



RADIAL meta-analysis: following the rules usually pays off

Matthew Wingo, Mario F. L. Gaudino

Department of Cardiothoracic Surgery, Weill Cornell Medicine, New York, NY, USA

Correspondence to: Mario F. L. Gaudino, MD, FEBCTS. Department of Cardiothoracic Surgery, Weill Cornell Medicine, 525 East 68th Street, New York, NY 10065, USA. Email: mfg9004@med.cornell.edu.

Response to: Kopjar T, Dashwood MR, Dreifaldt M, *et al.* No-touch saphenous vein as an important conduit of choice in coronary bypass surgery. *J Thorac Dis* 2018;10:S3292-6.

Submitted Oct 04, 2018. Accepted for publication Oct 18, 2018.

doi: 10.21037/jtd.2018.10.75

View this article at: <http://dx.doi.org/10.21037/jtd.2018.10.75>

We thank Dr. de Souza and colleagues for their careful and thorough evaluation of our recent patient-level meta-analysis (1). They have provided an excellent summary of our methods and findings which we will not spend time repeating here. Instead, we will give an adequate reply to their critique. The issues raised in their paper are important and deserve careful consideration. Our response will address the foremost of their concerns which is the exclusion of the Örebro study by Dreifaldt *et al.* from our analysis.

The Örebro trial was a randomized non-inferiority trial which used within patient randomization to compare radial artery (RA) and “no-touch” saphenous vein (ntSVG) grafts (2). Clinical endpoints were not recorded. It recruited 108 patients to receive one ntSVG and one RA graft to either the lateral (circumflex) territory or the inferior (right coronary) territory to complement the left internal thoracic artery graft to the left anterior descending artery. The endpoint was angiographic patency at a mean of 36 months. Completeness of follow-up was very good at 92%.

Having identified this article as part of our literature search at the beginning of the RADIAL project, we were reluctant to exclude the randomized data it provided. However, since there were no clinical endpoints recorded, this study was excluded from the primary analysis as lacking the outcome of interest. Several considerations prevented us from including it in our secondary outcome analysis of angiographic patency as well. In fact, while we included studies that used within patient randomization or ntSVG, we were hesitant to include those studies that used both (3). The reason for this is that for patient level meta-analysis, homogeneity of methodology and intervention are key to the validity of the analysis. The more variations are added,

the fewer valid conclusions can be made.

Another reason that we excluded this study was the fact that this was the only trial that did not use systematic anti-spasm therapy in patients with RA grafts. While there are significant differences in practice for the prevention of RA spasm (4), there is wide consensus that some strategy must be used. This was also noted in Dr. Tatoulis commentary on the Örebro study at the original time of publication (5). The lack of use of anti-spastic drugs in the postoperative period is unique of the Örebro study, contradict current recommendations (6), and does not reflect current practice (and clearly disadvantages RA, not ntSV, grafts).

Finally, the third and most important flaw of the Örebro trial is the incorrect use of the RA. As Dr. de Souza’s present commentary notes, the current guidelines suggest that the RA should only be used to bypass vessels with significant stenosis (7). Specifically, the 2011 ACCF/AHA guidelines recommend (class IIb) that the RA should only be used for a stenosis of >70% on the lateral territory and >90% on the inferior territory and the 2018 ESC/EACTS guidelines recommend a high-grade stenosis (7,8). This was not the case in the Örebro study where apparently no stenosis cut-off was used and the RA was anastomosed to target with stenosis <70% in 31% of the cases and <90% in 69% of the cases.

The text of the Örebro trial notes that 6 out of the 7 failed single RA grafts were used for targets in the inferior circulation. As mentioned, according to guidelines, the stenosis of the inferior territory vessel should exceed 90% in order to correctly use the RA. Table 2 of the Örebro trial shows that 46 out of 46 RA grafts where target stenosis exceeded 90% were patent, so the six failed RA grafts must have been misused for a less than 90% stenosis on

the inferior circulation. If the odds ratio is corrected to exclude only those six misused and failed RA grafts, then the difference in patency for the ntSVG and the RA grafts does not reach significance [odds ratio (OR) =2.3, 95% confidence interval (CI): 0.82–6.4, P=0.11]. This actually underestimates the misuse of the RA grafts in the Örebro trial, because as previously noted greater than 30% of RAs were anastomosed to targets with less than 70% stenosis. As one can see the patency rate of ntSVG at 36 months is not better than that of the correctly used RA.

In summary, if the Örebro trial had used the RA as current evidence suggests, it would have been included in our meta-analysis and its results would be much different. We, the RADIAL authors stand by our decision to exclude the trial from our study because of the methodological reasons listed above and the incorrect use of the RA.

The ntSVG is an intriguing technique with a plausible mechanism. Avoiding trauma and distention to the SVG may limit endothelial injury and prolong patency. However, at present no proof of its efficacy in improving patients' outcome has been provided. The same cannot be said for the RA which is now a class I indication (7). Dr. de Souza should probably focus his efforts on providing new more convincing data on the ntSVG, rather than questioning the published literature.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Cite this article as: Wingo M, Gaudino MF. RADIAL meta-analysis: following the rules usually pays off. *J Thorac Dis* 2018;10(11):E785-E786. doi: 10.21037/jtd.2018.10.75

References

1. Gaudino M, Benedetto U, Fremes S, et al. Radial-Artery or Saphenous-Vein Grafts in Coronary-Artery Bypass Surgery. *N Engl J Med* 2018;378:2069-77.
2. Dreifaldt M, Mannion JD, Bodin L, et al. The no-touch saphenous vein as the preferred second conduit for coronary artery bypass grafting. *Ann Thorac Surg* 2013;96:105-11.
3. Desai ND, Cohen EA, Naylor CD, et al. A randomized comparison of radial-artery and saphenous-vein coronary bypass grafts. *N Engl J Med* 2004;351:2302-9.
4. Cable DG, Caccitolo JA, Pearson PJ, et al. New approaches to prevention and treatment of radial artery graft vasospasm. *Circulation* 1998;98:II15-21; discussion II21-2.
5. Tatoulis J. Invited commentary. *Ann Thorac Surg* 2013;96:111.
6. Aldea GS, Bakaeen FG, Pal J, et al. The Society of Thoracic Surgeons Clinical Practice Guidelines on Arterial Conduits for Coronary Artery Bypass Grafting. *Ann Thorac Surg* 2016;101:801-9.
7. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2018. [Epub ahead of print].
8. Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2011;58:e123-210.