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Intra-operative and post-operative management of conduits for coronary artery bypass grafting: a clinical consensus statement of the European Society of Cardiology Working Group on Cardiovascular Surgery and the European Association for Cardio-Thoracic Surgery Coronary Task Force

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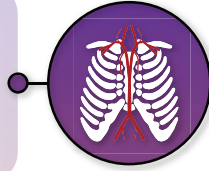
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Management of conduits for coronary artery bypass grafting

Conduit harvesting

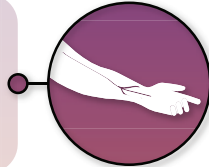
- Limited evidence on effect of skeletonized versus pedicled ITA harvesting on graft patency and cardiac outcomes
- Ultrasonic coagulation may be preferred for skeletonized ITA harvesting to avoid thermal injury



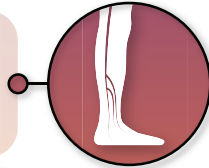
Conduit storage

- Abundant in vitro and observational clinical data show buffered solutions are superior to 0.9% saline and blood-based solutions for intraoperative storage of SVG
- No clinical data currently support use of endothelial damage inhibitors

- Observational data support pedicled RA harvesting to avoid endothelial injury
- Clinical benefit of RA grafting is based on studies using ORAH, limited data exist in support of ERAH

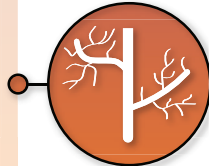


- Observational data suggest OVH is associated with better long-term SVG patency, but randomized evidence shows similar mid-term MACE outcomes between OVH and EVH



Antispasm therapy

- Observational data support use of oral vasodilator therapy for ≤ 1 year after RA-CABG
- Sex differences exist in the vascular reactivity of arterial grafts, and further evidence on sex-specific approaches to antispasm therapy is needed



Secondary preventive therapy

- Randomized evidence supports use of low to medium-dose aspirin (100–325 mg once daily) to prevent SVG occlusion
- Randomized and observational evidence supports addition of clopidogrel or ticagrelor to aspirin for 1 year to prevent SVG failure
- Ticagrelor may be preferred due to its potent and less variable antiplatelet effects, but should be avoided in patients at high bleeding risk
- No evidence exists for a benefit of P2Y12 inhibitor monotherapy or anticoagulants on SVG patency
- Use of statins is associated with attenuation of atherosclerotic plaque progression in SVG
- More evidence is needed to elucidate the role of PCSK9 inhibition in maintaining SVG patency



Intra-operative and post-operative management of conduits for coronary artery bypass grafting. CABG, coronary artery bypass grafting; ERAH, endoscopic radial artery harvesting; EVH, endoscopic vein harvesting; ITA, internal thoracic artery; MACE, major adverse cardiac events; ORAH, open radial artery harvesting; OVH, open vein harvesting; PCSK9, proprotein convertase subtilisin/kexin type 9; RA, radial artery; SVG, saphenous vein graft.

Abstract

The structural and functional integrity of conduits used for coronary artery bypass grafting is critical for graft patency. Disruption of endothelial integrity and endothelial dysfunction are incurred during conduit harvesting subsequent to mechanical or thermal injury and during conduit storage prior to grafting, leading to acute thrombosis and early graft failure. Late graft failure, in particular that of vein grafts, is precipitated by progressive atherogenesis. Intra-operative management includes appropriate selection of conduit-specific harvesting techniques and storage solutions. Arterial grafts are prone to vasospasm subsequent to surgical manipulation, and application of intra-operative vasodilatory protocols is critical. Post-operative management includes continuation of oral vasodilator therapy and selection of antithrombotic and lipid-lowering agents to attenuate atherosclerotic disease progression in conduits. In this review, the scientific evidence underlying the key aspects of intra- and post-operative management of conduits for coronary artery bypass grafting is examined. Clinical consensus statements for best clinical practice are provided, and areas requiring further research are highlighted.

Keywords: Coronary artery bypass grafting • Internal thoracic artery • Radial artery • Saphenous vein • Harvesting technique • Vasospasm • Graft failure

INTRODUCTION

Graft patency is the mechanism for the sustained clinical benefits of coronary artery bypass grafting (CABG). Continued patency of bypass grafts protects against spontaneous myocardial

infarction (MI) and reduces the need for repeat revascularization.¹ In the largest individual participant data pooled analysis on graft failure to date [seven randomized clinical trials (RCTs) involving 4413 patients and 13 163 grafts], graft failure was strongly associated with non-fatal cardiac events, as well as

mortality after CABG.² Graft failure is a multifactorial process that involves acute thrombosis, intimal hyperplasia, inflammation, spasm and atherosclerosis.³ Conduit harvesting techniques, intra-operative storage prior to reimplantation into the coronary circulation, and targeted pharmacotherapy therefore represent the key determinants to preserve the structural and functional integrity and, ultimately, the efficacy of CABG conduits. In this clinical consensus statement by the European Society of Cardiology (ESC) Working Group on Cardiovascular Surgery and the European Association for Cardio-Thoracic Surgery Coronary Task Force, we review the scientific evidence and provide best practice statements for the intra- and post-operative management of CABG conduits. We also highlight gaps in knowledge and future research directions.

