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Original Investigations

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Bayesian Interpretation of the EXCEL Trial and Other Randomized Clinical Trials of Left Main Coronary Artery Revascularization

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Key Points

Question

A randomized clinical trial (EXCEL; Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) of patients with left main coronary artery disease reported no significant difference between percutaneous coronary intervention and coronary artery bypass surgery in the composite outcome rate of death, stroke, or nonfatal myocardial infarction at 5 years; however, this interpretation is controversial, and whether bayesian analyses may assist resolution is unknown.

Findings

This bayesian reanalysis of EXCEL data suggested that the mean difference for the primary composite outcome was 3% less and for mortality was 1% less with coronary artery bypass surgery than with percutaneous coronary intervention at the 5-year follow-up; the estimated probability of more primary composite events with percutaneous coronary intervention was 95%

(virtually 100% when including repeated revascularization) and of more deaths was 99%. Similar results were observed when the totality of prior studies, based on a systematic review, was included.

Meaning

Bayesian analysis provided additional insights into the interpretation of randomized trial results, suggesting that percutaneous coronary intervention provides long-term results inferior to coronary artery bypass surgery for patients with left main coronary artery disease.

Abstract

Importance:

Patients with left main coronary artery disease have improved outcomes with coronary revascularization compared with medical therapy, but the choice of optimal revascularization technique is unresolved.

Objective:

To use bayesian methods to analyze the risk differences for patients with left main coronary artery disease randomized to treatment with coronary artery bypass surgery (CABG) compared with those randomized to percutaneous coronary intervention (PCI) in recent randomized clinical trials (RCTs).

Design, Setting, and Participants:

A systematic review using the PubMed database with the query string “(left main disease) and (PCI or CABG) and (5-year follow-up) and (clinical trial)” identified all RCTs from January 1996 to January 2020 comparing CABG to PCI for treatment of patients with left main coronary artery disease and with 5-year follow-up data. With the use of bayesian

methods, the largest and most publicized RCT (EXCEL; Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization; 2019) was reanalyzed (1) as an isolated entity using non-informative priors and (2) in the context of previous knowledge using informative priors derived from similar trials. Published aggregate data were used with assignments from each trial following the original intention-to-treat principle. Combining EXCEL data with varying levels of prior information using Bayes theorem provided final (posterior) probability distributions for primary and secondary outcomes.

Main Outcomes and Measures:

A composite end point of death, nonfatal myocardial infarction, and stroke was the primary EXCEL outcome and was accordingly the primary outcome for this reanalysis. Secondary analyses were performed for isolated all-cause mortality and for the composite outcome along with repeated revascularization procedures.

Results:

When EXCEL data were analyzed using the originally stated non-inferiority design, the 5-year primary outcome difference reported (2.8%; 95% CI, -0.9% to 6.5%) exceeded the predefined 4.2% non-inferiority margin; thus, the null hypothesis of PCI inferiority could not be rejected. By contrast, the present bayesian analysis of the EXCEL primary outcome estimated 95% probability that the 5-year primary outcome difference was increased with PCI compared with CABG and 87% probability that this difference was greater than 1 extra event per 100 patients treated. Bayesian analyses also suggested 99% probability that EXCEL total mortality was increased with PCI and 94% probability that this absolute difference exceeded 1 extra deaths per 100 treated. A systematic review identified 3 other RCTs that studied the same question. The incorporation of this prior knowledge

reduced the estimated probability of any excess mortality with PCI to 85%. For the secondary composite end point, which also included repeated revascularizations, there were estimated probabilities of 98% for at least 4 extra events and of 90% for at least 5 extra events per 100 patients treated with PCI.

Conclusions and Relevance:

Bayesian analysis assisted in RCT data interpretation and specifically suggested, whether based on EXCEL results alone or on the totality of available evidence, that PCI was associated with inferior long-term results for all events, including mortality, compared with CABG for patients with left main coronary artery disease.