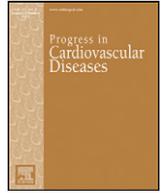




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The role of coronary artery bypass surgery versus percutaneous intervention in patients with diabetes and coronary artery disease ☆☆☆



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ABSTRACT

Patients with diabetes mellitus (DM) often exhibit a complex coronary anatomy, making coronary revascularization challenging. Coronary artery bypass grafting surgery (CABG) is currently considered the preferred revascularization method in patients with DM and multivessel disease. Percutaneous coronary intervention (PCI) has advanced with new stent generations having been developed in the recent years, but they have not yet been adequately compared against CABG in the population with DM. Comorbidities, such as renal disease and heart failure, lead to worse prognosis following a revascularization procedure and require especial consideration when choosing between CABG versus PCI. The presence of significant left main disease may also impose additional challenges to coronary revascularization, particularly when accompanied by the involvement of multivessel disease. Most of the evidence regarding revascularization in patients with DM is compiled from studies enrolling patients with stable ischemic heart disease, and trials with patients in the acute coronary syndrome setting are lacking.

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Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DES, drug-eluting stents; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; LV, left ventricular; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiovascular and cerebrovascular events; MI, myocardial infarction; MVD, multivessel coronary artery disease.

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Introduction

Diabetes mellitus (DM) is a global epidemic, and currently in North America, the prevalence of DM is approximately 11%.¹ Patients with DM have higher incidence of coronary artery disease (CAD) compared to the general population.² Choosing the proper revascularization strategy in these patients may be challenging, since DM is a marker of worse prognosis following coronary revascularization³ and approximately two-thirds of the patients have multivessel CAD (MVD).⁴ This paper will summarize the current evidence to best guide the optimal decision

of coronary revascularization in patients with DM, comparing coronary artery bypass grafting surgery (CABG) and percutaneous coronary intervention (PCI). Current gaps in evidence, such as the role of newer generation drug-eluting stents (DES), treatment of left main disease, and revascularization following an acute coronary syndrome (ACS) will also be discussed.

Main clinical evidence

The Bypass Angioplasty Revascularization Investigation (BARI) trial, published in 1996, randomized 1829 patients with MVD to undergo either balloon angioplasty or CABG and survival in both groups was similar after a follow-up of 5.4 years. Approximately one-fifth of the patients had medically treated DM and these patients had a survival benefit when undergoing CABG versus PCI (80.6% vs. 65.5%, $p = 0.003$ for the initial follow-up and 57.8% vs. 45.5%, $p = 0.025$ for the 10-year follow-up).^{3,5,6} These analyses formed the rationale for the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial, published in 2009, enrolling only patients with DM. Patients were randomized to medical therapy alone versus medical therapy added to the coronary revascularization strategy (PCI or CABG) chosen a priori by the attending physician.⁷ Approximately one-third of the 2368 patients were selected for the CABG stratum and two-thirds for the PCI stratum. Since the revascularization procedure was defined before randomization, this trial did not directly compare PCI versus CABG, but coronary revascularization versus medical therapy alone. The 5-year survival rates of the revascularization group and the medical therapy group were similar (88.3% vs. 87.8%, respectively, $p = 0.97$), as well as the rates of the composite of all-cause mortality, non-fatal myocardial infarction (MI) and non-fatal stroke (77.2% vs. 75.9%; $p = 0.70$). When compared to medical therapy, CABG resulted in a lower rate of major cardiovascular disease (CVD) events (22.4% vs. 30.5%; $p = 0.01$). The same benefit was not observed when comparing PCI versus medical therapy alone. Importantly, only one-third of the patients received a DES and only 20% of the patients had multivessel PCI. In the CABG group, 94.2% received an internal mammary-artery graft, with a mean of three distal anastomoses performed.⁷