Mechanisms and consequences of impaired endothelial function

The long-term patency of vein or arterial grafts is highly dependent on the anatomical integrity of the graft *in situ* and the anatomical and haemodynamic characteristics of the target vessel, but also the biology of the graft. The integrity and the biological 'health' of the endothelial layer of the graft are critical factors that determine its early patency given that trauma to the graft during harvesting and storage may lead to disruption of the endothelial layer exposing the subendothelial collagen to the circulating platelets, leading to acute graft thrombosis and failure early after CABG.³ This mechanism, together with technical anastomotic issues, lead to slow blood flow through the graft and largely explain the early thrombosis and graft failure observed in ~11% of saphenous vein grafts (SVGs) within the first few weeks post-surgery.^{4,5}

Beyond these mechanical factors, endothelial dysfunction [related to reduced endothelial nitric oxide (NO) bioavailability]

leads to redox dysregulation in the graft wall and triggers pro-inflammatory and pro-thrombotic mechanisms that may result in graft occlusion.^{3,6} Indeed, endothelial dysfunction related to clinical risk factors, such as smoking, diabetes or insulin resistance, obesity, and hypercholesterolaemia, is driven by activation of pro-oxidant enzymatic systems in the endothelial cell, such as nicotinamide adenine dinucleotide phosphate oxidases, which generate free radicals like superoxide (O₂⁻), damaging endothelial cell structures.⁷⁻⁹ The same redox dysregulation results in oxidative degradation of endothelial NO synthase (eNOS) co-factor tetrahydro-biopterin, which then induces eNOS uncoupling in the graft's endothelial cell, further increasing superoxide generation and endothelial dysfunction.^{8,10} On the other hand, late (>1 year) graft failure is often associated with intimal hyperplasia as part of atherogenesis. Clinical risk factors and the graft biology (e.g. redox dysregulation and endothelial dysfunction)¹¹ lead to proliferation and migration of smooth muscle cells and may also trigger the classic mechanisms of plaque formation, plaque rupture, and late graft failure. Size mismatch, particularly when larger SVGs are grafted to small coronary targets, may predispose to non-laminar flow patterns, which may lead to intimal hyperplasia or graft occlusion.¹² Grafts are also prone to spasm, driven by the imbalance between vasoconstrictors (e.g. thromboxane A₂ and endothelin) and vasodilators [e.g. NO, endothelial derived relaxation factor, and prostacyclin (PGI₂)] subsequent to endothelial dysfunction. Finally, evidence suggests that maintaining perivascular adipose tissue around the graft [internal thoracic artery (ITA) or SVG] could have a beneficial effect on graft patency,^{13,14} given that perivascular adipose tissue secretes a range of vasodilatory agents [e.g. adiponectin and hydrogen sulfide (H₂S)] that could improve endothelial function and the graft's overall redox state.^{15,16} An overview of the role of endothelial dysfunction and vascular redox dysregulation in graft failure is shown in Fig. 1.

