr, Marie-Claude Morice, A. Pieter Kappetein, Stuart J. Head, for the SYNTAX Extended Survival Investigators

Submitted

ABSTRACT

Objectives

To report the risk profile and 10-year survival of patients deemed ineligible for randomization and therefore enrolled in coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) nested-registries.

Background

The SYNTAX (Synergy between PCI with TAXUS and Cardiac Surgery) trial was a randomized study of patients with stable *de novo* three vessel (3VD) and/or left main coronary artery disease (LMCAD) eligible for CABG and PCI. Patients ineligible for randomization were entered into a PCI or CABG nested-registry.

Methods

This study is a prespecified subgroup analysis of the SYNTAX Extended Survival (SYNTAXES) study. Patients from the PCI and CABG nested-registries were followed to determine 10-year all-cause death (primary endpoint). Prespecified sub-analyses were performed for 3VD versus LMCAD, diabetes versus no diabetes, and among SYNTAX score tertiles.

Results

Ten-year all-cause death was 51.6% (99/192) in the PCI-registry and 25.9% (167/644) in the CABG-registry. In the PCI registry, 10-year all-cause death was 44.4% and 62.0% among 3VD and LMCAD patients, respectively (HR 0.56 [95% CI 0.37–0.83]; p=0.003). Diabetes did not affect 10-year all-cause death, while low versus high SYNTAX score did (34.1% vs. 63.4%, respectively) (HR 1·53 [95% CI 1.18–2.002]; p = 0.006). In the CABG-registry, all-cause death was not different according to 3VD, LMCAD, or SYNTAX score tertile. All-cause death occurred in 40.3% vs. 19.9% of patients with versus without diabetes (HR 2.44 [95% CI 1.80–3.31]; p < 0.001).

Conclusion

Patients in the CABG-registry showed excellent 10-year survival (all-cause death 25.9%). However, patients in the PCI-registry showed poor 10-year survival with an all-cause death rate exceeding 50%. Decisions on treatment strategies require a case-based heart team approach, weighing different aspects of comorbidities and treatment options.

Condensed Abstract:

The SYNTAX trial was an all-comer randomized study of patients with stable *de novo* three vessel and/or left main CAD eligible for either CABG or PCI by a heart team. We report 10-year survival of PCI-registry patients ineligible for CABG due to the presence of significant comorbidities increasing surgical risk, and CABG registry patients ineligible for PCI due to too extensive CAD. Ten-year all-cause death was 25.9% (167/644) and 51.6% (99/192) in the CABG- and PCI-registries, respectively. These results underline that long-term survival is impacted by cardiovascular risk factors and provide "real-world" insight regarding the interaction between CABG and PCI in high-risk CAD patients.

Keywords

SYNTAX; PCI; CABG; Extended Survival

INTRODUCTION

Coronary artery bypass grafting (CABG) has been considered the preferred treatment for stable multi-vessel and/or left main coronary artery disease (LMCAD) (1). Since the introduction of percutaneous coronary intervention (PCI), various randomized clinical trials have been conducted comparing PCI outcomes with those of CABG in this patient population (2-5). However, the randomized patients from these trials are considered highly-selected patients and may not adequately represent "real-world" patients with coronary artery disease regularly treated by cardiologists and cardiothoracic surgeons.

The SYNTAX (Synergy between PCI with TAXUS and Cardiac Surgery) trial was an all-comer randomized study that enrolled patients with stable *de novo* three vessel disease and/or left main CAD (CAD) deemed eligible by the heart team for either CABG or PCI. A major strength and novelty of the SYNTAX trial was that patients were excluded from randomization and entered into nested registries when significant comorbidities were present creating an increased surgical risk in the judgement of the heart team (e.g., the PCI-registry with CABG ineligible patients). Furthermore, patients were entered into a CABG-registry if the complexity of the CAD was deemed too extensive for optimal PCI outcomes (e.g., PCI ineligible patients) (6,7).

The SYNTAX trial reported clinical outcomes with up to 5-years follow-up, and The SYNTAX Extended Survival (SYNTAXES) study provided unique long-term data on all-cause death up to 10 years of follow-up (8,9). The present study reports the risk profiles and 10-year survival of those patients deemed ineligible for randomization and enrolled in the SYNTAX CABG and PCI nested-registries.

