seen in a subgroup of patients with aggressive coronary atherosclerosis. Conversely, the pathophysiologic response⁵ to the presence of an intravascular foreign body (stent) may also adversely affect the fate of the conduits used to graft stented coronary arteries. Stenting can cause prolonged endothelial dysfunction, as well as an acute and chronic inflammatory reaction, even during the late period, with involvement of the distal coronary artery and surrounding myocardium.⁵ This may adversely affect anastomosis sites in patients who subsequently undergo coronary artery bypass grafting.

A vexed question is whether the poor fate of venous conduits used to bypass coronary arteries with in-stent restenosis is due to aggressive atherosclerosis or to an inflammatory reaction involving downstream coronary artery beds. Although we do not know the distribution of occluded conduits with respect to stent locations, we cannot definitively point out the influences on graft patency. We therefore do not support inclusion of these data in meta-analyses.

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Reply to the Editor:

We thank Nezic and colleagues for their interest in our recent article.¹ We regret to point out, however, that Nezic and colleagues misrepresent data reported by Gaudino and associates.² In fact, 2 different analyses were reported in that study. First, Gaudino and associates² reported an angiographic comparison of radial artery (RA) and saphenous vein graft (SVG) conduits randomly assigned to target obtuse marginal coronary arteries (OMs) with previous stenting (study group) versus OMs without previous (control group). The results of this comparison were shown in Gaudino and associates’ Table 3,² which compared 20 RA conduits versus 20 SVG conduits from the study group and 20 RA conduits versus 20 SVG conduits from the control group. In addition, they reported angiographic results of other conduits not randomly assigned to complete revascularization in both the study and control groups (see Gaudino and associates’ Table 2²).

For the purpose of our meta-analysis of randomized, controlled trials, we included only conduits randomly assigned to target OMs. Therefore, in our study the Gaudino I study included RA versus SVG conduits randomly grafted to previously stented OMs, and the Gaudino II study included RA versus SVG conduits grafted to unstented OMs. The risk that intrastent restenosis would influence the results was exactly the same for all RA and SVG conduits used in the first cohort of patients (Gaudino I). Nezic and colleagues picked up data referring to conduits not randomly assigned to complete revascularization (see Gaudino and associates’ Table 2), thus completely misrepresenting the inclusion criteria adopted in our meta-analysis of randomized, controlled trials.

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META-ANALYSIS COVERS THE HORIZON WHEN THE LITERATURE SEARCH IS UNDERTAKEN THROUGH A KEYHOLE

To the Editor:

The meta-analytical review by Benedetto and colleagues¹ comparing failure rates of radial artery (RA) and saphenous vein (SV) conduits in coronary artery bypass grafting has several methodologic flaws that significantly limit its validity. Consequently, we strongly believe that both the data presented and the conclusion that “no definitive evidence supports the superiority of the RA over the SV in terms of graft failure rate”¹ cannot be accepted without challenge.

Benedetto and colleagues’ restrictive inclusion criteria¹ may have excluded data from several high-quality studies that considered different target lesions or used definitions of graft failure other than total graft occlusion or severe diffuse graft narrowing (string sign).¹ Angiographic stenosis of more than 50%, 70%, or 75%, for example, may cause symptomatic ischemia and may require repeated angiography. Finally, Benedetto and colleagues¹ appear to have excluded important studies in which assessment of angiographic patency was performed at a fixed interval as a secondary end point. These restrictive inclusion criteria compromise the

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. Metaregression 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