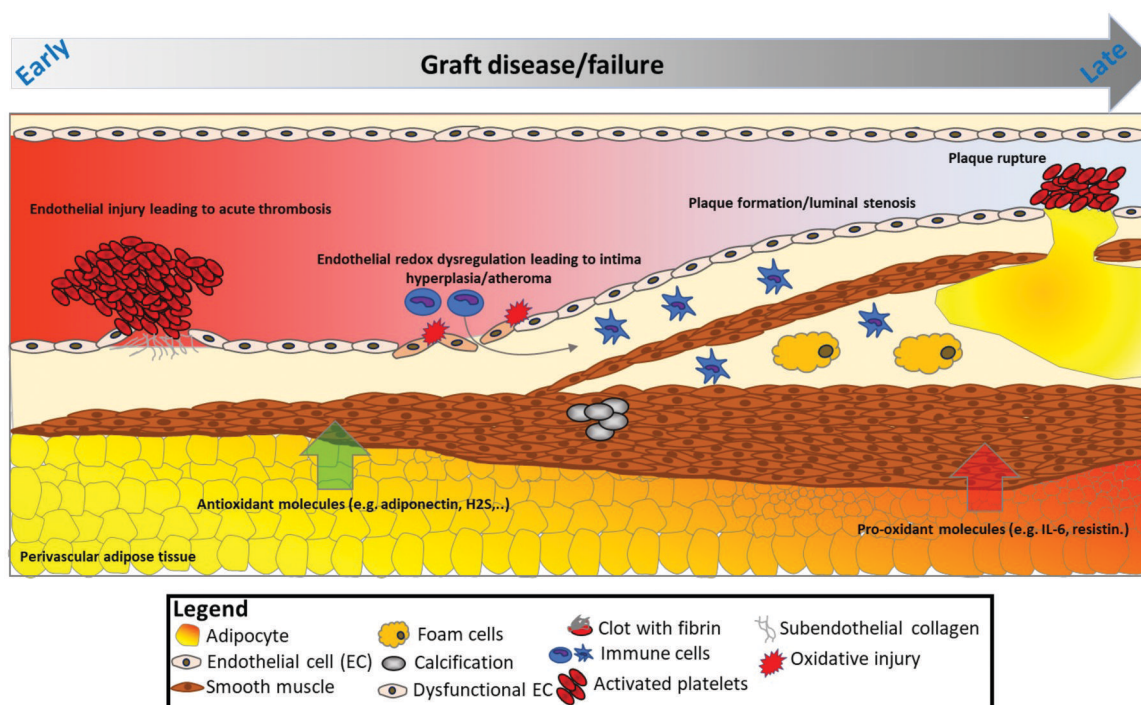


Figure 1: Graft failure: from early endothelial injury to late atherosclerotic plaque formation and rupture.

CONDUIT HARVESTING

Skeletonized vs. pedicled harvesting of arterial grafts

The ITA can be harvested as a pedicled graft (including perivascular fat, veins, and the endothoracic fascia) or as a skeletonized graft (without surrounding tissue). The skeletonized method is technically more challenging, but results in a longer and more versatile conduit that facilitates sequential and composite grafting, and has been shown to improve conduit flow (Fig. 2).¹⁷⁻¹⁹ Skeletonizing the ITA reduces sternal devascularization²⁵ and has been associated with lower risk of deep sternal wound infection in non-randomized studies and meta-analyses.^{20,21,26} This benefit is especially pronounced in diabetic patients and when harvesting bilateral ITAs.^{20,27} Patients with deep sternal wound infection have an increased risk of adverse short- and long-term clinical outcomes, including an increased mortality risk.^{28,29} However, recent reports have suggested that the skeletonized technique may result in lower patency rates and worse long-term clinical outcomes than the pedicled technique, probably as a result of mechanical trauma to the ITA during harvesting.²¹⁻²³ Limited evidence suggests that semi-skeletonized harvesting³⁰ may be associated with better results when compared with pedicled harvesting with respect to graft length and flow without increasing operative time, although there are insufficient data to compare the incidence of sternal wound complications or long-term clinical outcomes.³¹

While skeletonization of the radial artery (RA) theoretically attenuates potential sympathetic responses and vasoconstriction due to denervation,³² it does not result in significant added conduit length and is more frequently associated with endothelial damage.³³ When using non-skeletonized RA grafts, incising the RA fascia after harvesting for the entire length of the RA to allow for maximal dilatation and to protect against local constrictive fibrous bands may combine the advantages of both techniques.^{32,34} Limited skeletonization for 2-3 cm at the distal and proximal ends of the RA allows maximal dilatation at the anastomotic points and protects against accidental incorporation of any fibrous bands that may distort the anastomosis.³⁴ The gastroepiploic artery (GEA) is mainly used to revascularize the distal branches of the right coronary artery and has shown excellent

early and long-term patency rates when harvested as a pedicle including omental tissue.³⁵ As reported for other arterial grafts, skeletonization of the GEA results in larger diameter conduits and may prevent spasm due to arterial denervation and facilitate visual inspection and sequential anastomosis.³⁶ In observational studies, graft patency of skeletonized GEA conduits up to 4 years after surgery was either similar or superior to that of pedicled GEA conduits.³⁷

Electrocautery vs. harmonic scalpel harvesting

Conventional electrocautery enables easy and rapid harvest of the ITA. However, the heat that is transmitted to the artery can injure the endothelium leading to segmental vasospasm.^{38,39} Yoshida *et al.*⁴⁰ using scanning electron microscopy found nearly complete loss of endothelium on the flow surface of the ITA in the branch orifice area following monopolar cauterization vs. partial loss with bipolar cauterization. Bipolar electrocautery enables precise control of current and avoids random spraying of heat in contrast to monopolar electrocautery.⁴¹

The harmonic scalpel is an alternative to electrocautery and may be preferred when harvesting the ITA using a skeletonized technique. Ultrasonic coagulation generates lower temperature compared with electrocautery, which reduces thermal-related injuries and tissue charring⁴² as well as vasospasm.⁴³ Isomura *et al.*⁴³ found that the tissue temperature is $<80^{\circ}\text{C}$ when ultrasonic coagulation is used, while it is $>300^{\circ}\text{C}$ when electrocautery is used. In addition to generating less heat, ultrasonic coagulation produces less surgical smoke and requires fewer surgical clips. Urso *et al.*⁴⁴ in a randomized comparison of electrocautery vs. harmonic scalpel harvesting found that the intraoperative mean graft flow was similar with both techniques. Kieser *et al.*⁴⁵ in the largest observational series of harmonic ITA skeletonization found no significant differences in the risk of reoperation for bleeding [0.80, 95% confidence interval (CI) -3.20-4.80], ITA damage (0.25, 95% CI -1.10-1.60), sternal wound complications (-0.40, 95% CI -2.80-2.00), or peri-operative MI (0.70, 95% CI -2.60-4.00) compared with electrocautery.