The Synergy between percutaneous coronary intervention with Taxus and cardiac surgery (SYNTAX) trial randomized 1800 patients (approximately one-fourth with DM) with left main and/or MVD to either CABG or PCI with first-generation paclitaxel-eluting stent.⁸ At 1 year, a lower rate of all-cause death, MI, stroke and repeat revascularization (MACCE) was observed in the subgroup of patients with DM randomized to CABG (14.2% vs. 26.0%, relative risk: 1.83; 95%CI: 1.22 to 2.73, $p = 0.003$). The 5-year MACCE rates of the group with DM also favored CABG versus PCI (29.0% vs. 46.5%, $p < 0.001$).^{9,10} The Coronary Artery Revascularization in Diabetes (CARDia) trial randomized 510 patients with DM and stable CAD (SIHD; 60% with MVD) to either PCI (69% with DES) or CABG. The primary outcome was the composite of all-cause mortality, MI and stroke, which occurred in 10.5% of the CABG patients versus 13.0% in the PCI patients at 1 year (Hazard Ratio (HR): 1.25; 95% CI (Confidence Interval): 0.75 to 2.09, $p = 0.393$). Higher rates of non-periprocedural MI (5.5% vs. 1.2%, $p = 0.016$) and repeat revascularization (11.8% vs. 2.0%, $p < 0.001$) were also observed in the PCI group, as well as a trend to a higher stroke rate in CABG patients (2.8% vs. 0.4%, $p = 0.066$).¹¹ The U.S. Department of Veterans Affairs – Coronary Artery Revascularization in Diabetes (VA-CARDS) trial was stopped early due to slow recruitment, after enrolling only 25% of the planned population of patients with DM and complex CAD. The 2-year all-cause mortality in the CABG group was 5%, versus 21% for PCI (HR: 0.30; 95% CI: 0.11 to 0.80).¹²

In 2012, the landmark Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial was published by Farkouh and colleagues, randomizing 1900 patients with DM and MVD (without left main disease), most of them with stable CAD to undergo either CABG or PCI

with DES (mostly first-generation DES). After a mean follow-up of 3.8 years, CABG, when compared to PCI, reduced the composite rate of all-cause mortality, MI and stroke (18.7% vs. 26.6%, $p = 0.005$). CABG patients also experienced reduced isolated rates of MI (6.0% vs. 13.9%, $p < 0.001$) and had slightly higher rates of stroke (5.2% vs. 2.4%, $p = 0.03$).¹³ In 2018, the long-term survival report of the FREEDOM trial was published, comprising half of the original cohort of patients, followed for a median of 7.5 years. All-cause mortality was significantly lower in the CABG group than in the PCI arm (18.3% vs. 24.3%; $p = 0.01$) (Fig. 1).¹⁴ In subgroup analyses, younger patients, smokers and patients from centers in North America tended to have more pronounced benefits with surgical revascularization (p for interaction: 0.001; 0.01, and 0.02, respectively).

Recently, the applicability of the SYNTAX score when deciding between CABG vs. PCI in patients with DM and MVD from the FREEDOM trial was reported.¹⁵ The SYNTAX score, developed for the SYNTAX trial mentioned above, evaluates the anatomic complexity of the coronary tree and is commonly referenced in clinical guidelines as an aiding tool for choosing the optimal revascularization strategy in the general population of patients with stable CAD.^{8,16,17} This sub-analysis of the FREEDOM trial reported that the SYNTAX score was an independent predictor of MACCE (defined as the composite of death, MI, stroke and repeat revascularization) in patients with DM undergoing PCI, but not in those undergoing CABG.¹⁵ Additionally, regardless of the SYNTAX score category, the incidence of MACCE was higher in the PCI arm than in the CABG arm (low SYNTAX score: 36.6% vs. 25.9%, $p = 0.02$; intermediate SYNTAX score: 43.9% vs. 26.8%, $p < 0.001$; high SYNTAX score: 48.7% vs. 29.7%, $p = 0.003$) (Fig. 2). A pooled analysis of the SYNTAX, Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease (PRECOMBAT), and Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease (BEST) trials evaluated the role of the SYNTAX score in the population with DM ($n = 1068$ patients, two-thirds with MVD and one third with left main disease).¹⁸ Patients undergoing CABG had lower rates of the composite of all-cause death, MI, stroke, and repeat revascularization regardless of the SYNTAX score. Conversely, for the composite of death, MI and stroke (without repeat revascularization)