METHODS

Study Design and Patients

The present study is a prespecified subgroup analysis of the SYNTAXES study (NCT03417050), an investigator-driven extension of follow-up up to 10 years of the original SYNTAX trial (NCT00114972). The SYNTAX trial was a multicenter randomized controlled trial performed in 85 centers across 18 North-American and European countries. The trial design and rationale have been described previously (6,7). In summary, patients with stable *de novo* three-vessel disease (3VD) and/or LMCAD were screened for enrollment by the local heart team. During a multidisciplinary heart team discussion (consisting of a cardiothoracic surgeon, an interventional

cardiologist and a non-interventional cardiologist), a consensus was reached on whether both PCI with a first-generation paclitaxel drug-eluting stents and CABG would result in clinical equipoise, allowing the patient to be randomized for either treatment. Patients found ineligible to be randomized were included in nested CABG (PCI-ineligible patients) and PCI (CABG-ineligible patients) registries. (6,7). A random group of patients from the CABG registry (60%; n=649) and all PCI registry patients (100%; n=198) were selected to be followed-up (6,10).

Medical Ethical Committee approval for this study was granted at the institution of the principal investigators (Erasmus University Medical Centre, Rotterdam, Netherlands, reference: MEC-2016-716). The study protocol is consistent with the International Conference on Harmonization Guidance of Industry E6 Good Clinical Practice and the Declaration of Helsinki. Informed consent to obtain information on 10-year vital status was waived, and follow-up was performed in accordance with local law and regulations of each participating site. Survival data was obtained from electronic medical records or by query of national death registries.

Endpoints

The primary endpoint of this study was all-cause death at 10-year follow-up in patients entered into the PCI and CABG nested-registries. Prespecified sub-analyses for 10-year all-cause death were performed in subgroups of patients with 3VD versus LMCAD, the presence versus absence of diabetes, and according to coronary artery disease complexity defined by SYNTAX score tertiles (low; 0-22, intermediate; 23-32, and high; ≥33).

Definitions

The LMCAD subgroup consisted of patients in which the disease was either isolated or combined with single-vessel, two-vessel, or three-vessel CAD. The 3VD subgroup consisted of patients with CAD involving all three vessels in the absence of LMCAD. SYNTAX scores representing the extensiveness and complexity of CAD based on visual interpretation of the coronary angiogram assessed during heart team meetings were defined according to the classical tertiles; scores of 22 or lower defined as low, 23–32 as intermediate, and 33 or higher as high. Diabetes was defined as patients requiring treatment with oral agents or insulin (6,7,10). The European System for Cardiac Operative Risk Evaluation (EuroSCORE) was used to assess operative risk.

Statistical Analysis

The analyses were performed according to the as-treated principle. Patient characteristics were presented according to descriptive statistics and reported as proportions (%, count/sample size) or mean ± SD.

Sub-analyses were performed for LMCAD and 3VD, with or without diabetes, and SYNTAX score tertile. Kaplan-Meier curves were generated to measure the probability of all-cause death for patients entered in the PCI and CABG nested-registries (primary endpoint), as well as for prespecified subgroups (3VD, LMCAD, diabetes, no diabetes, and SYNTAX score tertiles; secondary endpoint). Patients with missing vital status were included in the time to event Kaplan Meier analysis and censored at the time of "lost to follow-up." Statistical comparison was performed by overall and pairwise log-rank testing with Benjamini-Hochberg correction, with a 2-sided p-value of 0.05 or less considered statistically significant. Cox proportional hazards models were used to estimate hazard ratios (HR) with 95% confidence intervals (CI) for sub-group comparisons. Analyses were performed with R, version 3.5.0 or higher (Foundation for Statistical Computing, Vienna, Austria).

RESULTS

From March 2005 through April 2007, 198 patients were included in the PCI and 1,077 patients in the CABG registries. Of the 198 patients in the PCI registry, 192 were treated with PCI, four patients were treated medically, one underwent CABG, and one patient withdrew consent. From the 1,077 patients in the CABG registry, 649 were randomly selected to be followed-up, and of which, 644 were treated with CABG, three did not receive treatment, and two were managed medically. Another nine patients were lost to follow-up, and three patients withdrew consent. Follow-up at 10 years was complete in 100% (192/192) of as-treated PCI Registry and in 100% (644/644) of the randomly selected as-treated CABG Registry patients.