In observational analyses of RA harvesting, harmonic scalpel induced less spasm and intimal injury compared with electrocautery^{46,47} and was associated with larger conduit luminal

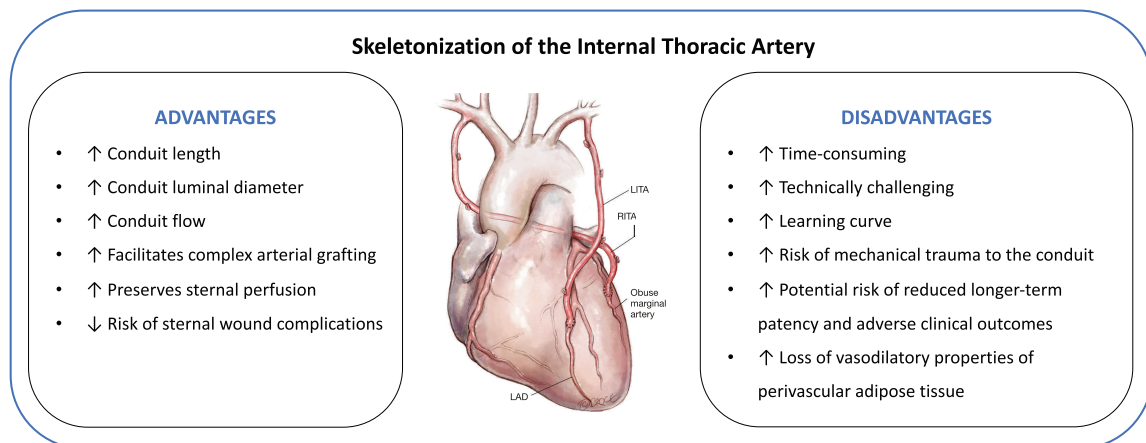


Figure 2: Advantages and disadvantages of the skeletonization technique for internal thoracic artery harvesting. The supporting evidence is based on data from meta-analyses of non-randomized studies and small randomized clinical trials and non-randomized studies.¹⁹⁻²³ LAD, left anterior descending artery; LITA, left internal thoracic artery; RITA, right internal thoracic artery. Image reproduced with permission from Taggart DP *et al.*²⁴

diameter. Nonetheless, no differences in intra-operative graft flow or post-operative graft patency were found.⁴⁷

Open vs. endoscopic harvesting techniques

The effectiveness of the endoscopic technique for SVG harvesting [endoscopic vein harvesting (EVH)] in reducing the incidence of harvesting site complications and post-operative pain, as well as increasing patient satisfaction and mobility relative to the open technique [open vein harvesting (OVH)], is well established⁴⁸ and supports the use of EVH as standard of care in patients who are at risk of leg wound complications (Fig. 3). A pooled analysis of 29 studies (11 919 patients) showed that the odds of wound complications (including abscess, necrosis, dehiscence, drainage, seroma, oedema, and haematoma) were significantly reduced by 71% with EVH compared with OVH [odds ratio (OR) 0.29, 95% CI 0.22-0.37, $P < .00001$].⁴⁸ However, patency data for EVH compared with OVH are mixed. Whereas two small RCTs with angiographic follow-up of 3 and 6 months, respectively, did not find a difference in the rate of SVG failure between EVH and OVH,^{49,50} observational evidence with longer angiographic follow-up, in particular the non-randomized *post hoc* analyses of the Project of Ex-vivo Vein Graft Engineering via Transfection (PREVENT)-IV⁵¹ and Randomized On/Off Bypass (ROOBY)⁵² trials, has suggested that EVH is associated with reduced long-term SVG patency.⁵³ A meta-analysis of 11 studies (18 131 patients) reported lower SVG failure rates with OVH at a mean follow-up of 2.6 years (OVH 17.7% vs. EVH 24.9%, OR 0.61, 95% CI 0.43-0.87, $P = .01$).⁵⁴ A meta-analysis that included only studies with angiographic follow-up > 1 year (5 studies, 5235 patients) also reported lower SVG patency with EVH (OR 0.80, 95% CI 0.70-0.91).⁵⁵ The Randomized Endovascular Graft Prospective (REGROUP) trial⁵⁶ did not find a significant

difference between OVH and EVH in the risk of the composite of death, MI, or repeat revascularization at a median follow-up of 2.78 years [15.5% vs. 13.9%, hazard ratio (HR) 1.12, 95% CI 0.83-1.51, $P = .47$] that was confirmed at median follow-up of 4.7 years (OVH 23.5% vs. EVH 21.9%, HR 0.92, 95% CI 0.72-1.18, $P = .52$).⁵⁷ Importantly, the REGROUP trial did not include angiographic follow-up and specified minimum harvester experience for both techniques, which has been shown to affect SVG quality.⁵⁸ In a comparison of OVH vs. EVH performed by experienced (>30 /month, >900 total cases) vs. less experienced (<3 /month, <100 total cases) harvesters, the incidence of SVG endothelial injury was significantly lower when grafts were procured by experienced harvesters and when using OVH.⁵⁸