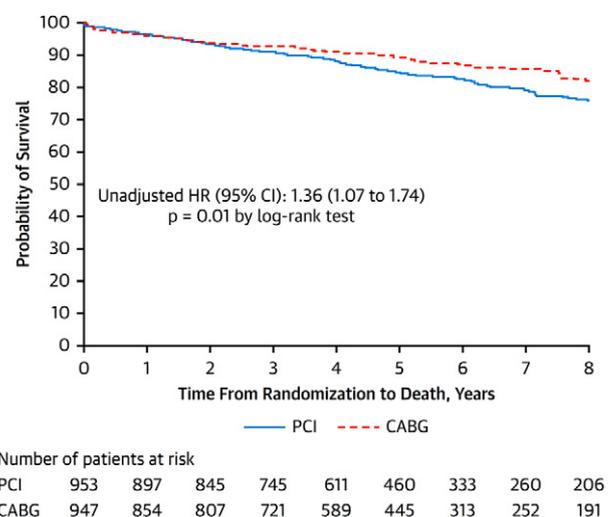


Fig. 1. Survival curve for the long-term all-cause mortality in the patients with diabetes and multivessel coronary disease from the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, according to revascularization strategy. CABG: coronary artery bypass grafting. PCI: percutaneous coronary intervention. Extracted from reference.¹⁴

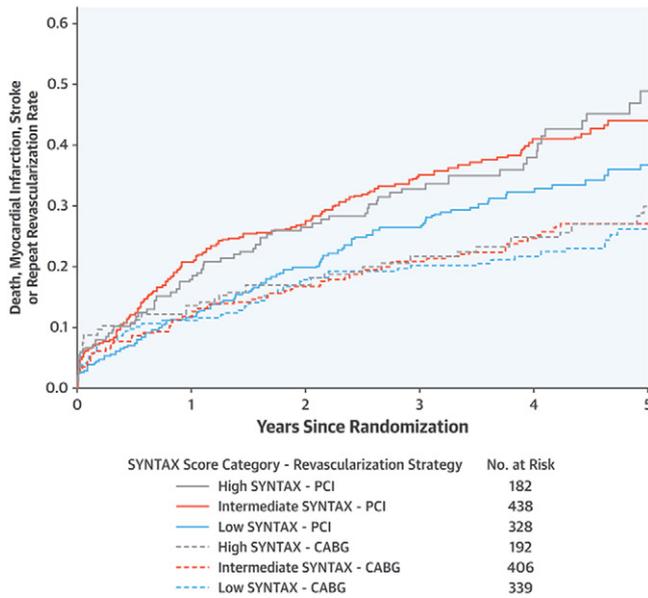


Fig. 2. Major adverse cardiac and cerebrovascular events (MACCE; all-cause mortality, myocardial infarction, stroke, and repeat revascularization) in patients with diabetes and multivessel coronary disease from the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, according to the revascularization strategy (CABG or PCI) and SYNTAX score category (low, intermediate or high). Unregard of the SYNTAX score category, the incidence of MACCE was higher in the PCI arm than in the CABG arm. CABG: coronary artery bypass grafting. PCI: percutaneous coronary intervention. SYNTAX: Synergy between percutaneous coronary intervention with Taxus and cardiac surgery. Extracted from reference.¹⁵

CABG was superior to PCI only in patients with high SYNTAX score (13.2% vs. 24.5%, $p = 0.018$).

What is consistent is that CABG reduces the rates of repeat revascularization and MI in patients with complex coronary anatomy and DM.¹⁹ When following these patients over more prolonged periods or when pooling data from different randomized trials, CABG is also related to reduced all-cause mortality, as shown in the long-term follow-up of the FREEDOM trial.¹⁴ Recently, a meta-analysis by Head and colleagues including 11 randomized trials reported a higher 5-year likelihood of death for patients undergoing PCI versus CABG ($n = 11,518$; HR: 1.20; 95%CI: 1.06 to 1.37; $p = 0.0038$), especially in patients with DM and MVD ($n = 3266$; HR: 1.48; 95% CI: 1.19 to 1.84; $p = 0.0004$; p for interaction: 0.0077).²⁰ As a downside, CABG was associated with a significantly higher stroke rate compared to PCI at 30 days (1.1% vs. 0.4%, $p < 0.001$) and 5 years (3.2% vs. 2.6%, $p = 0.027$), but not between 31 days and 5 years, suggesting that most CABG-related strokes occur in the first month of follow-up.²¹ A significant interaction was found for the population with DM, with a 5-year stroke rate of 2.6% for those treated with PCI versus 4.9% for CABG (HR: 0.52; 95%CI: 0.37 to 0.75; $p < 0.001$; p for interaction = 0.004).²¹ Results were not significant in patients without DM.