Patients included in the PCI registry were deemed either high-risk for CABG (70.7%), had no graft material for anastomosis (9.1%), refused CABG (5.6%), had small or poor quality of distal vessels (1.5%), or were excluded from randomization because of other reasons (13.1%). Reasons for inclusion in the CABG registry included complex coronary anatomy not ideal for PCI (70.9%), chronic total occlusion untreatable with PCI (22.0%), inability to take antiplatelet medication (0.9%), refusal to undergo PCI (0.5%), or other reasons (5.7%).

Patient Characteristics

The baseline characteristics of patients entered into the nested CABG and PCI-registries have been reported previously (10). In brief, compared to the randomized trial, PCI registry patients were older and at higher operative risk. Those in the CABG registry showed similar age and operative risk compared to the randomized

patients (Table 1). For both cohorts, coronary lesion complexity was higher in registry patients compared to the randomized patients.

Table 1. Baseline demographics and lesion characteristics in the registry and trial patients

Characteristics	Registry		Trial	
	PCI (n=192)	CABG (n=644)	PCI (n=903)	CABG (n=897)
Age, yrs.	71.2 ± 10.4 (192)	65.7 ± 9.4 (644)	65.2 ± 9.7	65.0 ± 9.8
Male	70.3% (135/192)	80.7% (520/644)	76.4% (690/903)	78.9% (708/897)
Comorbid risk factors				
Body mass index (kg/m^2)	28.0 ± 5.5 (191)	28.0 ± 4.6 (643)	28.1 ± 4.8	27.9 ± 4.5
Diabetes				
Any	35.4% (68/192)	29.7% (191/644)	25.6% (231/903)	24.6% (221/897)
Requiring insulin	15.1% (29/192)	9.2% (59/644)	9.9% (89/903)	10.4% (93/897)
Blood pressure ≥130/85 mm Hg	69.8% (134/192)	68.5% (441/644)	68.9% (622/903)	64.0% (574/897)
Hyperlipidemia	67.5% (129/191)	76.4% (480/628)	78.7% (705/896)	77.2% (686/889)
Cardiovascular history				
Smoking status	11.2% (21/188)	21.9% (140/639)	18.5 % (167/903)	22.0% (196/890)
Previous myocardial infarction	40.4% (76/188)	33.5% (211/629)	31.9% (285/893)	33.8% (300/887)
Previous stroke	7.8% (15/192)	5.5% (35/639)	3.9% (35/899)	4.8% (43/890)
Previous transient ischemic attack	7.9% (15/191)	5.6% (36/638)	4.3% (39/901)	5.1% (45/888)
Congestive heart failure	9.7% (18/186)	5.5% (35/633)	4.0% (36/898)	5.3% (47/880)
Carotid artery disease	10.4% (20/192)	12.3% (79/644)	8.1% (73/903)	8.4% (75/897)
Angina				
Stable	46.4% (89/192)	62.9% (405/644)	56.9% (514/903)	57.2% (513/897)
Unstable	38.0% (73/192)	21.6% (139/644)	29.0% (262/903)	28.0% (251/897)
Ejection fraction <30%	5.7% (11/192)	4.5% (29/644)	1.3% (12/891)	2.5% (22/875)
Additive EuroSCORE	5.8 ± 3.1 (192)	3.9 ± 2.7 (644)	3.8 ± 2.6 (903)	3.8 ± 2.7 (897)
Parsonnet score	14.4 ± 9.5 (192)	9.0 ± 7.1 (644)	8.5 ± 7.0 (903)	8.4 ± 6.8 (897)
Lesion complexity				
SYNTAX score	31.6 ± 12.3 (189)	37.8 ± 13.3 (632)	28.4 ± 11.5 (903)	29.1 ± 11.4 (897)
Total occlusion	36.5% (69/189)	56.4% (356/631)	24.2% (217/897)	22.1% (198/897)
Lesion characteristics				
Number of lesions	4.8 ± 1.9 (192)	3.9 ± 1.6 (644)	4.3 ± 1.8 (903)	4.4 ± 1.8 (897)
Left main coronary artery disease, any	41.1% (79/192)	47.5% (306/644)	39.5% (357/903)	38.8% (348/897)
Isolated	13.9% (11/79)	3.3% (10/306)	11.8% (42/357)	14.1% (49/348)
Plus one-vessel disease	19.0% (15/79)	11.4% (35/306)	18.8% (67/357)	20.4% (71/348)
Plus two-vessel disease	32.9% (26/79)	21.9% (67/306)	31.4% (112/357)	30.5% (106/348)
Plus three-vessel disease	34.2% (27/79)	63.4% (194/306)	38.1% (136/357)	35.1% (122/348)
Three-vessel disease only	56.8% (108/192)	51.6% (332/644)	60.5% (546/903)	61.2% (549/897)

