AKI, and conversion to open heart surgery, but higher rates of stroke and PPM at 30-days in TAVI patients with bicuspid compared with tricuspid AV.[2] Likewise, Halim et al. reported similar in-hospital mortality, stroke, and conversion to open heart surgery, but higher residual moderate or severe aortic insufficiency in TAVI patients with bicuspid compared with tricuspid AV utilizing mostly current generation devices.[3] However, in both aforementioned studies, the majority (>90%) of the procedures were performed in elective hemodynamically stable patients compared with our study, which exclusively evaluated outcomes in urgent/emergent TAVI procedures. The relatively worse outcomes in our study are likely due to decompensated HF, further compounded by anatomical and clinical challenges of TAVI in bicuspid valve such as heavily calcified valve with fused raphe, annular asymmetry, concomitant aortopathy, concern for suboptimal valve expansion in an orifice with 2 commissures, and possibly use of early generation devices compared with current generation devices which are known to have better procedural success and outcomes in bicuspid AV.[1,3]

Our study is limited by database, which lacks information on STS risk scores, valve types (early vs current generation), laboratory/imaging parameters, reasons necessitating urgent/emergent procedures, and long-term follow-up.

In conclusion, in this study of nationally representative cohort of TAVI patients undergoing urgent/emergent procedure, we found relatively worse in-hospital outcomes in patients with bicuspid compared with tricuspid AV.

Disclosures

The authors declare no conflict of interest.

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A Meta-Analysis of Cardiovascular Outcomes in Patients With Hypercholesterolemia Treated With Bempedoic Acid

Treatment with statins has led to significant reductions in cardiovascular events; however, not all patients could attain their target low-density lipoprotein (LDL) level despite treatment with maximally tolerated doses or without experiencing statin-related side effects.[1,2] Bempedoic acid, a small-molecule inhibitor of ATP-citrate lyase, a component of the cholesterol biosynthesis pathway was recently approved by the Food and Drug Administration for the treatment of patients with atherosclerotic cardiovascular disease (ASCVD).[3] However, the efficacy of bempedoic acid in cardiovascular event reduction remains unclear. Therefore, we performed a meta-analysis of randomized controlled trials (RCTs) comparing cardiovascular outcomes in patients treated with bempedoic acid compared with placebo in patients with hypercholesterolemia intolerant to or treated with maximally tolerated statin doses.

We performed a search of electronic databases including PubMed/Medline, Google Scholar, and ClinicalTrials.gov from inception till June 2020. We included RCTs evaluating the effect of bempedoic acid for the treatment of hypercholesterolemia in patients intolerant to or on maximum tolerated statin doses. We included participants from RCTs that were assigned to a daily dose of 180mg of bempedoic acid or placebo throughout the trial period and had reported on individual cardiovascular outcomes. The primary outcome of our meta-analysis was the incidence of five-point major adverse cardiovascular events (MACE) that includes, myocardial infarction, non-fatal stroke, cardiovascular mortality, hospitalization for unstable angina, and coronary revascularization. Secondary outcomes were hospitalization for heart failure and noncoronary revascularizations. Outcomes were analyzed as dichotomous variables, and risk ratios (RR) and their respective 95% confidence intervals (CI) were obtained using the Mantel-Haenszel method and a random-effects model was used. A two-tailed p-value <0.05 was used to indicate significance. Review Manager version 5.3 (RevMan; Cochrane Collaboration) was used to analyze all study data.

A total of 4 RCTs,[4–7] randomizing 3,483 patients (2,332 to bempedoic acid and 1,151 to placebo) were included in this meta-analysis. The mean age of study participants was 65.3 ± 9.3 years, and 58.2% of participants were men. At baseline, mean LDL was 132.6 ±

