Long-term forecasting and comparison of mortality in the Evaluation of the Xience Everolimus Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial: prospective validation of the SYNTAX Score II

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Aims
To prospectively validate the SYNTAX Score II and forecast the outcomes of the randomized Evaluation of the Xience Everolimus-Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) Trial.

Methods and results
Evaluation of the Xience Everolimus Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization is a prospective, randomized multicenter trial designed to establish the efficacy and safety of percutaneous coronary intervention (PCI) with the everolimus-eluting stent compared with coronary artery bypass graft (CABG) surgery in subjects with unprotected left-main coronary artery (ULMCA) disease and low-intermediate anatomical SYNTAX scores (<33). After completion of patient recruitment in EXCEL, the SYNTAX Score II was prospectively applied to predict 4-year mortality in the CABG and PCI arms. The 95% prediction intervals (PIs) for mortality were computed using simulation with bootstrap resampling (10 000 times). For the entire study cohort, the 4-year predicted mortalities were 8.5 and 10.5% in the PCI and CABG arms, respectively (odds ratios (OR) 0.79; 95% PI 0.43–1.50). In subjects with low (≤22) anatomical SYNTAX scores, the predicted OR was 0.69 (95% PI 0.34–1.45); in intermediate anatomical SYNTAX scores (23–32), the predicted OR was 0.93 (95% PI 0.53–1.62). Based on 4-year mortality predictions in EXCEL, clinical characteristics shifted long-term mortality predictions either in favour of PCI (older age, male gender and COPD) or CABG (younger age, lower creatinine clearance, female gender, reduced left ventricular ejection fraction).

Conclusion
The SYNTAX Score II indicates at least an equipoise for long-term mortality between CABG and PCI in subjects with ULMCA disease up to an intermediate anatomical complexity. Both anatomical and clinical characteristics had a clear impact on long-term mortality predictions and decision making between CABG and PCI.

Keywords
Left main • Percutaneous coronary intervention • Coronary artery bypass surgery • SYNTAX score • SYNTAX Score II • Mortality • Drug-eluting stents

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Introduction

Coronary artery bypass graft (CABG) surgery was introduced in 1967 with the aim of relieving angina pectoris, enhancing quality of life and improving survival. In patients with unprotected left-main coronary artery (ULMCA) disease, the superiority of CABG over optimal medical treatment has been demonstrated in multiple studies and meta-analyses and has been the standard of care for over 30 years.

Percutaneous coronary intervention (PCI) was introduced into clinical practice in 1977 and was initially considered appropriate only for single-vessel disease. With the advent of drug-eluting stents (DES), long-term outcomes after PCI have markedly improved in patients with more complex coronary artery disease. Specifically for ULMCA disease, numerous registries and three randomized trials have compared outcomes in subjects treated with either CABG or PCI. Consequently, the prevailing international revascularization guidelines recommend revascularization of ULMCA with CABG or PCI in subjects with SYNTAX scores that are low for both CABG or PCI and class I recommendation for CABG or PCI (level of evidence A) and intermediate for PCI (level of evidence B for both). The same guidelines recommend against revascularization with PCI of ULMCA disease with high SYNTAX scores and intermediate SYNTAX score, respectively. These recommendations are based on similar 5-year mortality and myocardial infarction, with a lower incidence of stroke and increased risk of repeat revascularization with PCI compared with CABG in subjects with ULMCA disease and lower anatomical complexity.

The introduction of the newer-generation everolimus-eluting stent (EES)—with proven marked improvements in both safety and efficacy—has prompted the design of the randomized Evaluation of Xience Everolimus-Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization (EXCEL) Trial.

Aiming to improve decision making between CABG and PCI in patients with complex coronary artery disease, the SYNTAX Score II combines anatomic and clinical factors. Importantly, the SYNTAX Score II was developed in the landmark, all-comers, randomized SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) Trial where selection bias would have been minimal, and externally validated in two real world registries. In addition, the SYNTAX Score II has been included in international revascularization guidelines.