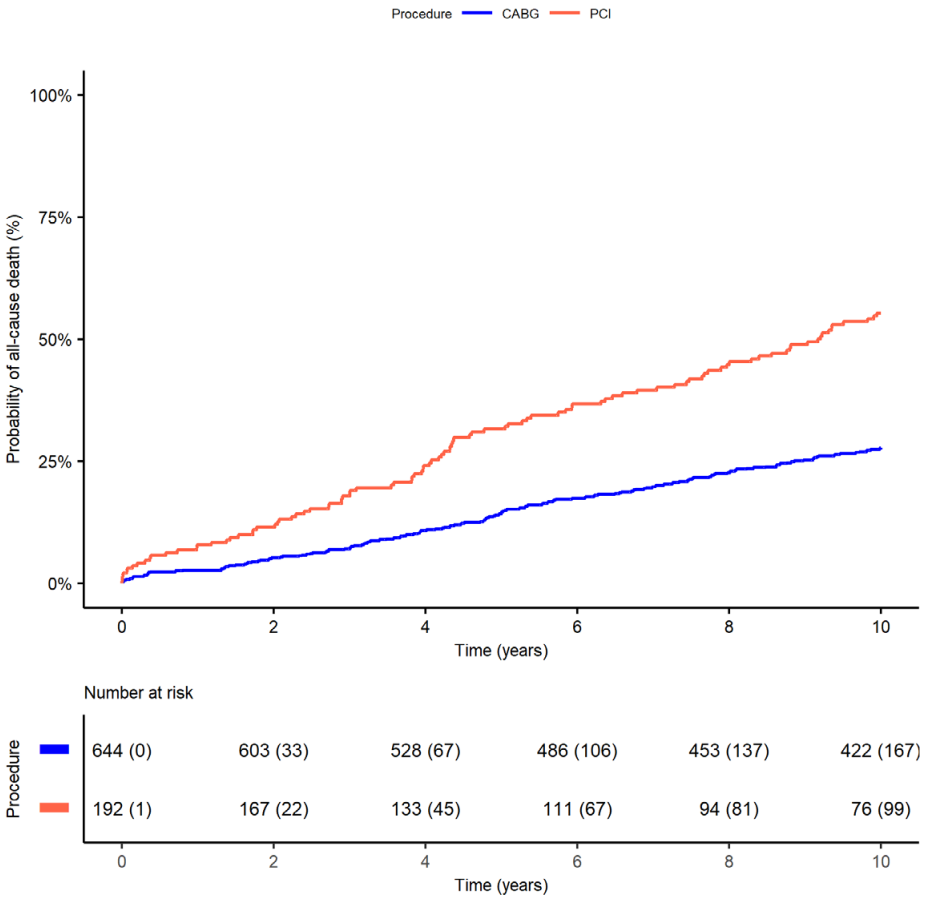
Values are mean SD (N) or % (n/N)), unless otherwise noted. Percentages might not sum to 100% as a result of rounding

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; SYNTAX = Synergy between PCI with TAXUS and Cardiac Surgery; EuroSCORE = European System for Cardiac Operative Risk Evaluation.

Primary endpoint

PCI Registry

The primary endpoint of all-cause death at 10 years occurred in 51.6% (99/192) of patients entered into the PCI nested-registry (Central Illustration) compared to 27% (244/903) in the PCI arm of the randomized trial.



Central Illustration. Kaplan-Meier curves for primary analysis of 10-year all-cause death in coronary artery bypass grafting (CABG in blue) and percutaneous coronary intervention (PCI in red) registries, respectively.

Ten-year all-cause death was significantly lower for patients with 3VD as compared to those with LMCAD (44% (48/108) vs. 62% (49/79), respectively; HR 0.56 [95% CI 0.37–0.83]; p = 0.003) (Figure 1A).

