Reduced risk of myocardial infarct and revascularization following coronary artery bypass grafting compared with percutaneous coronary intervention in patients with chronic kidney disease

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Coronary atherosclerotic disease is highly prevalent in chronic kidney disease (CKD). Although revascularization improves outcomes, procedural risks are increased in CKD, and unbiased data comparing coronary artery bypass grafting (CABG) and percutaneous intervention (PCI) in CKD are sparse. To compare outcomes of CABG and PCI in stage 3 to 5 CKD, we identified randomized trials comparing these procedures. Investigators were contacted to obtain individual, patient-level data. Ten of 27 trials meeting inclusion criteria provided data. These trials enrolled 3993 patients encompassing 526 patients with stage 3 to 5 CKD of whom 137 were stage 3b–5 CKD. Among individuals with stage 3 to 5 CKD, survival through 5 years was not different after CABG compared with PCI (hazard ratio [HR] 0.99, 95% confidence interval [CI] 0.67–1.46) or stage 3b–5 CKD (HR 1.29, CI 0.68–2.46). However, CKD modified the impact on survival free of myocardial infarction: it was not different between CABG and PCI for individuals with preserved kidney function (HR 0.97, CI 0.80–1.17), but was significantly lower after CABG in stage 3–5 CKD (HR 0.49, CI 0.29–0.82) and stage 3b-5 CKD (HR 0.23, CI 0.09–0.58). Repeat revascularization was reduced after CABG compared with PCI regardless, of baseline kidney function. Results were limited by unavailability of data from several trials and paucity of enrolled patients with stage 4–5 CKD. Thus, our patient-level meta-analysis of individuals with CKD randomized to CABG versus PCI suggests that CABG significantly reduces the risk of subsequent myocardial infarction and revascularization without affecting survival in these patients.

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More than 10% of the adult U.S. population have chronic kidney disease (CKD),[1] which is associated with increased cardiovascular morbidity and mortality.[2,3] Standard cardiovascular therapies have the potential to decrease morbidity and mortality, but utilization of established cardiovascular therapies including coronary angiography and revascularization procedures has remained lower in individuals with CKD than in patients with relatively preserved kidney function.[4,5]

Although this selective underutilization of coronary revascularization in a population at high cardiovascular risk ("renalism"[5]) could represent inappropriate therapeutic nihilism, recent trials have failed to demonstrate efficacy of standard medical therapies in patients on dialysis,[6,7] whereas the majority of large cardiovascular trials have excluded individuals with CKD, raising important questions about the efficacy or safety of other accepted cardiovascular therapies in this population. Indeed, patients with CKD experience higher perioperative mortality[8,9] after coronary artery bypass grafting (CABG), are at higher risk of acute kidney injury after CABG surgery or percutaneous coronary intervention

(PCI),[10,11] and have generally much higher overall mortality[12,13] compared with the subjects enrolled in landmark trials comparing CABG and PCI, in whom advanced kidney dysfunction was uncommon.[8] Therefore, a dedicated, CKD-specific comparison of the risks and benefits of PCI and CABG is needed to define the optimal role for each therapy in the setting of impaired kidney function.

Although several retrospective comparisons of PCI and CABG among individuals with CKD undergoing coronary revascularization for clinical indications have generally favored CABG,[14–16] the potential for indication bias and residual confounding remains an important concern with nonrandomized studies in this area. To provide highest level of evidence, we conducted a systematic review of the literature and, subsequently, a detailed, individual-level meta-analysis of patients with moderate to severe CKD from published randomized trials comparing CABG and PCI.

RESULTS

Study identification and characteristics

Our prespecified literature search identified 1111 citations (Figure 1). After title and abstract review, 75 citations were examined in detail; however, 48 were excluded because they failed to meet the specified inclusion criteria. A total of 27 eligible trials were identified for inclusion, but 17 had to be excluded for the following reasons: data no longer available ($n = 3$),[17–19] insufficient data to calculate the estimated glomerular filtration rate (eGFR) ($n = 7$),[20–26] unable to contact the investigators despite multiple attempts ($n = 3$),[27–29] and investigators unable ($n = 2$)[30,31] or unwilling ($n = 2$)[32,33] to share data.