Controlling of risk factors for progression of CAD is also important in the post-revascularization period.²² Patients with DM who are able to adequately control blood pressure, cholesterol and glucose levels, refrain from smoking, eat a balanced and healthy diet and practice physical activities routinely are less likely to die or have a cardiovascular event following a revascularization procedure.^{23,24} As a general guidance, achieving blood pressure of $<130/80$ mmHg, HbA1c $< 7.0\%$ and low-density lipoprotein cholesterol (LDL-C) levels of at least 70 mg/dL are recommended targets in this population.²⁵ Patients should be engaged in achieving these goals during routine clinic visits, since compliance to optimal medical therapy or lifestyle modification interventions is challenging, even in the setting of a randomized clinical trial.^{26,27}

New-generation stents

New-generation DES have been used in the recent years, including in patients with DM, with the hope that they could bridge the gap between CABG and PCI outcomes in this population. Newer generation stents may overcome the higher risks of local stent complications found in patients with DM (such as stent thrombosis and restenosis), but it is unreasonable to expect that a focal intervention (PCI) will be able to optimally deal with the diffuse coronary disease commonly found in this population.^{28,29}

A direct randomized comparison of newer generation DES versus CABG in patients with DM is critically lacking and the best evidence currently available is derived from observational and pooled analyses. A 2012 meta-analysis reported that, in patients with DM, DES compared to bare-metal stents were related to lower rates of target vessel revascularization and similar incidence of stent thrombosis, MI and death, also suggesting that everolimus-eluting stents were more efficacious and safer compared to sirolimus, paclitaxel and zotarolimus eluting stents.³⁰ In the Taxus Element versus Xience Prime in a Diabetic Population (TUXEDO) – India trial, first-generation paclitaxel-eluting stents were not non-inferior to second-generation everolimus-eluting stents regarding the composite of cardiac death, target-vessel MI, or ischemia-driven target-vessel revascularization at the 1-year in 1830 patients with DM. In fact, paclitaxel stents resulted in higher rates of ischemia-driven target-lesion revascularization (HR: 2.18; 95%CI: 1.20 to 3.95; $p = 0.009$), cardiac death or target-vessel MI (HR: 1.69; 95%CI: 1.04 to 2.75; $p = 0.03$) and stent thrombosis (HR: 5.08; 95%CI: 1.74 to 14.87; $p < 0.001$).³¹

When compared with CABG, a 2014 meta-analysis reported increased mortality rates with paclitaxel or sirolimus DES and similar mortality with second-generation everolimus (rate ratio (RR): 1.11; 95%CI: 0.67 to 1.84) and zotarolimus DES (RR: 1.45; 95%CI: 0.31 to 8.81) in >20 thousand patients with DM.³² A registry-based analysis from the State of New York, comprising 8096 propensity-score matched patients with DM and MVD, reported that, when compared to CABG, patients undergoing PCI with everolimus DES had a lower risk of death (HR: 0.58; 95%CI: 0.34 to 0.98; $p = 0.04$) and stroke and higher risk of MI in the first 30 days of follow-up. In the long-term follow-up (4 years), the occurrence of death was similar between treatments (HR: 1.12; 95%CI: 0.96 to 1.30; $p = 0.16$) when complete revascularization was attained, which happened only in 20% of the PCI patients. For the remaining 80% patients, PCI with everolimus DES was associated with increased rates of death compared to CABG (HR: 1.20; 95%CI: 1.01 to 1.42; $p = 0.03$; p for interaction = 0.05). A lower risk of stroke (HR: 0.76; 95%CI: 0.58 to 0.99; $p = 0.04$) and a higher risk of MI (HR: 1.64; 95%CI: 1.32 to 2.04; $p < 0.0001$) were also observed in the everolimus PCI versus CABG patients.³³ The BEST trial compared PCI with everolimus DES versus CABG in 880 patients with MVD, 40% with DM. The trial was stopped prematurely, due to enrolment difficulties, and outcome comparisons should be evaluated with caution. The rates of the primary composite of all-cause death, MI or target-vessel revascularization at 2 years were 7.9% in the CABG group and 11.0% in the PCI group ($p = 0.32$ for noninferiority). After a median follow-up of 4.6 years, these rates were 10.6% in the CABG arm and 15.3% in the PCI arm (HR: 1.47; 95%CI: 1.01 to 2.13; $p = 0.04$ for superiority). A more pronounced reduction in the primary outcome favoring CABG was observed in the subgroup with DM in the long-term follow-up (HR: 2.24; 95% CI: 1.25 to 4.00; p for interaction: 0.06).³⁴