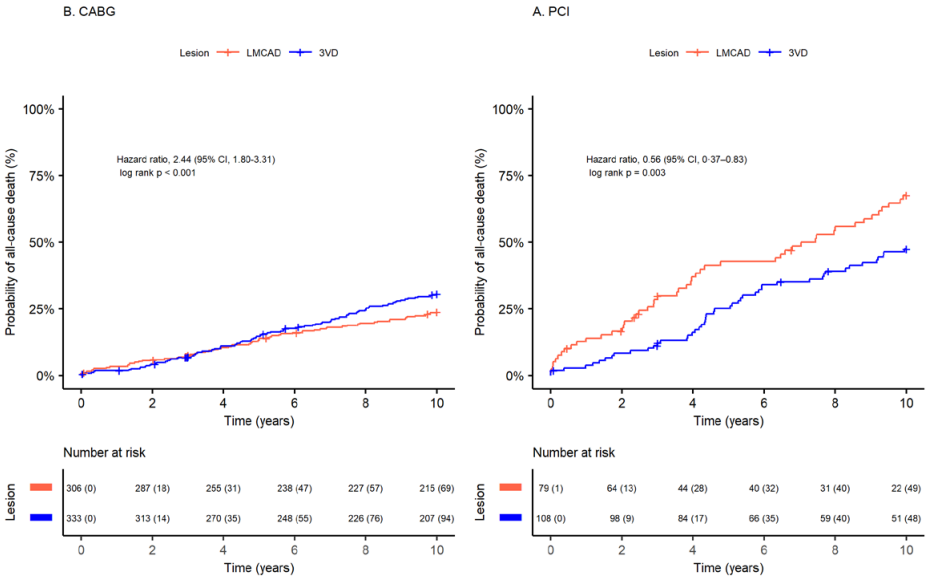


Figure 1. Kaplan-Meier curves of the three-vessel disease vs. left main disease analysis of 10-year all-cause death in (A) percutaneous coronary intervention (PCI) and (B) coronary artery bypass grafting (CABG) registries, respectively.

Among PCI patients with or without diabetes, the 10-year all-cause death occurred in 52.9% (36/68) and 50.8% (63/124), respectively (HR 1.15 [95% CI 0.76–1.74]; p = 0.49; Figure 2A).

All cause death at 10 years was 34.1% (15/44) for patients with a low SYNTAX score (<22; n=44; mean 16.5 ± 5.1), 50.8% (32/63) for patient with intermediate SYNTAX score (23-32; n=63; mean 27.7 ± 2.8), and 63.4% (52/82) in patients with high SYNTAX score (>33; n=82; mean 42.4 ± 9.2) (HR 1·53 [95% CI 1.18–2.002]; p = 0.006; Figure 3A). There was no significant difference in all-cause death between low- and intermediate-SYNTAX score groups (p = 0.11) or intermediate- and high-SYNTAX score groups (p = 0.11). However, a significant difference was observed between the low- and high-score groups (p = 0.006). Incomplete revascularisation was 63.5% (122/192).

CABG Registry

The primary endpoint of all-cause death at 10 years occurred in 25.9% (167/644) of patients after CABG (Central Illustration). This compared to 24% (211/897) 10-year all-cause death in the CABG arm of the randomized trial.

The 10-year all-cause death was 28.3% (94/332) in 3VD as compared to 22.5% (69/306) in LMCAD patients (HR 1.31 [95% CI 0.96–1.78]; p = 0.09) (Figure 1B). Sub-group

analysis revealed a significant difference in 10-year all-cause death for 40.3% (77/191) patients with versus without diabetes (19.9% (90/453); HR 2.44 [95% CI 1.80–3.31]; p < 0.001; Figure 2B).