Although numerous risk scores and prospective trials are available in the medical literature, their performances are reported when the outcomes are already known. The aim of the present study is to apply the SYNTAX Score II in the ongoing EXCEL trial, in order to prospectively validate the SYNTAX Score II before independent reporting of the outcomes of the trial, forecast the 4-year mortality outcomes in the PCI and CABG arms, and to describe how anatomical and clinical characteristics impact on the long-term mortality predictions and decision making between CABG and PCI.

Methods

Study population

The EXCEL trial (clinicaltrials.gov identifier: NCT01205776) is an international, prospective, unblinded, randomized multicenter trial that enrolled 1905 subjects in 131 centres. Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization was designed to establish the safety and efficacy of the EES (XIENCE PRIME™ or XIENCE V® or XIENCE Xpedition™ or XIENCE PRO™) and PCI in patients with ULMCA disease. Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization adopted an enrolment criteria of subjects with ULMCA disease up to intermediate anatomical complexity (SYNTAX Score < 33), with minimal exclusion criteria to allow meaningful comparisons between revascularization modalities (Supplementary material online, Table S1). The information on the trial endpoints and sample size calculation is also available in the Supplementary material online.

Following diagnostic angiography demonstrating significant ULMCA disease and the consensus of the local Heart Team (qualified participating interventional cardiologist and cardiac surgeon), subjects were consented and randomized 1:1:1 (i) PCI with the EES or (ii) CABG. All randomized patients were scheduled to undergo follow-up telephone contact or office visit up to 5 years post-procedure.

The primary endpoint of the EXCEL trial is the composite measure of all-cause mortality, myocardial infarction or stroke [modified Rankin Scale (mRS) ≥ 1 and increase by ≥ 1 from baseline] at a median follow-up interval of 3 years post-index procedure.

SYNTAX Score II

The SYNTAX Score II has been described previously. In brief, the SYNTAX Score II augments the purely anatomical SYNTAX score with anatomical and clinical factors that were shown to alter the threshold value of the anatomical SYNTAX score in order for equipoise to be achieved between CABG and PCI for long-term mortality. The SYNTAX Score II is composed of the anatomical SYNTAX score, presence of ULMCA disease, and six clinical characteristics [age, creatinine clearance (CrCl), left ventricular ejection fraction (LVEF), gender, chronic obstructive pulmonary disease (COPD) and peripheral vascular disease (PVD)]. The SYNTAX Score II allows for 4-year mortality predictions to be made following revascularization with CABG or PCI to aid decision making between CABG and PCI. Importantly, the SYNTAX Score II was developed in the randomized SYNTAX Trial (n = 1800) and externally validated in the multinational DELTA (n = 2891) and Credo-KYOTO (n = 3896) registries.

Using the actual baseline clinical and angiographic data from each enrolled patient in EXCEL, the SYNTAX Score II was calculated for each patient. Scores were assigned for the presence and magnitude of each predictor directly based on the Cox proportional hazards model coefficients generating different scores and 4-year mortality predictions for PCI and CABG. To mirror conventional clinical practice, investigator reported anatomical SYNTAX Scores were used in the analysis.

Statistical analysis

Categorical variables are presented as numbers and percentages and are compared with the χ² test. Continuous variables are expressed as mean ± SD or median with interquartile range (IQR), and are compared using the Student’s t-test or Wilcoxon rank-sum test based on their
distributions. Within EXCEL, SYNTAX Score II predictor values were >99% complete with the exception of LVEF which was 95.1% complete. An advanced multiple imputation strategy which takes the correlation between all potential predictors (method of chained equations) was used to account for missing values as previously described.\(^{19}\)