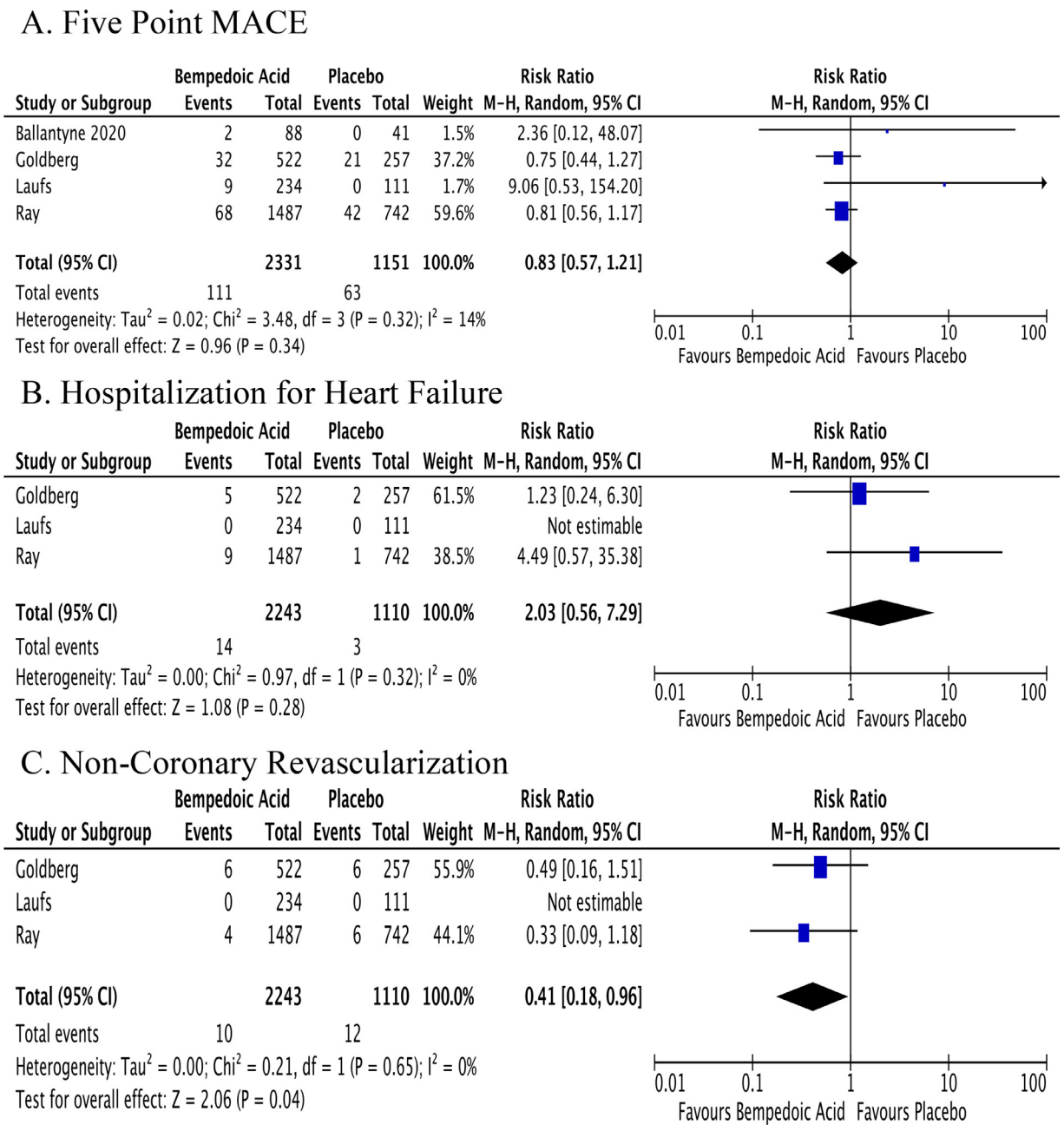

Figure 1. Forest plot of cardiovascular outcomes in patients treated with bempedoic acid compared to placebo. (*A*) Five point major adverse cardiovascular events (MACE). (*B*) Hospitalization for heart failure. (*C*) Noncoronary revascularization procedures. CI = confidence interval; MACE = major adverse cardiovascular event; M-H: Mantel-Haenszel.