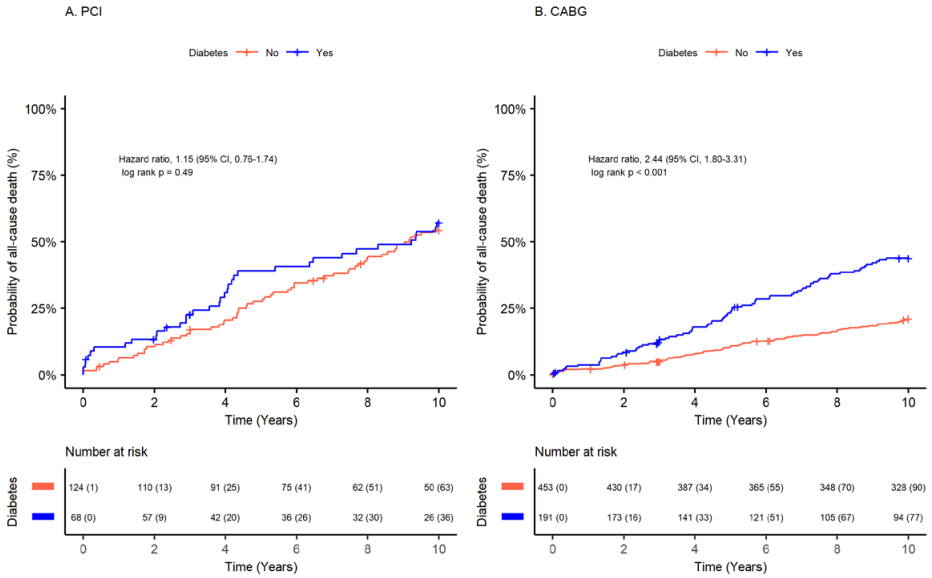


Figure 2. Kaplan-Meier curves of the diabetes vs. no diabetes analysis of 10-year all-cause death in (A) PCI and (B) CABG registries, respectively. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

All-cause death at 10 years was 17.7% (12/68) in low SYNTAX score patients (<22; n=68; mean 16.8 ± 4.1), 24.2% (39/161) in intermediate SYNTAX score patients (23-32; n=161; mean 28.2 ± 2.7), and 28.0% (113/403) in high SYNTAX score patients (>33; n=403; mean 45.2 ± 10.1; HR 1·27 [95% CI 0·99–1·62]; p = 0.16; Figure 3B). The difference in all-cause death was not statistically significant between the different score tertiles. Incomplete revascularisation was 25.3% (163/644).

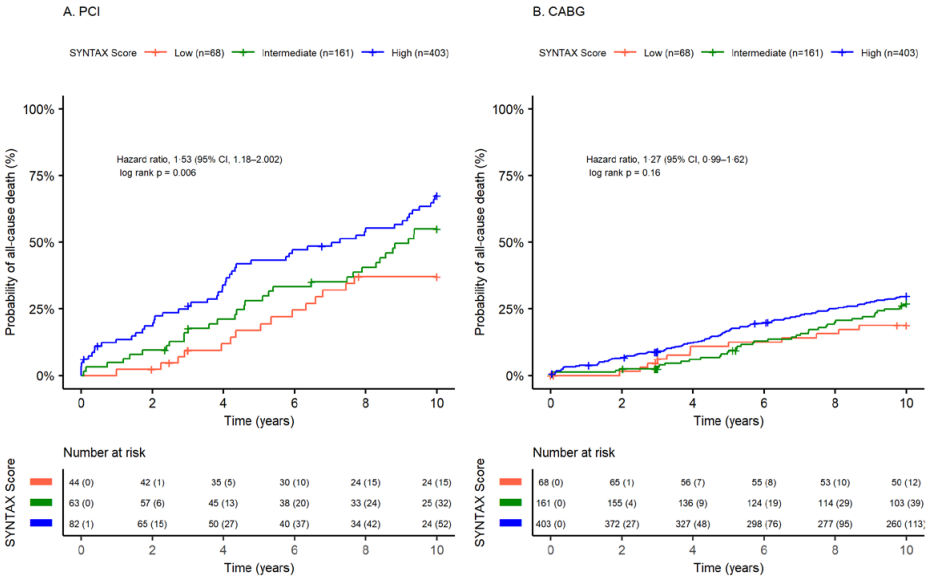


Figure 3. Kaplan-Meier curves for primary analysis of 10-year all-cause death in (A) percutaneous coronary intervention (PCI) and (B) coronary artery bypass grafting (CABG) registries, respectively, in the pre-specified SYNTAX score tertile subgroups.

DISCUSSION

The SYNTAXES study is the first to assess 10-year survival after PCI with drug-eluting stents and CABG in patients with *de novo* three-vessel and/or left main disease (8). The SYNTAX trial only randomized patients in whom both PCI and CABG would lead to clinical equipoise and entered all patients ineligible for randomization into nested-registries (7). There were 6.4% (198/3075) of all-comers with 3VD or LMCAD considered ineligible to undergo surgical revascularisation mainly due to systemic factors including frailty and comorbidities, and more than one-third, 35% (1077/3075), were deemed poor candidates for PCI, mainly due to the extent, diffuse nature and complexity of their coronary disease (7,10). This study provides important long-term insight into survival after PCI and CABG by extending follow-up to 10 years for complex patients with coronary artery disease deemed appropriate for only one revascularisation strategy.