**Comparison of predicted 4-year mortality between CABG and PCI arms**

The individual predicted mortality and the odds ratio (OR) of the two randomized revascularization strategies were calculated using the SYNTAX Score II. To determine the 95% PIs, the trial was simulated 10,000 times and generated 4-year mortality from predictions based on consecutive bootstrap samples\(^{20}\) of the original SYNTAX trial (Figure 1).\(^{17,21}\) A prediction interval is an estimate of an interval in which future observations will fall, with a certain probability, compared with what has already been observed (SYNTAX trial).\(^{21}\) All data analyses were performed using R version 2.15.3.\(^{23}\)

**Results**

Between 29 September 2010 and 6 March 2014, 2909 patients with ULMCA disease were screened and 1905 subjects randomized to CABG (n = 957) or PCI (n = 948) (Figure 2).

Subjects in the two randomization arms were well balanced with regards to baseline demographic and clinical characteristics included in the SYNTAX Score II (Table 1). Overall, the median age was 66.0 (IQR 59.0–73.0) years, 76.3% male, 24.7% female, 7.8% COPD and 8.6% PVD. The median LVEF was 60.0% (IQR 52.0–63.0%), median CrCl 85.0 mL/min (IQR 66.8–106.2 mL/min) and the median anatomical SYNTAX score 21.0 (IQR 15.0–26.0).

**SYNTAX Score II 4-year mortality predictions in the cohorts**

The predicted mortality was 8.5% (95% PI 5.4–11.9%) in the PCI arm and 10.5% (95% PI 6.6–15.1%) in the CABG arm (OR 0.79; 95% PI 0.43–1.50%) (Table 2).

Figure 3 demonstrates the first 1000 trial simulations. Based on numerical differences in 4-year mortality predictions, 77.9% of trial simulations (n = 7790) favoured PCI and 22.1% of trial simulations (n = 2210) favoured CABG. In 55.2% of trial simulations (n = 5520) 4-year mortality predictions between CABG and PCI could not be separated with statistical significance (P > 0.05). 40.4% (n = 4040) of trial simulations had mortality predictions separated with statistical significance (P < 0.05) in favour of PCI, and 4.4% (n = 440) had mortality predictions separated with statistical significance (P < 0.05) in favour of CABG.

**Anatomical complexity**

Anatomical complexity had a clear impact on mortality predictions. In subjects with low (<22) and intermediate,\(^{21–32}\) anatomical SYNTAX scores the predicted OR were 0.69 (95% PI 0.34–1.45) and 0.93 (95% PI 0.53–1.62), respectively (Table 2).

In the low SYNTAX score group, 54.2% (n = 5420) of mortality predictions were similar (P > 0.05) between CABG and PCI; in the intermediate SYNTAX score group, 84.1% (n = 8410) of mortality predictions were similar (P > 0.05) between CABG and PCI (Figure 3).

Mortality predictions that were separated with statistical significance (P < 0.05) in favour of PCI were 43.7% (n = 4370) in the low SYNTAX score group, compared with 11.3% (n = 1130) in the intermediate SYNTAX score group. Conversely, mortality predictions that were separated with statistical significance (P < 0.05) in favour of CABG were 2.1% (n = 210) in the low SYNTAX score group, compared with 4.6% (n = 460) in the intermediate SYNTAX score group.

**Impact of clinical characteristics**

Clinical characteristics had a clear impact on 4-year mortality predictions (Table 2, Figure 4). In both arms the subgroup with the highest predicted mortalities was PVD [22.5% (95% PI 11.3–36.1%) in the PCI arm and 26.5% (95% PI 13.1–41.7 in the CABG arm)].

Based on 4-year mortality predictions, older age, male gender and COPD favoured PCI, whereas younger age, lower CrCl, impaired LVEF and female gender favoured CABG (Figure 4).