Challenging sub groups

Comorbidities

The presence of comorbidities, advanced age and frailty may make difficult the revascularization strategy choice between CABG and PCI. Depending on the prognosis of the non-cardiac baseline comorbidities,

patients and physicians may favor the more immediate peri-procedural risk profiles, and not the possible long-term CVD benefits, when deciding between PCI versus CABG.³⁵ Accordingly, in the long-term follow-up of the FREEDOM patients, a significant interaction was observed between the revascularization strategy and age, as mentioned previously. Patients younger than the trial median age at randomization (63.3 years; $n = 950$) were able to experience a larger benefit from CABG over PCI, compared to older patients (p for interaction = 0.001).¹⁴

Dedicated studies about coronary revascularization in patients with DM and chronic kidney disease (CKD) are lacking and most of the current evidence originated from exploratory analyses. In the FREEDOM trial, 451 patients had CKD, defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² and with a mean eGFR of 47 mL/min/1.73m². When compared with patients without CKD, CKD patients were older and had a higher burden of comorbidity, which culminated in a higher rate of the composite of all-cause death, MI and stroke in these patients over a median follow-up of 3.8 years (HR: 1.48; 95% CI: 1.16 to 1.89; $p = 0.002$). No interaction was found between the revascularization strategy and the CKD subgroup for any clinical outcome (HR for all-cause death, MI and stroke comparing CABG vs. PCI in patients with CKD: 0.73; 95%CI: 0.50 to 1.05; p for interaction = 0.83).³⁶ Recently, a pooled analysis of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE), BARI 2D, and FREEDOM trials compared outcomes of patients with DM and CKD following a revascularization procedure. A total of 1058 patients had CKD (21.4% of the whole pooled population). CKD patients had a higher probability of all-cause death, MI and stroke compared to patients with normal renal function at 4.5 years (HR: 1.48; 95% CI: 1.28 to 1.71; $p = 0.0001$) (Fig. 3). When comparing CABG vs. PCI in the CKD subgroup, no interaction was found, although the point estimates tended to favor CABG, particularly in patients with more advanced CKD, i.e. eGFR <45 mL/min/1.73 m² (HR for all-cause death, MI and stroke: 0.68; 95% CI: 0.39 to 1.19; $p = 0.17$).³⁷

Regarding left ventricular (LV) dysfunction, most revascularization trials either excluded these patients or had a low representation of them in their final population. In the FREEDOM trial, <2% of the patients had a LV ejection fraction (LVEF) <40% and no interaction was observed in this subgroup regarding the incidence of major CVD events or all-cause mortality both during the original and extended follow-up.^{13,14} A retrospective propensity-matched registry analysis from the province

of Alberta, Canada combined all revascularization procedures performed in patients with DM, MVD and LV dysfunction from 2004 to 2016 ($n = 1738$). A total of 56% of the patients had LVEF between 35% and 49%, the remaining having LVEF lower than 35%. When compared to CABG, PCI was associated with higher rates of MACCE (all-cause death, MI, stroke and repeat revascularization) in both LVEF strata over a mean follow-up of 50 months (HR: 1.97; 95%CI 1.64 to 2.35, $p < 0.001$ for LVEF between 35% and 49% and HR: 2.28; 95%CI: 1.79 to 2.90, $p < 0.001$ for LVEF<35%). PCI was also associated with increased all-cause mortality (HR: 1.34; 95%CI: 1.07 to 1.68, $p = 0.001$ for LVEF between 35% and 49% and HR: 1.62; 95%CI: 1.20 to 2.22, $p = 0.002$ for LVEF<35%), with similar rates of stroke compared to CABG.³⁸