At 10-year follow-up, the primary endpoint of all-cause death occurred in 25.9% of patients entered in the CABG-registry, and 51.6% of patients entered in the PCI-registry. In comparison, 10-year all-cause death in the SYNTAX trial was 23.5% (211/897) in CABG patients and 27.0% (244/903) in PCI patients (HR 1.17 [95% CI

0.97–1.41, p=0.09]) (8). This shows that patients who were deemed suitable for CABG had excellent 10-year survival both in the registry as in the randomized-arm of the SYNTAX trial. However, patients that were found unsuitable to undergo CABG and were entered into the PCI nested-registry showed a much worse 10-year survival prognosis compared to the PCI randomized-arm of the trial. The possible explanation could be the older age, significant comorbidities, and frailty among PCI-registry patients. It is important to note that more patients with depressed left ventricular ejection fraction (<30%) were included in the PCI nested-registry than in the PCI arm of the SYNTAX trial (5.7% vs 1.3%), which may be linked to worse outcomes. In our study, the high-risk profile of patients due to extensive comorbidities dictated treatment strategy and thereby allocated those patients to the PCI registry rather than the CABG registry.

Patients with LMCAD had significantly higher all-cause death compared with 3VD patients within the PCI registry (Table 2). Patients stratified by the type of coronary artery disease within the CABG registry had similar all-cause death rates (Table 2). The LMCAD cohort in the PCI registry had 25.3% (20/79) chronic total occlusions and 12.7% (10/79) trifurcation lesions, which may explain the high incomplete revascularisation rate of 63% (122/192). Moreover, 36.9% (45/122) of patients with incomplete revascularisation in the PCI registry had left main coronary disease.

It is important to note that there have been significant improvements in PCI techniques since the SYNTAX and SYNTAXES PCI registry enrollment. This was well demonstrated in the SYNTAX II study that incorporated physiologic assessment. Physiologic assessment was performed in 75.5% of the lesions, leading to treatment deferral of 24.5% of the stenoses (11). Furthermore, post-implantation intravascular ultrasound was performed in 76.4% of the lesions leading to stent optimization and post-dilation in 30.2% of the stented lesions (12). Additionally, the advances and improvements in techniques addressing chronic total occlusion have been associated with improved procedural outcomes (12). Intravascular ultrasound (IVUS) is also used to optimize LM PCI in current daily practice and has been recommended by multiple society guidelines (13).

In the CABG registry, patients with 3VD 10-year all-cause death occurred in 28.2% (94/332) of patients compared to 20.6% (113/549) in the randomized CABG cohort. Furthermore, CABG registry patients in the LMCAD subgroup had better long-term outcomes compared to the trial patients, as demonstrated by an all-cause death of 22.5% (69/306) compared to 28.2% (98/348), respectively.

Table 2. Outcomes in the PCI and CABG registry

Outcomes	PCI	CABG
Overall		
10-year all-cause mortality	51.6% (99/192)	25.9% (167/644)
SYNTAX score ≥33	43.4% (82/189)	63.8% (403/632)
SYNTAX score 23-32	33.3% (63/189)	25.5% (161/632)
SYNTAX score ≤22	23.3% (44/189)	10.8% (68/632)
Chronic total occlusion	36.5% (69/189)	56.4% (356/631)
Incomplete revascularisation	63.5% (122/192)	25.3% (163/644)
Left main coronary artery disease		
Overall 10-year all-cause mortality	62.0% (49/79)	22.5% (69/306)
SYNTAX score ≥33	47.3% (36/76)	68.2% (206/302)
SYNTAX score 23-32	26.3% (20/76)	17.5% (53/302)
SYNTAX score ≤22	26.3% (20/76)	14.2% (43/302)
Diabetes	30.4% (24/79)	25.2% (77/306)
Chronic total occlusion	25.3 % (20/79)	44.9% (135/301)
Incomplete revascularisation	57.0% (45/79)	22.9% (70/306)
Three-vessel disease		
Overall 10-year all-cause mortality	44.4% (48/108)	28.2% (94/332)
SYNTAX score ≥33	42.6% (46/108)	59.9% (194/324)
SYNTAX score 23-32	37.0% (40/108)	33.0% (107/324)
SYNTAX score ≤22	20.4% (22/108)	7.1% (23/324)
Diabetes	40.7% (44/108)	33.7% (112/332)
Chronic total occlusion	44.4% (48/108)	67.6% (219/324)
Incomplete revascularisation	68.5% (74/108)	27.7% (92/332)