The effectiveness of the endoscopic RA harvesting (ERAH) technique compared with open RA harvesting (ORAH) in reducing the incidence of arm wound complications, including infection,⁴⁸ haematoma,⁴⁸ and incisional pain,⁵⁹ is consistent with the benefits of endoscopic harvesting of the SVG (Fig. 3). However, similarly, there are concerns that ERAH may adversely affect RA patency and cardiac outcomes due to potential mechanical injury to the endothelium.

This consideration is particularly important for a predominantly muscular and highly spastic conduit such as the RA. Whereas older studies have reported no difference between ORAH and ERAH,^{60,61} a more contemporary organ bath study showed that ORAH was associated with better preservation of endothelial function compared with ERAH.⁶² Meta-expertise bias, short follow-up, and low statistical power, reported that ERAH was associated with similar 30-day and longer-term mortality and graft patency rates compared with ORAH.^{63,64} No adequately powered RCT exists evaluating a strategy of ORAH vs. ERAH on cardiac outcomes. The vast majority of the evidence in support of the efficacy and safety of RA grafting is based on

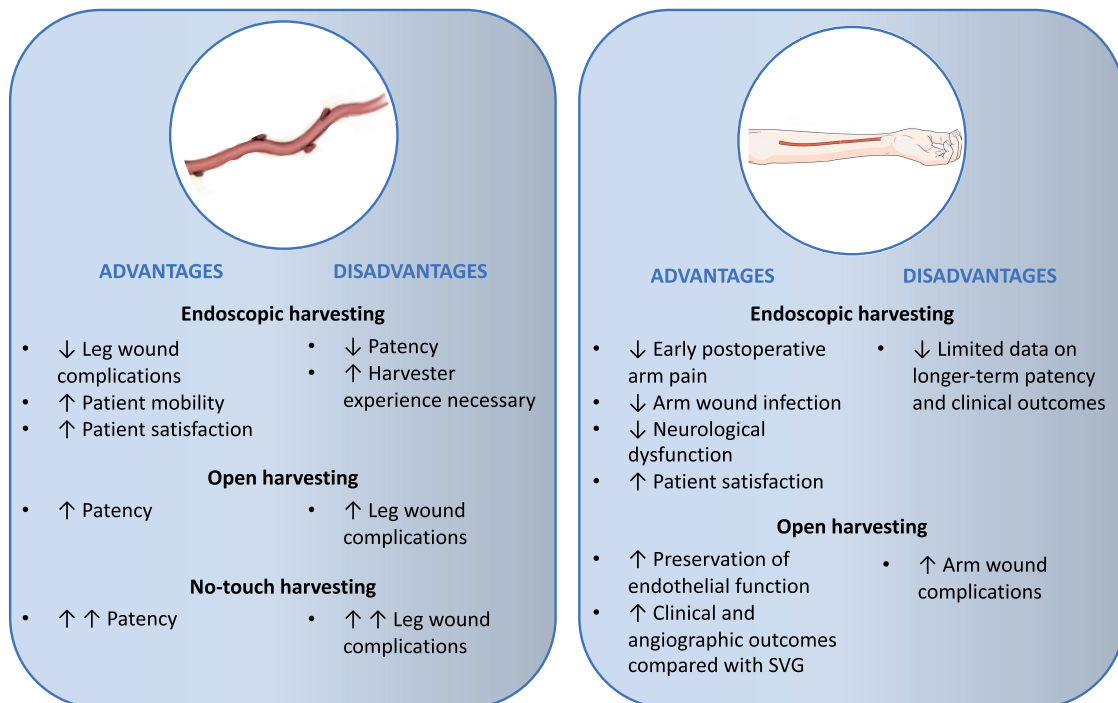


Figure 3: Advantages and disadvantages of harvesting techniques for the saphenous vein (left) and radial artery (right). SVG, saphenous vein graft. Parts of the figure were drawn using Servier Medical Art (smart.servier.com) licensed under a Creative Commons Attribution 4.0 International Licence (<https://creativecommons.org/licenses/by/4.0/>).

studies that used ORAH. Open radial artery harvesting should therefore currently be considered standard of care.