Acute coronary syndromes

Most of the evidence concerning the choice of the optimal revascularization strategy in patients with DM was obtained from patients with SIHD, and few studies have focused in patients with an ACS.³⁹ Consequently, only one-third of the patients with DM and MVD in the United States undergo CABG following a non-ST segment elevation MI.⁴⁰ In the FREEDOM trial, approximately 30% of the patients had a recent ACS preceding enrollment and outcomes were similar in this group compared to the overall population.¹³ A sub-analysis of the Acute Catheterization and Early Intervention Triage Strategy (ACUITY) trial including 326 propensity-matched patients with DM, MVD and a non ST-segment elevation ACS reported lower 1-year rates of all-cause death, MI and ischemia-driven repeat revascularization with CABG compared to PCI (17.3% vs. 30.1%, $p = 0.01$), mainly driven by reductions in repeat revascularization.⁴¹ The best evidence currently available in the ACS setting is a large observational registry-based analysis, pooling all revascularization procedures in the province of British Columbia, Canada from 2007 to 2014. Among 2947 patients with DM, MVD and ACS, CABG, compared to PCI, was associated with lower 30-day rates of the MACCE composite of all-cause death, MI and stroke (4.3% vs. 8.2%, $p < 0.01$) and MI (1.8% vs. 6.1%, $p < 0.01$), with a small absolute increase in the stroke rates (1.6% vs. 0.8%, $p = 0.04$). In the long-term follow-up between 31 days and 5 years, CABG led to lower rates of MACCE (20.8% vs. 33.4%; $p < 0.01$), all-cause death (12.4% vs. 22.3%; $p < 0.01$), MI (9.9% vs. 17.6%, $p < 0.01$) and similar rates of stroke (6.2% vs. 5.8%, $p = 0.97$).⁴² A randomized clinical trial in the ACS setting is urgently needed.⁴³

Left main disease

The treatment of left main disease with either CABG or PCI has been evaluated in recent clinical trials, enrolling different proportions of patients with DM. Importantly, left main disease was an exclusion criterion for the FREEDOM trial.¹³ In a pooled analysis of the SYNTAX and PRECOMBAT trials, including all patients with left-main disease ($n = 1305$), CABG compared to PCI led to lower 5-year rates of all-cause death, stroke, MI or repeat revascularization (23.0% vs. 28.3%; $p = 0.045$), mainly driven by reductions in repeat revascularization (10.8% vs. 19.5%; $p < 0.001$). No interaction was observed in the subgroup with DM (28% of the whole population, p for interaction = 0.38).⁴⁴ The Nordic-Baltic-British left main revascularization (NOBLE) study randomized 1201 patients with left main disease, 15% of them with DM, to undergo either CABG or PCI. In the overall population, CABG was superior to PCI in reducing the primary outcome of all-cause mortality, MI, stroke, and repeat revascularization at 5 years (18% vs. 28%, $p = 0.0044$).⁴⁵

The Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial randomized 1905 patients with left main disease with low or intermediate SYNTAX score to revascularization with either CABG or PCI with second-generation DES. PCI was noninferior to CABG regarding the incidence of the primary outcome, a composite of all-cause death, stroke