**Diabetes**

In subjects with diabetes, predicted mortality was 9.9% (95% PI 5.6–14.7%) in the PCI arm and 11.4% (95% PI 6.4–17.3%) in the CABG arm (OR 0.86 (PI 0.40–1.90; Table 2). Similar analyses in non-diabetics yielded predicted mortalities of 7.9% (95% PI 4.8–11.3%) in the PCI arm and 10.2% (95% PI 6.2–14.8%) in the CABG arm (0.75 (PI 0.39–1.48)).

**Discussion**

The main findings of the study are: (i) The prospective use of a decision-making and risk prediction tool (SYNTAX Score II) was feasible in a large-scale randomized trial on completion of enrolment of subjects, in which the follow-up results were unknown and blinded; (ii) based on the SYNTAX Score II, we predicted a 77.9% chance of a lower 4-year mortality in the PCI arm of the EXCEL trial, with a 40% chance that this will achieve statistical significance in favour of PCI; (iii) The interplay between angiographic and clinical characteristics has an important impact on decision-making and risk stratification of patients with ULMCA disease.

**SYNTAX Score II and prospective mortality predictions**

The unprecedented aspect of the present study was to prospectively validate the SYNTAX Score II in a randomized trial that is still ongoing, despite completion of enrolment of patients, with expected reporting of the primary outcome in another 2 years. It is important to emphasize that outcomes of EXCEL are being collected, analysed and reported by an independent clinical events committee (CEC), and that the current analyses were performed with all authors completely blinded to any outcome data.

A second unique aspect of the present study was to report the
Figure 1 Schematic representation of the SYNTAX Score II predictions used in the Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization trial. (A) The mortality predictions of percutaneous coronary intervention and coronary artery bypass graft for each patient enrolled in the Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization trial were calculated using the SYNTAX Score II. The pie chart represents the individual risk of 4-year mortality (red slice). (B) Based on individual mortality predictions, patients’ outcomes were simulated to obtain the 4-year mortality in both trial arms. (C) To determine the 95% prediction intervals steps A and B were repeated 10 000 times with 4-year mortality predictions based on consecutive bootstrap samples of the original SYNTAX trial.
predicted long-term mortality of a randomized trial following completion of patient enrolment, blinded and prior to the actual reporting of the trial. This was only possible because the SYNTAX Score II was developed in the randomized SYNTAX trial—consisting of a population with complex coronary artery disease (ULMCA disease or de novo three-vessel disease)—and importantly where selection bias was minimal secondary to the unique all-comers design of SYNTAX. In addition, the SYNTAX Score II has shown consistent and solid predictive performances in two multicenter registries for CABG and PCI-treated patients with left-main and/or complex coronary artery disease.14,16

The SYNTAX Score II predicted a 55.2% likelihood that there will not be a statistically significant difference in mortality between the PCI and CABG arms of EXCEL at 4 years. This is likely to be secondary to the clinical profile of the patients recruited in EXCEL. On average subjects in EXCEL had preserved LVEF, reasonable renal function, were predominantly male, and importantly more complex coronary artery disease (SYNTAX score ≥33) was a key exclusion criteria. In the SYNTAX trial, female gender, reduced LVEF, lower CrCl, higher anatomical SYNTAX scores and younger age were all shown to favour CABG.14,16,22

The combination of these angiographic and clinical profiles is therefore likely to explain the predicted favourable results for PCI, despite similar baseline clinical characteristics in the CABG and PCI arms of EXCEL. The present study therefore does not imply that PCI reduces mortality in all ULMCA revascularization, but predicts that subjects with ULMCA disease with a lower anatomical and risk profile may potentially derive a prognostic benefit from undergoing PCI, whilst more complex disease and a higher risk clinical profile would remain the domain of CABG on the grounds of prognosis.