37.5 mg/dL, 66.4% of patients were on maximum tolerated statin therapy, and 32.7% had diabetes mellitus. Cardiovascular outcome data were available for 3,482 patients (99.9%) with a mean follow-up duration of 35 weeks (range 12 to 54 weeks). Four trials reported data on five point MACE.[4–7] Overall, there was no statistically significant difference in the risk of 5 point MACE (4.8% vs 5.5%; RR: 0.83 [95%CI, 0.57 to 1.21]; p = 0.34, I^2 = 14%) (Figure 1A) in patients randomized to bempedoic acid compared to placebo. A total of 3 RCTs reported on hospitalizations for heart failure and on noncoronary revascularization.[5–7] There was no significant reduction in hospitalizations for heart failure (0.9% vs 0.8%; RR: 2.03 [95%CI, 0.56 to 7.29]; p = 0.28, I^2 = 0%) (Figure 1B); however, there was a significant 59% risk reduction in non-coronary revascularization procedures in the bempedoic acid group compared to placebo (0.45% vs 1.1%; RR: 0.41 [95%CI, 0.18 to 0.96]; p = 0.04, I^2 = 0%) (Figure 1C).

In this study, there was a significant reduction in non-coronary revascularization procedures while there were no observed significant reductions in MACE or heart failure hospitalizations among patients treated with bemedpoic

acid compared to placebo in patients with hypercholesterolemia treated with maximally tolerated medical therapy with residual risk for future ASCVD. Meanwhile, pro-protein convertase subtilisin/Kexin type 9 inhibitors, a class 1 recommendation for the secondary prevention of ASCVD in patients at very high risk for future ASCVD, have been shown to significantly reduce LDL levels and MACE in a meta-analysis of 35 trials.[8,9] One explanation for the lack of efficacy of bempedoic acid in reducing MACE is the relatively short follow-up period in individual trials. Limitations of this meta-analysis include the lack of individual patient-level data and the absence of trials with follow-up data extending beyond one year.

In conclusion, this study demonstrates that the significant reductions in LDL levels in patients treated with bempedoic acid compared to placebo reported in individual trials were not consistent with significant reductions in MACE. Meanwhile, a significant 59% reduction in noncoronary revascularization procedures was observed. Therefore trials with adequate power to detect efficacy outcomes and extended follow-up intervals are needed to delineate the benefit of bempedoic acid on cardiovascular outcomes.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Drug-Eluting Stents Versus Bypass Surgery for Left Main Disease: An Updated Meta-Analysis of Randomized Controlled Trials With Long-Term Follow-Up

Debate is ongoing regarding the optimal mode of revascularization for patients with left main coronary artery disease (LMCAD). Longer-term follow-up from randomized trials has recently become available. We recently published a study-level meta-analysis that demonstrated similar mortality after percutaneous coronary intervention (PCI) with drug-eluting stents (DES) when compared with coronary artery bypass grafting (CABG).[1] There were also no differences in cardiac death, stroke or myocardial infarction (MI), although there was a greater risk of unplanned revascularization after PCI. A limitation of this study was that only 1 trial had data beyond 5 years, that for all-cause mortality only from the SYNTAX trial.[2] An open question thus remains as to whether CABG will outperform PCI during long-term follow-up.

The PRECOMBAT trial, in which 600 patients with LMCAD were randomized to PCI with sirolimus-eluting stents versus CABG, has now reported 10-year data.[3] Unlike SYNTAX, the PRECOMBAT trial reported detailed long-term outcomes on major adverse cardiovascular events, including MI, stroke, and revascularization. We therefore performed an updated meta-analysis to better inform clinicians, patients, and guideline committees with regards to the long-term clinical outcomes seen with the 2 therapies.

Methods

The present analysis was conducted in accordance with published PRISMA guidance and prospectively registered (CRD42020163240). We systematically identified all randomized clinical trials comparing PCI with DES and CABG in patients with LMCAD. The primary efficacy endpoint was all-cause mortality. Secondary endpoints were cardiac death, MI, stroke, and unplanned revascularization. All analyses were by intention-to-treat, and all outcomes assessed as relative risks (RRs). The last available follow-up was used for all trials. Random-effects meta-analyses were performed using the restricted maximum likelihood estimator. Methods otherwise were as recently described in detail.[1]

Results

There were 5 eligible trials[2–6] in which 4,612 patients were included. The weighted mean follow-up duration was 74.9 months. Baseline characteristics are shown in Table 1. There was no