The remaining 10 trials comprised the analytical dataset and included the following trials: Angioplasty Versus Minimally Invasive Surgery Trial (AMIST)[34]; Bypass Angioplasty Revascularization Investigators Trial (BARI)[35]; Cisowski *et al.*[36]; Argentine Randomized Study: Coronary Angioplasty with Stenting Versus Coronary Bypass Surgery in Multivessel Disease (ERACI II)[37]; German Angioplasty Bypass Surgery Investigation (GABI)[38]; Study of Unprotected Left Main Stenting Versus Bypass Surgery (Le MANS)[39]; Diegeler *et al.*[40]; Medicine, Angioplasty, or Surgery Study (MASS 1)[41]; Medicine, Angioplasty, or Surgery II Study (MASS 2)[42]; and Veterans Affairs Cooperative Study 385, the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME).[43]

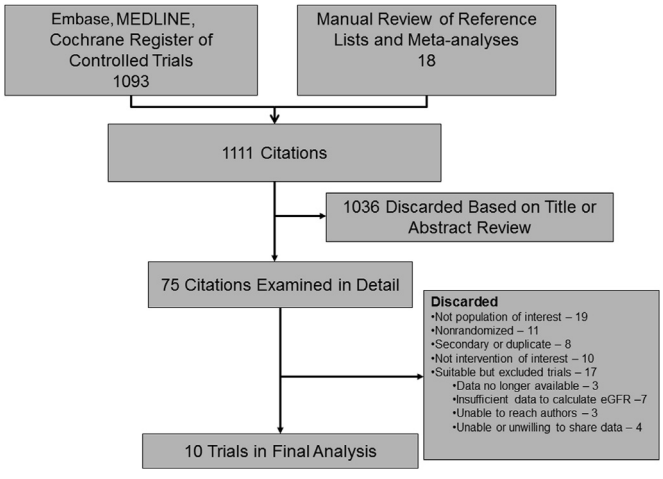

Figure 1 | Flow diagram of study selection.

All studies used central and concealed randomization and intention-to-treat analyses of outcomes. However, in 2 studies, outcomes assessors were not blinded to treatment assignment.[34,36] Loss to follow-up was generally low, but exceeded 10% in 2 studies[34,38] (Table 1).

The majority of trials completed enrollment between 1991 and 2001 with the exception of a single trial that completed enrollment in 2002[36] and the Le Mans trial, which enrolled subjects from 1997 to 2008.[39] As shown in Table 1, stents were used in all but 2 studies,[38,41] and off-pump bypass techniques were available for CABG patients in 5 studies.[34,36,39–41] Four studies required multivessel disease for inclusion,[35,37,38,42] whereas 4 excluded individuals with multivessel coronary disease.[34,36,40,41] One study (AMIST)[34] did not collect data on at least 1 covariate, leading to systematic missingness. Eligible studies for which we were unable to obtain data were qualitatively similar to included studies in terms of sample size, year enrolled, revascularization technique, inclusion criteria, and the range of relative risks of study outcomes following PCI compared with CABG (Supplementary Tables S1 and S2).

Baseline characteristics of study subjects

The study cohort included 3993 randomized subjects (CABG: 1994, PCI: 1999,) with 17,131 person-years (PY) of post-intervention follow-up time (post-CABG: 8528 PY, post-PCI: 8603 PY). There were 526 individuals with stage 3 or worse CKD with 1856 PY of follow-up (CABG: 892 PY, PCI: 964 PY), and 137 with stage 3b or worse CKD (20 with stage 4 and 5 CKD) with 402 PY of follow-up (CABG: 195 PY, PCI: 207 PY). There were 7 individuals with stage 5 CKD. Baseline characteristics of the enrolled patients and those with CKD are shown in Tables 2 and 3. Individuals with and without CKD were mostly similar, but those with CKD tended be older, and a higher percentage of those with CKD were female.

Survival

All-cause mortality rates were similar after CABG or PCI and were higher among individuals with CKD (CABG: 5.6/100 PY, PCI: 5.5/100 PY) compared with those with preserved kidney function (CABG: 2.1/100 PY, PCI: 2.3/100 PY).

On primary multiple imputation–based analysis adjusted for all covariates of interest, mortality did not differ between patients randomized to CABG versus PCI among individuals with relatively preserved kidney function (hazard ratio [HR] 0.90, 95% confidence interval [CI] 0.73–1.11), those with stage 3 to 5 CKD (HR 0.99, 95% CI 0.67–1.46), those with stage 3a CKD (HR 0.79, 95% CI 0.47–1.33), or those with stage 3b to 5 CKD (HR 1.29, 95% CI 0.68–2.46)