### Table 1  SYNTAX score II baseline variables

<table>
<thead>
<tr>
<th></th>
<th>PCI</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomical SYNTAX score (IQR)</td>
<td>21.0 (15–26)</td>
<td>20.0 (15.0–25)</td>
</tr>
<tr>
<td>Age (years) (IQR)</td>
<td>66.0 (59.0–73.0)</td>
<td>66.0 (60.0–73.0)</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min) (IQR)</td>
<td>85.7 (66.2–107.5)</td>
<td>84.6 (67.1–105.0)</td>
</tr>
<tr>
<td>LVEF (IQR)</td>
<td>60.0 (52.0–62.0)</td>
<td>60.0 (52.0–63.0)</td>
</tr>
<tr>
<td>Left main coronary artery disease, n (%)</td>
<td>948 (100)</td>
<td>957 (100)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>226 (23.8)</td>
<td>214 (22.4)</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>67 (7.1)</td>
<td>81 (8.5)</td>
</tr>
<tr>
<td>PVD, n (%)</td>
<td>97 (10.3)</td>
<td>84 (8.8)</td>
</tr>
</tbody>
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PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; IQR, interquartile range; COPD, chronic pulmonary obstructive disease; PVD, peripheral vascular disease.
Impact of anatomic complexity in risk predictions

Unprotected left-main coronary artery disease should be regarded as a heterogeneous pathology when considering the choice of revascularization modality. The anatomical complexity of the left main may vary from a single lesion in the shaft to distal trifurcation disease and its association with more complex downstream (three-vessel) disease. These variances may influence the capacity of PCI to achieve complete revascularization, the number of stents implanted and complexity of interventional techniques employed. Moreover, incomplete revascularization and anatomical complexity have been directly correlated to late all-cause mortality following PCI.24–26 This was exemplified in the PCI arm of the left-main subgroup of SYNTAX, where the incidence of 5-year all-cause mortality was shown to markedly increase in subjects with a SYNTAX score ≥ 33 (5-year mortality 20.9%) compared with subjects with a SYNTAX score < 33 (5-year mortality 7.9%).

Conversely, in subjects undergoing CABG, anatomical complexity has been shown to not affect long-term prognosis, as exemplified in the CABG arm of the left-main subgroup of SYNTAX, where the incidence of 5-year all-cause mortality remained almost unchanged in subjects with a SYNTAX score ≥ 33 (5-year mortality 14.1%) compared with subjects with a SYNTAX Score < 33 (5-year mortality 15.1%).24 In the present analysis, although the PIs were wide, the expected mortality favoured PCI in the low (<22) anatomical SYNTAX score group (7.3% vs. 10.3%), and was practically equiposed between PCI and CABG in the moderate (>22) anatomical SYNTAX score group (10.1% vs. 10.8%; Table 2).

The aforementioned reasons explain why the risk predictions in EXCEL are not at variance with results of the recent randomized comparisons between CABG and PCI.16 Al Ali et al. pooled the results of three randomized trials of first-generation DES vs. CABG in left-main coronary artery disease and demonstrated that PCI did not reduce the overall mortality (HR 1.08; 95% CI 0.75–1.57), since the global outcomes reflected a composite of lower and higher mortality related to simple and more complex coronary anatomy.16 In contrast, EXCEL set an exclusion criteria of a SYNTAX score ≥ 33, thereby selecting subjects with less complex coronary artery disease and therefore potentially more favourable results for PCI.

