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EDITORIAL COMMENT

The Pursuit of a Perfect Conduit*

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The last decades proved coronary artery bypass graft (CABG) to be the most durable and complete treatment of coronary artery disease. Kolessov et al[1] showed, in the early sixties, no better graft than the internal thoracic artery (ITA) was found. Indeed, it has particular characteristics that make it so unique: rarely affected by atherosclerosis, it delivers a high quantity of nitric oxide to the coronary downstream, thus functioning similarly to a flap more than a graft. The well-known limitations are that there are only 2 ITAs in the body, the circulation depends on the subclavian artery, which sometimes is severely affected by atherosclerosis, and patients with comorbidities such as diabetes, obesity, and chronic obstructive pulmonary disease could not benefit from double ITAs harvesting due to challenges in sternal wound healing. On the other hand, the Y grafts make the treated coronary territory dependent on 1 single source. Although saphenous veins are considered the "gold resource" for the patient, sometimes, it is not all gold that glimmers. Veins can be affected by varicose dilations, have valves, and act in the condition of low hemodynamic stress. Another significant limitation is diameter mismatch, considering the critical complexity in harvesting and morbidity after harvesting both saphenous (and radial grafts). Additional challenges are the situations when a graft must be placed in emergency. Dealing with all these limitations of autologous conduits makes CABG more of an art than a science. Needless to say, the need for a solution obsesses the great minds in this field. The ideal graft should correspond to the following criteria: unlimited availability, not requiring surgery during preparation, customized dimension in different diameters and lengths to avoid mismatch, sufficient radial force to act in conditions of high hemodynamic stress, and sufficiently porous to serve as a matrix to be populated by circulating progenitors of endothelial cells. To date, a wide range of materials have been explored as tissue-engineered vascular grafts (TEVGs). TEVGs are composed of diverse materials: synthetic, natural, or mixture. At least 5 types of grafts were further evaluated in patients that underwent CABG[2]: glutaraldehyde-fixed human umbilical vein grafts, cryopreserved saphenous allograft vein, dialdehyde starch-treated bovine internal thoracic artery grafts, no-react bovine internal mammary artery, autologous endothelial cell-seeded expanded polytetrafluoroethylene (e-PTFE) grafts, de-endothelized and cryopreserved allograft veins seeded by autologous endothelial cells. The first 4 types of grafts showed very poor patency and therefore were not recommended as alternative choices for CABG in patients.

In this issue of *JACC: Basic to Translational Science*, Ono et al[3] propose a restorative vascular graft (RVG) as an alternative solution. To create the necessary porous architecture for endothelialization, they employed electrospinning of the PTFE tube as the manufacturing method. The polymer fiber morphology, interfiber bonding, and pore interconnectivity were controlled to promote microvessel growth through the wall to supply endothelial cells to populate the length of the graft with a confluent endothelium. The host environment of the preclinical model (sheep) was used as an in vivo bioreactor to promote cells to populate and grow in a porous scaffold of a synthetic tube. Using the coronary site of implantation in this preclinical model was challenging and ambitious; most of the studies using ovine preclinical models (13 in total) used a carotid site of implantation, a considerably larger diameter of the target vessel.[4]

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The aggregated patency rate at 6 months was 90.9% (10/11) for the RVGs, and 72.7% (8/11) of the implanted RVGs were patent when considering all surviving RVG animals in aggregate after 1 year of implantation. A very promising and critically important finding is that RVGs maintained an overall uniform and nondilating lumen throughout the study when analyzed by quantitative angiography. There are few data available, if any, to compare with the results of this preclinical study. Some data from human studies showed promising results. Autologous e-PTFE grafts revealed a 90.5% patency after 7.5- to 48-month follow-up,[5] whereas de-endothelized and cryopreserved allograft veins seeded by autologous endothelial cells with reported patency of 50% after 9-month follow-up showed zero patency after 32 months.[6] When comparing the 2 types of grafts, the synthetic e-PTFE seems much better than the cryopreserved allograft, indicating that elimination of immunogenicity in the allografts cannot be fully achieved by cryopreservation and therefore needs to be further improved by using other methodologies such as decellularization. No human studies are testing small-diameter TEVGs for CABG after 2008. The 2 points of concern in the present study are the 2 unscheduled deaths for the RVG animals, with the autopsies revealing a recanalized thrombus in the distal graft in 1 animal and a mid-graft occlusion in another one. One open question is whether the delamination of the neointima tissue by the optical coherence tomography catheter, which usually does not happen in native vessels, is a sign of immature neoendothelium. More data regarding the electron microscopy analysis of the tissue of the grafts from the sacrificed animals should be provided to answer this question. The second point that needs to be considered when translating to clinical application is the severe blood loss during the graft sealing step in an animal with a low platelet count. However, considering the arduous experimental setup of the ovine CABG model, the study presented encouraging safety results that will help to enable its clinical translation.

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REFERENCES

1. Kolessov VI. Mammary artery-coronary artery anastomosis as method of treatment for angina pectoris. *J Thorac Cardiovasc Surg*. 1967 Oct;54(4):535–544.

2. Desai M, Seifalian AM, Hamilton G. Role of prosthetic conduits in coronary artery bypass grafting. *Eur J Cardiothorac Surg*. 2011;40(2):394–398.

3. Ono M, Kageyama S, O'Leary N, et al. 1-Year patency of biorestorative polymeric coronary artery bypass grafts in an ovine model. *J Am Coll Cardiol Basic Trans Science*. 2023;8:19–34.

4. Fang S, Ellman DG, Andersen DC. Review: tissue engineering of small-diameter vascular grafts and their in vivo evaluation in large animals and humans. *Cells*. 2021;10(3):713. https://doi.org/10.3390/cells10030713

5. Laube HR, Dude J, Rutsch W, Konertz W. Clinical experience with autologous endothelial cell-seeded polytetrafluoroethylene coronary artery bypass grafts. *J Thorac Cardiovasc Surg*. 2000;120(1):134–141.

6. Herrmann FEM, Lamm P, Wellmann P, Milz S, Hagl C, Juchem G. Autologous endothelialized vein allografts in coronary artery bypass surgery - long term results. *Biomaterials*. 2019;212:87–97.

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