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Commentary: Is this a case in which we know what we don't know what we don't know?

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Current guidelines recommend early invasive revascularization strategies in patients with non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS).¹ Adoption of primary percutaneous coronary intervention (PCI) over the years has led to a substantial decrease in mortality in acute coronary syndrome (ACS); nevertheless, coronary artery bypass grafting (CABG) remains a staple for patients with ACS, particularly in those with left main or complex multivessel coronary artery disease or anatomy unsuitable for PCI.² Despite the conclusive benefit of revascularization in NSTEMI-ACS,³ there are limited data comparing the long-term effectiveness of PCI compared with CABG,⁴ as most large trials comparing these 2 modalities are either under-representative of (ie, NOBLE [Nordic-Baltic-British left main revascularization], FREEDOM [Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease])^{5,6} or completely exclude patients with ACS (ie, SYNTAX [Synergy between PCI with TAXUS and Cardiac Surgery]).⁷

Hamaya and colleagues⁸ conducted a systematic review and meta-analysis consolidating the limited available data; 3 randomized controlled trials (RCTs) and 8 observational studies. The authors found an association with survival benefit of CABG with longer follow-up length, which is consistent with the pattern seen in many large coronary RCTs such as Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease (EXCEL).⁹

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CENTRAL MESSAGE

Early invasive revascularization is imperative in non-ST elevation acute coronary syndrome. While there may be survival benefit with surgical revascularization, evidence is limited.

The authors should be commended for the design of the meta-analysis, as they reconstructed time-to-event analysis from survival curves to create restricted mean survival time differences, avoiding violation of the proportional hazard ratio assumption. However, the study faces several challenges, mainly due to lack of availability of data in the literature, which led to numerous assumptions to complete the analysis.

After exclusion of studies with incomplete raw data or outdated publication date, the authors were left with only 1 pooled RCT and 5 observational trials, representing a limited, predominately nonrandomized sample size. Importantly, the findings of survival advantage of CABG over PCI were solely driven by the single trial with greater than 5-year follow-up, and moreover there were no statistically difference in mean survival between each group at any particular cutoff year.

Furthermore, there are a number of indications with established surgical benefit, such as diabetes,^{5,10} multivessel,⁷ and left main disease.⁶ Given the study's composition of mainly observational data, a large degree of variance in coronary anatomy, patient risk profile, and diabetic status in the included patients is expected, which is reflected statistically by the moderate degree of between-study heterogeneity. It assumes appropriate clinical selection of revascularization techniques; however, the study is inevitably vulnerable to confounding, which may introduce bias.

Given these limitations, one must be cautioned to conclude the superiority of either method of

revascularization in NSTEMI-ACS from this meta-analysis alone. At most, it may suggest a trend toward survival advantage with CABG compared with PCI with long-term follow-up. Despite many limitations, this study highlights the scarcity of evidence within revascularization in ACS, calling for further randomized evidence. While awaiting results from the randomized trial, severe coronary artery disease (MILESTONE) <https://clinicaltrials.gov/ct2/show/NCT01311323>, our focus with managing patients with NSTEMI-ACS should continue to include the Heart Team approach,¹ considering patients' coronary anatomy, surgical risk, diabetic status, and comorbidity profile to guide optimal revascularization strategy.

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