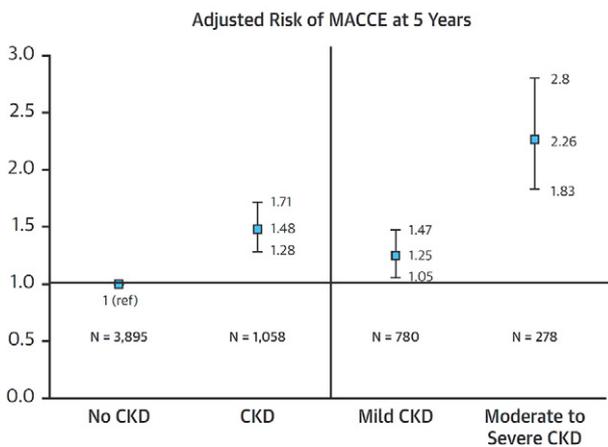


Fig. 3. Patients with diabetes and chronic kidney disease (CKD) are more likely to experience a major adverse cardiovascular or cerebrovascular event (MACCE, the composite of all-cause mortality, myocardial infarction or stroke) compared to patients with DM but without CKD. This holds true both for patients with mild (eGFR between 45 and 60 mL/min/1.73 m²) and moderate to severe (eGFR <45 mL/min/1.73 m²) renal dysfunction. Data from a pooled analysis of the patients with diabetes in the COURAGE, BARI-2D, and FREEDOM trials (trial acronyms in the text). eGFR: estimated glomerular filtration rate. Extracted from reference.³⁷

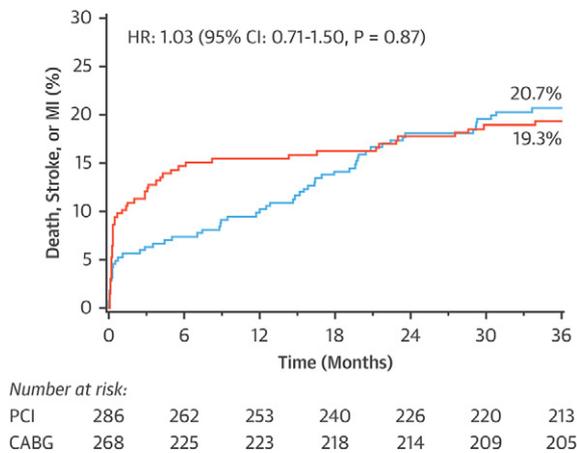


Fig. 4. Composite of all-cause mortality, stroke, and myocardial infarction (MI) for patients with diabetes and left main disease undergoing CABG (red line) vs. PCI (blue line) in the Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial. CABG: coronary artery bypass grafting. PCI: percutaneous coronary intervention. Extracted from reference.⁴⁷

and MI at 3 years (15.4% vs. 14.7%, noninferiority p -value = 0.02).⁴⁶ Randomization was stratified according to the presence of DM (approximately 30% of the trial population) and results in this subgroup were recently reported.⁴⁷ Relative to patients without DM, DM was associated with a higher 3-year incidence of the primary outcome (20.0% vs. 12.9%; $p < 0.001$), and no interaction between revascularization strategy and DM was observed (PCI vs. CABG HR for the primary outcome in the subgroup with DM: 1.03; 95%CI: 0.71 to 1.50; $p = 0.87$; p for interaction: 0.82) (Fig. 4). In this analysis, patients with DM, left main disease and an intermediate SYNTAX score had a lower risk of all-cause death when undergoing CABG compared to PCI (9.6% vs. 19.6%, $p = 0.04$). This was not observed in patients with low SYNTAX score, although no formal interaction was present (p for interaction = 0.32). In the previously mentioned meta-analysis by Head, no difference in 5-year mortality rate was observed in 1120 patients with DM and left main disease undergoing either CABG or PCI (13.4% vs. 16.5%; HR: 1.34; 95%CI: 0.93 to 1.91; $p = 0.11$).²⁰ Caution is advised when interpreting these results, since patient selection, differences in outcome definitions and assessment among trials and statistical power of subgroup analyses may lead to bias.⁴⁸ It is possible that DM would not be a good discriminator for choosing the best revascularization strategy in patients with left main disease, especially in the absence of concomitant MVD, but this hypothesis still needs to be tested in dedicated trials.⁴⁹

Conclusions

For most patients with DM and MVD, CABG is the revascularization strategy of choice, as demonstrated in several studies. The best approach in specific situations, such as patients with an ACS or left main disease, is still controversial and the available evidence, mostly non-randomized, is not conclusive. Particularly in these cases, a thorough discussion with the Heart Team, considering also comorbidities, coronary anatomy complexity, and patient preferences, is key for individualizing the decision-making process regarding the optimal strategy for coronary revascularization.

Declaration of Competing Interest

None.

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