ΜΙΑ ΕΝΑΝΤΙ ΔΥΟ ΕΣΩ ΜΑΣΤΙΚΩΝ ΑΡΤΗΡΙΩΝ ΣΤΗΝ ΧΕΙΡΟΥΡΓΙΚΗ ΜΥΟΚΑΡΔΙΑΚΗ ΕΠΑΝΑΙΜΑΤΩΣΗ

Είναι η χρήση των δύο έσω μαστικών ανώτερη άλλων μορφών αρτηριακής επαναιμάτωσης;
ι άλλαξε μετά την δημοσίευση των 5ετών αποτελεσμάτων της ART (Arterial Revascularization Tria

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y is the mammary artery so special and what protects it from erosclerosis?

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The internal mammary artery (IMA) grafts have been associated with long-term patency and improved survival as compared to saphenous vein grafts (SVGs). Early failure of IMA is attributed to poor surgical technique and less with thrombosis. Similarly, bypass surgery especially with the use of IMA has also been shown to be superior at 1-year as well as over five years compared to percutaneous procedures, including the use of drug-eluting stents for the treatment of coronary artery disease. The superiority of IMAs over SVGs

can be attributed to its striking resistance to the development of atherosclerosis. Structurally its endothelial layer shows fewer fenestrations, lower intercellular junction permeability, greater anti-thrombotic molecules such as heparin sulfate and tissue plasminogen activator, and higher endothelial nitric oxide production, which are some of the unique ways that make the IMA impervious to the transfer of lipoproteins, which are responsible for the development of atherosclerosis. A better comprehension of the molecular resistance to

responsible for the development of atherosclerosis. A better comprehension of the molecular resistance to the generation of adhesion molecules that are involved in the transfer of inflammatory cells into the arterial wall that also induce smooth muscle cell proliferation is needed. This basic understanding is crucial to championing the use of IMA as the first line of defense for the treatment of coronary artery disease.

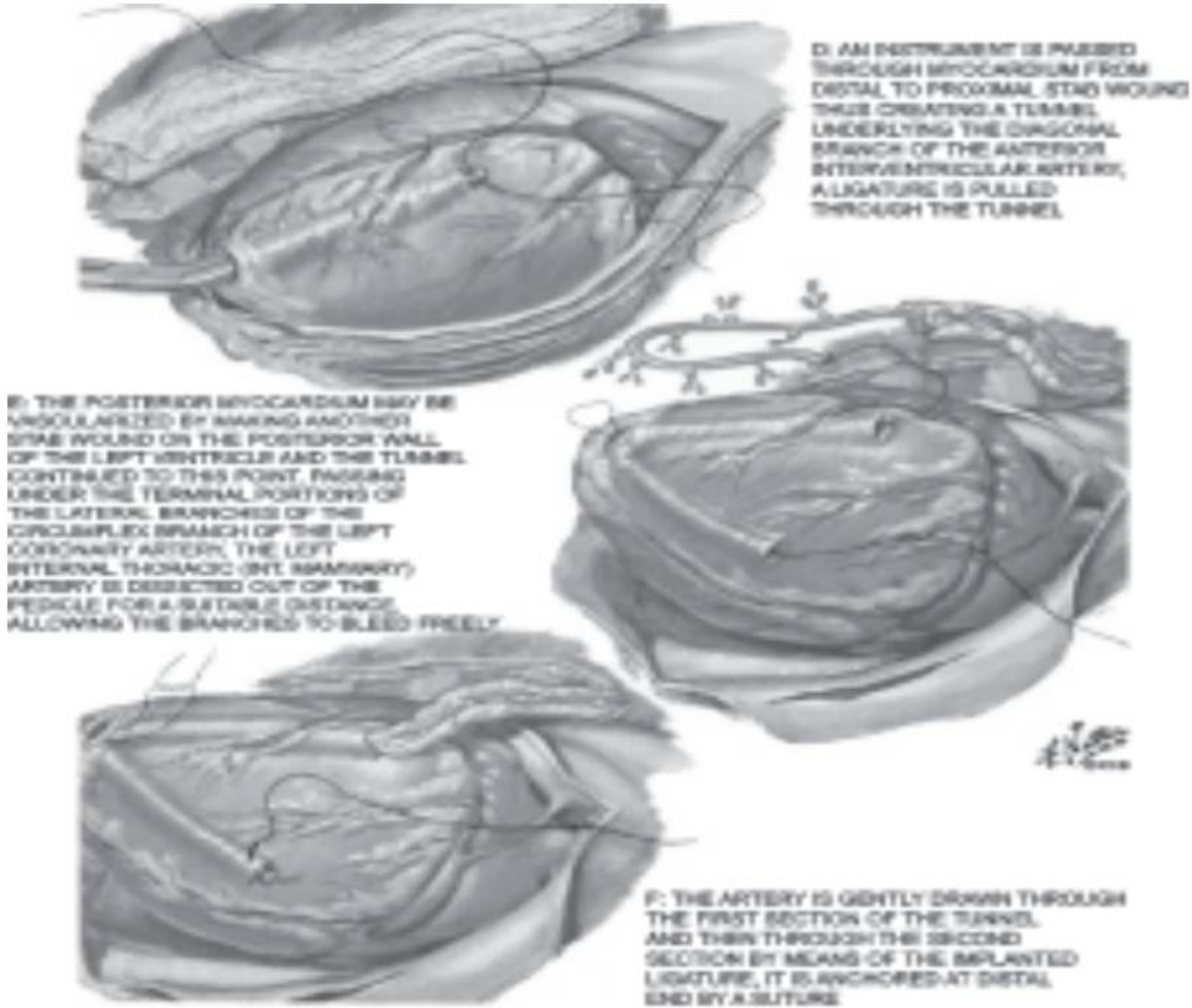

Figure 1: *Veinberg operation done for cardiac ischaemia*

Endothelium-Derived Hyperpolarizing Factor in Human Internal Mammary Artery Is 11,12-Epoxyeicosatrienoic Acid and Causes Relaxation by Activating Smooth Muscle BK_{Ca} Channels