Impact of clinical characteristics in risk predictions

The predictions provided by the SYNTAX Score II displayed in the Figure 4 deserve detailed examination since clinical characteristics markedly affect the simulation patterns. Although it was shown that certain subsets of patients were more likely to have a mortality reduction with PCI or CABG, it is important to emphasize that the associated mortality impact was not exclusively derived from these factors alone. The underlying principle of the SYNTAX Score II being that it balances the interaction of anatomical complexity and six clinical variables that were shown to directly affect decision making on the most appropriate revascularization modality, and not each individual anatomical/clinical characteristic (Supplementary material online, Figure S1). Within the SYNTAX Score II, younger age,
Figure 3 First 1000 4-year mortality simulations of the Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization trial on the SYNTAX Score II. Each dot represents one simulated trial mortality in both randomization arms based on individual predictions. The diagonal line represents identical mortality for coronary artery bypass graft and percutaneous coronary intervention. A dot plotted to the left of the diagonal line favours coronary artery bypass graft (actual percentages shown in top left corner), and to the right favours percutaneous coronary intervention (actual percentages shown in bottom right corner). Simulated trials with a significant (\(P \leq 0.05\)) mortality difference between coronary artery bypass graft and percutaneous coronary intervention are coloured black (actual percentage shown in parentheses in respective corners). Simulated trials with a non-significant (\(P > 0.05\)) mortality difference between coronary artery bypass graft and percutaneous coronary intervention are coloured grey.
female gender, impaired renal function and reduced LVEF were shown to favour CABG compared with PCI on long-term prognostic grounds. As a result, patients with these specific characteristics were shown to derive a prognostic benefit from CABG, even when the anatomical complexity was lower. Conversely, older age, preserved renal and left ventricular function, and COPD were shown to favour PCI compared with CABG on long-term prognostic grounds. As a result, patients with these specific characteristics were shown to derive a prognostic benefit from PCI, even when the anatomical complexity was higher.

Diabetes

Diabetes has previously been shown not to be an independent predictor of mortality in the CABG or PCI arms of the SYNTAX trial, nor to have an interaction effect between CABG and PCI for long-term mortality when the end organ manifestations of diabetes were accounted for, as exemplified in the SYNTAX Score II.\textsuperscript{14,22} Conversely, the FREEDOM trial demonstrated a reduction in mortality in diabetics with predominantly three-vessel disease treated by CABG compared with first-generation drug-eluting stents at a...
median follow-up of 3.8 years. Importantly, ULMCA disease was an exclusion criteria in FREEDOM and is what prompted the presentation of mortality predictions in the diabetic subset of EXCEL. Notably in EXCEL, the presence of diabetes was associated with an increase in predicted mortality within both the CABG and PCI arms. Additionally, the predicted benefits of PCI were less pronounced in diabetics compared to non-diabetics, but remained similar to CABG (Figure 5; Table 2). In essence, despite the fact that diabetes was not contained within the SYNTAX Score II, the systemic metabolic effect of diabetes (such as age, CrCl, LVEF and other factors in the SYNTAX Score II) were associated with an increase in the patient risk profile and less favourable mortality predictions for PCI.14,28,29

The SYNTAX Score II and medical advances

Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization was designed to study the impact of revascularization on ULMCA disease, incorporating changes in medical therapies, PCI technology and techniques, and advances in CABG that were introduced since the completion of the SYNTAX trial. For example, as the SYNTAX Score II was developed in the SYNTAX trial which—exclusively used the first-generation paclitaxel-eluting TAXUS stent, it is not inconceivable that the PCI arm of EXCEL may outperform the mortality predictions made in the present study. In EXCEL, the workhorse drug-eluting stent was the EES (XIENCE). The randomized comparisons of everolimus- vs. paclitaxel-eluting stents were designed and powered for a combination of angiographic, ischemic and safety outcomes, and have consistently shown the EES to be associated with more favourable outcomes compared with paclitaxel-eluting stents.9–12 In addition, the largest patient level meta-analysis (n = 4989) of the SPIRIT clinical program has shown that EES was superior to paclitaxel-eluting stents in reducing all-cause mortality (3.2 vs. 5.1%, HR: 0.65, 95% CI: 0.49–0.86; P = 0.003.13 It is however important to emphasize that this difference was only driven by a lower non-cardiac mortality in the EES group and left-main revascularization was an exclusion criteria.13 More specifically in subjects undergoing ULMCA revascularization, a recent systematic review comparing EES with first-generation DES (n = 2231) and a propensity match study (n = 344) have shown no statistically significant differences in all-cause mortality.30,31 Furthermore, even within the SYNTAX Trial, when all stent thrombosis related deaths were removed, the impact on mortality reductions was shown to be modest (definite stent 0.5% reduction in mortality, definite to probable stent thrombosis 1.5% reduction in mortality).32,33

