

Letters to the Editor

generalizability of the study. More importantly, however, they prevent full consideration of all relevant available evidence. A PubMed search reveals 6 randomized, controlled trials comparing the patency of RA and SV conduits, but only 5 (or more accurately 4 separate article) were included in this study. Furthermore, no justification was given for ignoring the 36 nonrandomized studies that have compared many thousands of angiograms. Because all relevant studies were not included, several clinically important variables were not examined, such as long-term (>5 years) conduit patency, which is a more relevant end point when selecting revascularization strategy than is the 22-month mean angiographic follow-up reported.¹

Closer inspection of the extracted data, discussion, and study methodology reveals several critical flaws that compromise the study findings. The correct observational long-term patency data of the RAPCO (Radial Artery Patency and Clinical Outcome) trial can be found in a later article authored by Hayward and associates² (angiographic follow-up time 60 months, RA patency 89.1%, SV patency 82.4%), but Benedetto and colleagues¹ selected an earlier report, possibly because they focused on failure rate rather than patency. Meta-regression of only 5 studies is flawed for several statistical reasons.³ Benedetto and colleagues¹ have concluded on the basis of results with unknown heterogeneity that patency is comparable between RA and SV conduits and that the time of follow-up does not affect the accuracy of the overall estimate of patency. These conclusions are not possible unless early, midterm, and long-term patencies have been examined in a stratified manner, because different mechanisms are responsible for graft failure at different time horizons. Other sources of heterogeneity, for example the quality of reporting of the angiographic patency, do not appear to have been investigated. Although the authors stated

that I^2 was calculated, this value was not reported.

The flawed methodology, results, and conclusions of this study have introduced an even more distorted view of the existing evidence. Benedetto and colleagues assessed the literature through a key hole and consequently cannot see the evidence horizon. This perspective misinforms clinical decision making and misguides the focus of future research. This article is an example of fast-track publication of a poorly conducted meta-analysis without consideration of the potential causes of heterogeneity and without taking into account characteristics of angiographic patency that justify its use as a surrogate outcome.

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Reply to the Editor:

We would like to underline some fundamental issues concerning meta-analyses that Athanasiou and colleagues seem to have forgotten in their letter.

First, in cardiac surgery, as in other clinical fields, conclusive evidence should be addressed by the analysis of randomized, controlled trials (RCTs) when available. Observational studies frequently reach distorted conclusions because they are influenced by confounding. For example, no RCT has ever confirmed the benefits of beating-heart coronary surgery implied by observational studies.¹

In addition, graft failure is an outcome strongly influenced by the quality of target vessels.² It is reasonable to suppose that in clinical practice, radial artery conduits have been used for good quality target vessels, whereas saphenous vein grafts have been used on poorer quality vessels to complete revascularization. This concern in observational cohorts may not confidently be controlled for by any risk adjusted-analysis but is completely eliminated by randomization. Therefore for this topic, RCTs, even with their limitations, are largely better than any observational cohort study. Even a keyhole is preferable to a black hole. There is thus no reason to conduct a meta-analysis on observational distorted results when several RCTs are fortunately available. Despite these considerations, Athanasiou and colleagues love to read and publish meta-analyses of nonrandomized comparative studies, even when a large body of RCTs is available. They therefore reach conclusions³ completely discordant with RCTs,⁴ and it is hard to justify the exceptions made for selection bias related to nonrandomized design.

Second, the Editor of this *Journal* is interested in brief contributions. As stated in the Information for Authors, brief communications provide an option to have an article published in a more rapid fashion. Therefore our work is not an example of fast-track publication but rather is in line with the policy of this *Journal*. As Athanasiou and colleagues can see, several meta-analyses of RCTs on different topics in cardiac surgery are published

in the Brief Research Reports section of this *Journal*. Because such brief communications should contain no more than 750 words, we could not report all aspects of our literature research, statistical analysis, results, considerations, and conclusions. Reviewers and editors, however, found our work to be worthy of publication. Are Athanasiou and colleagues perhaps complaining about the ability of the Editor or reviewers of this *Journal*? Is one of them suggesting himself as the new Editor of this *Journal*?