High-pressure distension

During preparation, the SVG is frequently distended using a handheld syringe to overcome graft spasm and check for leaks. Manual distension leads to intraluminal pressures in excess of 600 mmHg⁶⁵ that results in endothelial and medial damage⁶⁶ that has been associated with reduced patency rates.⁶⁷ Galea *et al.*⁶⁸ found that apoptosis was increased in SVGs after distension with 350 mmHg for 2 min. Levels of eNOS remained unchanged in SVGs distended with 100 and 200 mmHg but were significantly lower in SVGs distended with 300 mmHg.⁶⁹ Stigler *et al.*⁷⁰ showed that distension pressures above 50 mmHg were associated with incrementally increased endothelial cell loss and neointimal proliferation. At 50, 100, and 300 mmHg pressures, endothelial loss levels assessed by CD31 immunostaining were 29%, 54%, and 91%, respectively. Although only limited data exist, a pressure-controlling syringe may be helpful in preventing excess graft dilatation and subsequent endothelial damage.

NO-TOUCH SVG

Mechanism of benefit

Ahmed *et al.*⁷¹ performed multiple studies assessing changes associated with no-touch (NT) compared with conventional (CON) SVG harvesting using discarded segments of human SVGs from the operating room. On light microscopy, endothelial cushions were present in the NT-SVGs while the endothelial surface was flattened with loss of endothelial integrity in the CON-SVGs. In addition, after dilatation, the total wall thickness was typically greater after NT than CON-SVG harvesting.⁷² On transmission electron microscopy, the medial smooth muscle cells had a normal appearance in the NT-SVGs but were non-uniform in the CON-SVGs.⁷¹ Others have documented the appearance of markers of smooth muscle cell activation, potential precursors of intimal hyperplasia, in the CON compared with the NT-SVGs.⁷³ Furthermore, the adventitial layer consisting of connective tissue, fat, vasa vasorum, and perivascular nerves is preserved in the NT-SVGs, while it is removed with CON-SVG harvesting. Studies with and without retention of the surrounding tissue showed partial reduction of distension-induced endothelial injury in the NT-SVGs.⁷² The basis for this protective effect may include partial buttressing of the SVG which then limits conduit overdilatation. Other possible mechanisms are preservation of eNOS activity, which is highly expressed in the adventitia tissue,⁷² and certain adipose specific markers such as leptin and adiponectin which are expressed in the perivascular fat.⁷⁴ More recent studies have shown that the phenotype of perisaphenous and peri-ITA fat has similarities with the perivascular fat of atherosclerosis-prone vessels such coronary arteries or the aorta.⁷⁵ Finally, some data suggest that the vasa vasorum of NT-SVGs remain patent unlike with CON-SVGs.⁷⁶

Angiographic and clinical outcomes

A recently published network meta-analysis of 18 graft patency RCTs (6543 patients and 8272 grafts) concluded that graft

occlusion was substantially reduced [risk ratio (RR) 0.56; 95% CI, 0.44-0.70] at a mean follow-up time of 3.5 years compared with the CON-SVG and that the NT-SVG and RA were ranked as the best conduits.⁷⁷ Tian *et al.*⁷⁸ in an RCT that included 2655 patients showed that SVG occlusion on computed tomography angiography (CTA) was significantly reduced for NT-SVG grafts compared with CON-SVG both at 3 months (2.8% vs. 4.8%, OR 0.57, 95% CI 0.41-0.80, $P < .001$) and at 12 months (3.7% vs. 6.5%, OR 0.56, 95% CI 0.41-0.76, $P < .001$). The SWEDEGRAFT registry-based RCT (NCT03501303) compares NT-SVG vs. CON-SVG in 900 patients with a primary endpoint of graft failure on protocol-specified CTA imaging or death at 2 years.⁷⁹ To date, there is no convincing evidence for better cardiac outcomes when using the NT-SVG compared with the CON-SVG.⁵³ No-touch saphenous vein graft harvesting is however associated with a significantly higher risk of leg wound complications (Fig. 3).⁵³ Tian *et al.*⁷⁸ reported that the NT technique was associated with higher rates of leg wound surgical interventions at 3 months (10.3% vs. 4.3%; OR, 2.55; 95% CI, 1.85-3.52; $P < .001$). Minimally invasive NT-SVG harvesting techniques have recently been described,^{80,81} including one approach whereby the NT-SVG is harvested endoscopically with the perivascular tissue intact,⁸² thus combining the advantage of endoscopic harvesting with respect to harvest site complications and the improved patency of NT-SVG.