Values are mean SD (N) or % (n/N)), unless otherwise noted. Percentages might not sum to 100% as a result of rounding

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; SYNTAX = Synergy between PCI with TAXUS and Cardiac Surgery;

There was a stepwise increase in all-cause-death associated with higher SYNTAX scores. All-cause death between the low- and high- SYNTAX score tertiles within the PCI registry were significantly different (p =0.006), while there was no significant difference in all-cause death within the CABG registry patients stratified by the SYNTAX score tertile.

Study limitations: The present findings should be appraised in the light of some limitations. First, only 60% of the patients in the CABG Registry were followed for 10 years. Nonetheless, the selection of those included for follow-up was random, and there were no differences in baseline characteristics compared to those who were not followed-up (10). Second, the PCI registry contains a relatively small number of patients; therefore, some of the results should be interpreted with caution. Finally, explorative subgroup analyses by lesion subsets could not be performed due to the low patient number in separate groups.

CONCLUSION

In the SYNTAX trial, patients who were deemed ineligible for PCI due to coronary disease complexity and instead enrolled in the CABG-registry showed excellent 10-year survival comparable to patients who were randomized to undergo CABG. Conversely, patients too frail to undergo CABG who were enrolled in the PCI-registry showed poor 10-year survival. Thus, patients with extensive coronary disease should ideally undergo CABG when at all feasible. Furthermore, this study shows that treatment strategy decisions should be made through a case-based heart team approach during which different aspects of comorbidities and treatment options are considered.

Abbreviations

CABG =	coronary artery bypass
CI =	confidence interval
HR =	hazard ratio
LMCAD =	left main coronary artery disease
PCI =	percutaneous coronary intervention
SYNTAX =	Synergy between PCI with TAXUS and Cardiac Surgery
SYNTAXES =	SYNTAX Extended Survival
3VD =	three-vessel disease

REFERENCES

1. Hlatky MA, Boothroyd DB, Bravata DM et al. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. Lancet 2009;373:1190-1197.
2. Gruntzig A. Transluminal dilatation of coronary-artery stenosis. Lancet 1978;1:263-263.
3. Serruys PW, Ong ATL, van Herwerden LA et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: the final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. J Am Coll Cardiol 2005;46:575-581.
4. Rodriguez AE, Baldi J, Fernández Pereira C et al. Five-year follow-up of the Argentine randomized trial of coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease (ERACI II). Journal Am Coll Cardiol 2005;46:582-588.
5. Hueb W, Lopes NH, Gersh BJ et al. Five-year follow-up of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation 2007;115:1082-1089.
6. Ong ATL, Serruys PW, Mohr FW et al. The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study: design, rationale, and run-in phase. Am Heart J 2006;151:1194-1204.
7. Serruys PW, Morice M-C, Kappetein AP et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med2009;360:961-972.
8. Thuijs D, Kappetein AP, Serruys PW et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. Lancet 2019;394:1325-1334.
9. Mohr FW, Morice MC, Kappetein AP et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013;381:629-38.
10. Head SJ, Holmes DR, Jr., Mack MJ et al. Risk profile and 3-year outcomes from the SYNTAX percutaneous coronary intervention and coronary artery bypass grafting nested registries. JACC Cardiovasc Interv 2012;5:618-625.
11. Campos CM, Stanetic BM, Farooq V et al. Risk stratification in 3-vessel coronary artery disease: Applying the SYNTAX Score II in the Heart Team Discussion of the SYNTAX II trial. Catheter Cardiovasc Interv 2015;86:E229-38.
12. Escaned J, Collet C, Ryan N et al. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. Eur Heart J 2017;38:3124-3134.
13. Räber L, Mintz GS, Koskinas KC et al. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. Eur Heart J 2018;39:3281-3300.