Athanasiou and colleagues will be astonished to read that our conclusions are supported and confirmed in a Letter to the Editor from Takagi and associates,⁵ which is an update to our work. Is even Takagi's work an example of fast-track publication of a poorly conducted meta-analysis? Are Athanasiou and colleagues the only researchers who can publish reliable meta-analyses?

Looking to an another "evidence horizon," meta-analysis and systematic review of non-RCTs by Athanasiou and colleagues have encouraged the use of minimally invasive great saphenous vein harvesting in coronary artery bypass grafting.⁶ These conclusions have been strongly disputed by a recent very large study published in the *New England Journal of Medicine*.

Sometime, even a great researcher looks into a black hole.⁷

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TOTAL OCCLUSION AND STRING SIGN OF RADIAL ARTERY VERSUS SAPHENOUS VEIN GRAFT CONDUITS: AN UPDATED META-ANALYSIS To the Editor:

We read with great interest the article by Benedetto and associates.¹ In their meta-analysis of 5 randomized, controlled trials, they demonstrated no significant advantage of radial artery (RA) relative to saphenous vein graft (SVG) conduits in coronary artery bypass grafting for "graft failure" including "total occlusion" and "string sign" (random-effects risk difference [RD], -0.40; 95% confidence interval [CI], -0.128 to 0.048; $P = .372$). More recently, however, Hayward and collaborators² updated the results of the Radial Artery Patency and Clinical Outcomes (RAPCO) trial that were originally reported by Buxton and colleagues³ in 2003. We performed an updated meta-analysis of randomized, controlled trials of RA versus SVG conduits in coronary artery bypass grafting for "total occlusion," "string sign," and "graft failure" ("total occlusion" plus "string sign").

Although Buxton and colleagues³ estimated graft patency in only 24 RA and 22 SVG conduits in the RAPCO trial, Hayward and collaborators² performed protocol angiography in 53 patients assigned to receive RA conduits and 60 patients assigned to receive SVG conduits at mean follow-up of 5.5 years. In total, our meta-analysis included data on 1176 grafts (592 RA and 584 SVG). Pooled analysis of the 5 trials, including updated results² of the RAPCO trial, demonstrated a statistically significant reduction in "total occlusion" (random-effects RD, -0.07; 95% CI, -0.12 to -0.03; $P = .0009$; **Figure 1, A**) but a statistically significant increase in "string sign" (random-effects RD, 0.04; 95% CI, 0.02 to 0.07; $P = .0002$; **Figure 1, B**) with RA relative to SVG, resulting in a statistically nonsignificant reduction in "graft failure" ("total occlusion" plus "string sign," random-effects RD, -0.05; 95% CI, -0.13 to 0.02; $P = .16$; **Figure 1, C**). Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual trials one at a time and recalculating the pooled RD estimates for the remaining studies. Exclusion of any single trial from the analysis of "total occlusion" did not substantively alter the overall result of our analysis. Although elimination of any single trial except for the Radial Artery Patency Study (RAPS)⁴ from the analysis of "string sign" did not substantially change the pooled estimate, exclusion of the RAPS, which included the largest number of grafts, demonstrated a statistically nonsignificant increase in "string sign" (random-effects RD, 0.02; 95% CI, -0.02 to 0.05; $P = .30$) with RA relative to SVG. Although elimination of any single trial except for the RAPS⁴ from the analysis of "graft failure" ("total occlusion" plus "string sign") did not substantially change the pooled estimate, exclusion of the RAPS demonstrated a statistically significant reduction in "graft failure" (random-effects RD, -0.09; 95% CI, -0.17 to 0.00; $P = .04$) with the RA relative to SVG.