## Title page.

Comments on "Comparison of alternate preparative techniques on wall thickness in coronary artery bypass grafts: The HArVeST randomized controlled trial".

## HArVeSTing vein grafts under different preparative techniques: raising more questions than answers.

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In the recently published HArVeST randomised control trial Angelini and colleagues describe a study on 4 groups of patients receiving saphenous vein (SV) grafts harvested with pedicle of surrounding fat removed (conventional, CT) or with pedicle intact ('no-touch', NT). <sup>1</sup> It is implied that NT grafts were prepared using the technique described by Souza et al.<sup>2</sup> Grafts were also flushed by syringe with heparinised blood (conventional high pressure test) or with blood at systemic pressure (low pressure test). Wall thickness and lumen diameter were assessed using intravascular ultrasound (IVUS) at 12 months. Wall thickness was also measured on histological sections from grafts retrieved prior to completion of proximal anastomoses.

A number of issues arise regarding various aspects of this study, in particular relating to the treatment of SVs at harvesting and the methods used to assess graft morphology. Rather than merely citing Souza's NT technique, a more detailed description of the harvesting procedure is needed as are representative examples of graft explants as previously presented by Souza et al.<sup>3</sup> In the HArVeST methods, distension was examined on veins that were "...touched as little as possible..." with the authors referring to their earlier biochemical study where no histology or morphometric analysis was performed. Important methodological information is lacking. Were high and low pressures measured and, if so, what were they? For histology, were SV segments perfusion or immersion fixed and were frozen or paraffin sections used? Was 'wall' or 'media' thickness measured and how was morphometry achieved? Representative histology examples should be included to illustrate altered graft architecture when comparing the different harvesting techniques and the effects of high- vs lowpressure distension. In distended CT perivascular fat is absent, the adventitia and vasa vasorum damaged and the media thinner than NT SVs as shown previously (figure 1). <sup>4,5</sup> Such details are essential when assessing the degree of vascular damage to CT and NT SVs. The IVUS data presented in the HArVeST trial was performed over ~12 months with no images shown. Conventional lowpressure 'tended' to yield a thinner vessel wall compared with high-pressure testing, but the difference was not significant. Also, lumen diameter in NT and CT remained 'similar'. These results are in contrast to the previous IVUS study of Johansson et al<sup>6</sup> that presents images taken at up to 8.5 years after CABG. Here there was a significantly lower number of multiple plaques in NT versus CT grafts. In addition, there were fewer advanced plaques with lipid and less plaque thickness in NT vs CT grafts with NT grafts maintaining a wider lumen (figure 2).

While the HArVeST trial was performed over 12 months authentic NT SVs provide superior grafts at up to 16 years follow up. For any study, such as the HArVeST trial, more information is required when describing both the surgery as well as the laboratory techniques used. The lack of such information will inevitably impact on the ability of others to repeat published data and to reliably compare harvesting techniques.

## References

- Angelini GD, Johnson T, Culliford L, Murphy G, Ashton K, Harris T, Edwards J, Clayton G, Kim Y, Newby AC, Reeves BC, Rogers CA. Comparison of alternate preparative techniques on wall thickness in coronary artery bypass grafts: The HArVeST randomized controlled trial. J Card Surg. 2021 Mar 12. doi: 10.1111/jocs.15477.
- 2. Souza DSR, Johansson B, Bojö L, et al. Harvesting the saphenous vein with surrounding tissue for CABG provides long-term graft patency comparable to the left internal thoracic artery: results of a randomized longitudinal trial. J Thorac Cardiov Surg. 2006;132(2):373-75.
- Souza DS, Arbeus M, Botelho Pinheiro B, Filbey D. The no-touch technique of harvesting the saphenous vein for coronary artery bypass grafting surgery. Multimed Man Cardiothorac Surg. 2009 Jan 1;2009(731):mmcts.2008.003624. doi: 10.1510/mmcts.2008.003624.
- 4. Dashwood MR, Savage K, Tsui JC, Dooley A, Shaw SG, Fernández Alfonso MS, Bodin L, Souza DS. Retaining perivascular tissue of human saphenous vein grafts protects against surgical and distension-induced damage and preserves endothelial nitric oxide synthase and nitric oxide synthase activity. J Thorac Cardiovasc Surg. 2009;138(2):334-40.
- Dashwood MR, Tsui JC. 'No-touch' saphenous vein harvesting improves graft performance in patients undergoing coronary artery bypass surgery: a journey from bedside to bench. Vascul Pharmacol. 2013;58(3):240-50.
- 6. Johansson BL, Souza DS, Bodin L, Filbey D, Loesch A, Geijer H, Bojö L. Slower progression of atherosclerosis in vein grafts harvested with 'no touch' technique compared with conventional harvesting technique in coronary artery bypass grafting: an angiographic and intravascular ultrasound study. Eur J Cardiothorac Surg. 2010;38(4):414-9.

## Figures and legends.

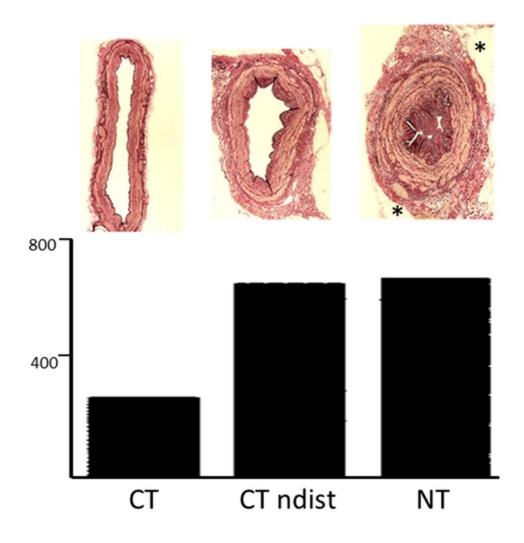


Figure 1. Media thickness of saphenous vein grafts.

Top. Representative elastic van Gieson stained transverse paraffin sections of saphenous veins. \* indicates the intact cushion of surrounding perivascular fat in the NT vein. Bottom. Histograms showing mean media thickness (in  $\mu$ m), measured between the internal and external elastic lamina, of conventional/distended at 300 mm Hg (CT) when compared with conventional non-distended (CT ndist) and no-touch/non-distended (NT) saphenous veins assessed by morphometric analysis (Modified from reference 4).

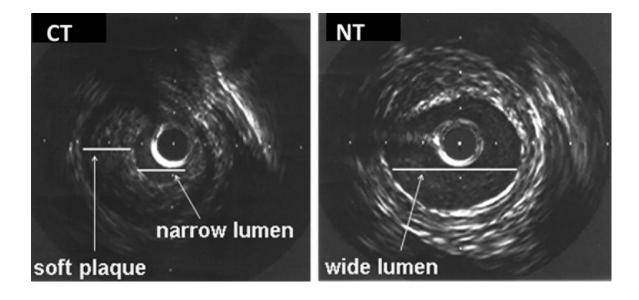


Figure 2. IVUS images of CT and NT SV grafts.

An intravascular ultrasound assessment of grafts showed that in the CT veins large soft plaques commonly appeared that reduced the lumen diameter considerably while NT veins maintain a wide lumen. (Modified from reference 8).