Best practice clinical consensus statements: conduit harvesting	Strength of evidence
<ul style="list-style-type: none"> Use the skeletonized technique to harvest the ITA in patients at high risk of sternal wound complications, particularly when harvesting bilateral ITAs 	Meta-analyses of non-randomized studies and small RCTs ^{20,21,26}
<ul style="list-style-type: none"> Use an endoscopic SVG harvesting technique in patients at risk of leg wound complications, considering harvester experience 	Single large RCT, ⁵⁶ meta-analyses of non-randomized studies and small RCTs ⁴⁸
<ul style="list-style-type: none"> Use an open, preferably no-touch, SVG harvesting technique in patients at low risk of leg wound complications 	Large RCT, ⁷⁸ meta-analyses of non-randomized studies and RCTs ^{54,55}
Avoid high-pressure distension of SVGs, using a pressure-controlling syringe when possible	Multiple <i>in vitro</i> studies ^{65,70}

Conduit storage

The evidence on the effect of conduit storage solutions is mixed, and data are derived mainly from *in vitro* studies (Fig. 4). Traditionally, heparinized 0.9% saline or autologous whole blood (AWB) has been used in clinical practice.⁸³ However, at a pH of 5.5, saline is acidic and has been shown to cause endothelial damage when used as an *ex vivo* storage solution.^{84,85} Unlike circulating blood which is under arterial and venous pressure, extracorporeal blood is under atmospheric pressure, which results in loss of partial pressure of CO₂ and causes the pH of blood to rapidly become alkaline. Loss of endothelial and smooth muscle cell viability has been shown to occur even after short-term exposure to slightly alkaline solutions at a pH of 8.0.⁸⁶ Whereas some studies have shown less endothelial injury,

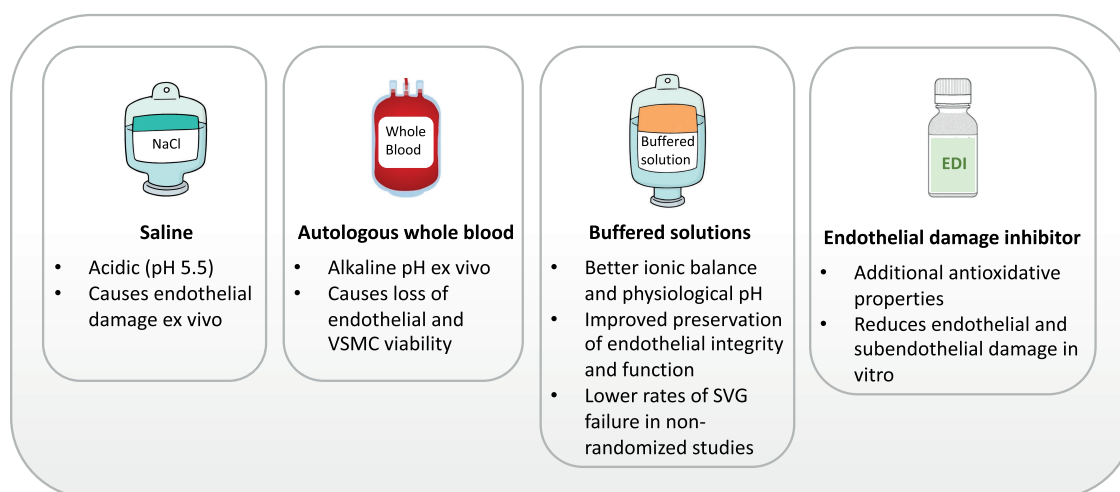


Figure 4: Comparison of solutions for intra-operative conduit storage. SVG, saphenous vein graft.

inflammatory changes, and tissue necrosis with the use of AWB compared with saline,⁸⁴ other studies did not find a difference between the two solutions.⁸⁷ In functional tests, AWB was superior to saline with regard to contraction and relaxation rates, likely due to improved preservation of vascular contractile and endothelial function.⁸⁸⁻⁹¹

Buffered solutions (such as University of Wisconsin preservation solution, histidine-tryptophan-ketoglutarate, TiProtec, and He solutions) provide better ionic balance and physiological pH, and *in vitro* studies have shown improved preservation of endothelial structural integrity and function compared with both AWB and saline.⁹² A *post hoc* analysis of the PREVENT-IV trial showed that use of buffered solutions was associated with lower rates of SVG failure and possibly better clinical outcomes.⁹³ There is evidence to suggest that AWB may increase the susceptibility of the RA to spasm⁹⁴ and a buffered asanguineous solution may be preferred for intra-operative storage of the RA.^{32,34}

An endothelial damage inhibitor (EDI) is a buffered solution with antioxidative, radical-scavenging, and eNOS-supporting properties that were developed based on the GALA formulation (reduced glutathione, L-ascorbic acid, and L-arginine).⁹⁵ In a small RCT using multidetector CTA, lower mean SVG wall thickness at 12 months was found for SVGs treated with EDI compared with saline.⁹⁶ Recent *ex vivo* studies using EDI on SVGs^{97,98} as well as RA grafts⁹⁹ have suggested significant reduction of endothelial and subendothelial damage and reduced levels of reactive oxygen species that correlated with a reduction of hypoxic damage (eNOS and caveolin-1) and significant increase of oxidation-reduction potential when compared with standard buffered solutions^{98,99} and saline or AWB.⁹⁷ No comparative studies of EDI vs. other buffered storage solutions have been performed with regard to graft patency or clinical outcomes. Use of EDI increases the cost of the CABG procedure.¹⁰⁰

The temperature of the storage solution is probably important in endothelial protection, but evidence is limited. Bush *et al.*⁶⁷ reported that the best protection is achieved at room temperature and 37°C, whereas temperature at 4°C causes separation at the basal membrane and spherical changes in cells.