Limitations

The major limitation of the present study is also its greatest strength, namely the complete absence of the EXCEL trial outcomes (expected in the fall of 2016). We therefore cannot verify that the SYNTAX Score II predictions are accurate. However, predicting today the results of a randomized trial which will not be known for 2 years, assuming these predictions are reasonably borne out, opens the door for how future randomized trials may be considered whilst the longer-term (5 year) results of EXCEL are awaited. In addition, the present study will also enable unbiased validation of the SYNTAX Score II, fostering understanding of the multiple risk factors involved in ULMCA disease and decision making on the most appropriate revascularization modality. Although we are not using risk prediction for the primary endpoint of the trial, all-cause death is a hard, reproducible endpoint not subject to adjudication bias or definitional variation.

Figure 5  First 1000 4-year mortality simulations of the Evaluation of the Xience Everolimus-Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left-Main Revascularization trial on the SYNTAX Score II according to the presence or absence of diabetes mellitus. See Figure 4 legend for text in interpreting figure. As illustrated, the presence of diabetes was associated with an increase in predicted mortality within both the coronary artery bypass graft and percutaneous coronary intervention arms, with the predicted benefits of percutaneous coronary intervention being less pronounced in diabetics compared with non-diabetics. DM, diabetes mellitus.
Conclusions
In the large-scale, prospective randomized EXCEL trial, the SYNTAX Score II indicated at least an equipoise for long-term mortality between CABG and PCI in subjects with ULMCA disease with low and intermediate anatomical complexity. Clinical characteristics had a clear impact on long-term mortality predictions and decision making between CABG and PCI. The accuracy of these mortality predictions will be compared with the actual individual outcome data from EXCEL in the coming years.

Supplementary material
Supplementary material is available at European Heart Journal online.

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References
A rare cause of cardiogenic shock

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A 49-year-old woman without medical history was admitted following out-of-hospital cardiac arrest. She had complained of chest pain and EKG demonstrated sinus rhythm with ST-elevation in lead AVR and diffuse ST-depression. She then developed ventricular fibrillation, and received CPR and urgent cardiac catheterization. In the laboratory, she was in cardiogenic shock for which inotropes and IABP support were started. Angiography demonstrated normal coronary arteries. Left ventricular end-diastolic pressure was 16 mmHg and there was no gradient between LV and aorta. Left ventricular angiography demonstrated a poor left ventricular function, and aortography was normal. Echocardiography was not informative (TTE: poor windows, TEE impossible due to traumatic tongue swelling). She died 7 h after admission because of refractory shock.

Autopsy demonstrated a 2 cm large papillary tumour located on the arterial side of the aortic valve, attached by a pedicle stuck to the left- to non- coronary cusp commissure (Panel A, left main ostium shown at the calliper’s right lower angle). We found no coronary embolic material. Light microscopy of the tumour showed multiple papillary fronds, consisting of a central core of dense and surrounded by a layer of loose connective tissue and covered by endothelial cells, confirming papillary fibro-elastoma (Panel B, × 6.25, H&E). Review of the LV angiogram demonstrated an oscillating structure in the aortic root (Panels C and D, Supplementary material online, Movie, RAO view).

Cardiac papillary fibro-elastomas are usually an incidental finding, but may present with thrombo-embolism or, in this case, mechanical obstruction of a (left main) coronary ostium. Timely recognition might prevent poor outcome.

EKG, electrocardiogram; CPR, cardiopulmonary resuscitation; IABP, intra-aortic balloon pump; LVEDP, left ventricular end-diastolic pressure; LV, left ventricle; TTE, transthoracic echocardiography; TEE, transoesophageal echocardiography; H&E: haematoxylin & eosin (stain).

Supplementary Material is available at European Heart Journal online.

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