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Background—Left internal mammary arteries (LIMAs) synthesize endothelium-derived hyperpolarizing factor (EDHF), a short-lived K^+ channel activator that persists after inhibition of nitric oxide (NO) and prostaglandin synthesis. EDHF hyperpolarizes and relaxes smooth muscle cells (SMCs). The identity of EDHF in humans is unknown. We hypothesized that EDHF (1) is 11,12-epoxyeicosatrienoic acid (11,12-EET); (2) is generated by cytochrome P450-2C, CYP450-2C; and (3) causes relaxation by opening SMC large-conductance Ca^{2+}-activated K^+ channels (BK_{Ca}).

Methods and Results—The identity of EDHF and its mechanism of action were assessed in 120 distal human LIMAs and 20 saphenous veins (SVs) obtained during CABG. The predominant EET synthesized by LIMAs is 11,12-EET. Relaxations to exogenous 11,12-EET and endogenous EDHF are of similar magnitudes. Inhibition of EET synthesis by chemically distinct CYP450 inhibitors (17-octadecynoic acid, *N*-methylsulfonyl-6-(2-propargyloxyphenyl)hexanamide), or a selective EET antagonist (4,15-epoxyeicosa-5(*Z*)-enoic acid) impairs EDHF relaxation. 11,12-EET activates a BK_{Ca} current and hyperpolarizes LIMA SMCs. Inhibitors of BK_{Ca} but not inward-rectifier or small-conductance K_{Ca} channels abolish relaxation to endogenous EDHF and exogenous 11,12-EET. BK_{Ca} and CYP450-2C mRNA and proteins are more abundant in LIMAs than in SVs, perhaps explaining the lack of EDHF activity of the SV. Laser capture microdissection and quantitative RT-PCR demonstrate that BK_{Ca} channels are primarily in vascular SMCs, whereas the CYP450-2C enzyme is present in both the endothelium and SMCs.

Conclusions—In human LIMAs, EDHF is 11,12-EET produced by an EDHF synthase CYP450-2C and accounting for ≈40% of net endothelial relaxation. 11,12-EET causes relaxation by activating SMC BK_{Ca} channels. (***Circulation.*** **2003;107:769-776.)**

Key Words: lasers ■ ion channels ■ bypass ■ cytochromes

Human left internal mammary arteries (LIMAs) are relatively resistant to atherosclerosis and make superb bypass conduits with better long-term patency rates than saphenous vein (SV) grafts.[1] The advantage of the LIMA may be the result of its superior endothelial function. LIMAs produce more of the antithrombotic vasodilators prostacyclin and nitric oxide (NO) and more endothelium-derived hyperpolarizing factor (EDHF) than SVs.[2] Although bioassays suggest that EDHF is present in LIMAs, its identity and mechanism of relaxation remain unknown. EDHF is a short-lived, endogenous, endothelium-derived vasodilator that acts independently of the NO-cGMP pathway and persists after effective inhibition of NO synthase (NOS) and prostaglandin H synthase (PGHS).[3] EDHF activity is elicited by acetylcholine (ACh) and bradykinin (BK). EDHF activates K^+ channels and causes hyperpolarization of arterial smooth muscle cells (SMCs), thereby inhibiting voltage-gated Ca^{2+} channels, lowering cytosolic Ca^{2+}, and promoting relaxation (Figure 1; Reference 3).

In animals, EDHF has been variously identified as an epoxyeicosatrienoic acid (EET) synthesized by one or more isoforms of cytochrome P450 (CYP450),[4,5] an endogenous cannabinoid (anandamide),[6] or even the K^+ ion itself.[7] The subcellular mechanism for the effects of EDHF is also controversial. Proposed effector pathways include activation of SMC K^+ channels (either Ca^{2+}-sensitive K^+ channels, K_{Ca}

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GINAL ARTICLE

aphenous Vein Graft Failure after Coronary Artery ypass Surgery: Insights from PREVENT IV

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hods and Results—We examined 1828 participants in the PREVENT IV trial undergoing protoc dated follow-up angiography 12-18 months post-CABG or earlier clinically-driven angiography. comes included patient- and graft-level angiographic VGF (≥75% stenosis or occlusion). Variable selected using Fast False Selection Rate methodology. We examined relationships between ables and VGF in patient- and graft-level models using logistic regression without and with eralized estimating equations. At 12-18 months post-CABG, 782 of 1828 (42.8%) patients had V 1096 of 4343 (25.2%) vein grafts had failed. Demographic and clinical characteristics were simi ween patients with and without VGF, though VGF patients had longer surgical times, worse targe y quality, longer graft length, and more frequently underwent endoscopic vein harvesting. After ivariable adjustment, longer surgical duration (odds ratio [OR] per 10-minute increase 1.05, 95% idence interval [CI] 1.03-1.07), endoscopic vein harvesting (OR 1.41, 95% CI 1.16-1.71), poor et artery quality (OR 1.43, 95% CI 1.11-1.84), and postoperative use of clopidogrel or ticlopidine 1.35, 95% CI 1.07-1.69) were associated with patient-level VGF. The predicted likelihood of VG graft-level model ranged from 12.1-63.6%.

Vein graft failure: from pathophysiology to clinical outcomes

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