Best practice clinical consensus statements: conduit storage	Strength of evidence
<ul style="list-style-type: none"> • Avoid the use of 0.9% saline for intra-operative graft storage 	Multiple <i>in vitro</i> studies ⁸⁹
<ul style="list-style-type: none"> • Use buffered solutions for storage of SVGs 	Large non-randomized study ⁹³
<ul style="list-style-type: none"> • Asanguineous solutions for storage of the RA may be preferred to reduce susceptibility to spasm 	<i>In vitro</i> study and expert opinion ^{32,94}

PREVENTION AND TREATMENT OF ARTERIAL GRAFT SPASM

Pathophysiology of arterial graft spasm

The mechanisms of vasospasm in arterial CABG grafts have been described by He and Taggart.¹⁰¹ Vasospasm may be precipitated by vasoconstrictor substances (spasmogens), which in arterial grafts include endothelium-derived contracting factors (e.g. endothelin-1), prostaglandins (e.g. thromboxane A₂), alpha-adrenoceptor agonists (e.g. norepinephrine), and platelet-derived substances (e.g. serotonin), among others.¹⁰¹ Arterial grafts such as the ITA and RA are predominantly alpha-adrenoceptor vessels with a high constriction responsiveness to norepinephrine. In comparison with the ITA, the RA has higher receptor-mediated contractility to endothelin, angiotensin II, vasopressin, serotonin, and thromboxane A₂. Vasospasm in arterial grafts may also be related to endothelial dysfunction.¹⁰¹ The intact endothelium prevents spasm of the graft by releasing endothelium-derived relaxing factors (e.g. NO and PG₁₂) which balance vasoconstriction and relaxation in arterial grafts. Whereas the ITA has better endothelial function and releases more NO and other vasorelaxing factors, the RA and GEA have less eNOS expression and require more active pharmacologic interventions.¹⁰¹ The diameter of the ITA is inversely correlated with its tendency for spasm, suggesting that the distal end of the ITA should not be harvested.¹⁰² Aspirin exhibits vasoconstrictive properties and inhibits arachidonic acid-dependent vasodilator pathways even at low doses (75-300 mg).¹⁰³

Sex-related differences in arterial graft physiology

Radial artery size and flow are smaller in women,^{104,105} whereas ITA segments have been noted to be comparable in size between women and men,¹⁰⁶ and both are more likely to be related to body size rather than sex.

Internal thoracic artery endothelial cells in post-menopausal women show impaired expression of messenger RNA for eNOS and reduced eNOS protein levels compared with men,¹⁰⁷ suggesting NO-mediated endothelial dysfunction. This is consistent with the findings of lower levels of vasodilators (including NO) and higher levels of vasoconstrictors in the circulating blood of women vs. men.¹⁰⁸ It is unclear if these differences contribute to function or the propensity for graft spasm in either sex. Sex differences in vascular reactivity, plasma levels of mediators of microvascular tone, and pharmacologic responses have been described and postulated to be related to higher levels of NO or eNOS in younger women due to higher levels of oestrogen.¹⁰⁸

The presence of oestrogen is postulated to delay cellular senescence by a NO-dependent mechanism, and menopause would thus lead to less NO bioavailability and impaired endothelial metabolism.¹⁰⁷

Endothelial cyclooxygenase pathway-mediated ITA hypersensitivity to serotonin and to alpha¹-adrenergic stimuli in women may be a biological mechanism contributing to post-operative ITA graft spasm in women,¹⁰⁹ and excessive ITA graft constriction in women administered catecholamines.¹¹⁰ Table 1 summarizes the sex differences in vascular reactivity responses of *ex vivo* ITA segments to mediators of vascular tone.

VASODILATORY PROTOCOLS

Intra-operative protocols

Papaverine is the most widely used agent for vasodilation of the ITA. Papaverine can either be injected into endothoracic fascia before harvesting or topically applied after harvesting and the ITA covered with a papaverine-soaked gauze.¹¹⁴ Several studies have shown the beneficial effect on ITA graft flow after periarterial or intraluminal administration of papaverine.¹¹⁵ Intraluminal papaverine administration may increase vasodilation over topical administration, but it is associated with the risk of intimal injury.^{116,117} Sodium nitroprusside has also been shown to be a potent vasodilator when used topically on the ITA, but is less frequently used.¹¹⁸

Several RA bath options have been described.^{32,119} The most commonly used topical vasodilating agents for the RA in clinical practice are calcium channel blockers (CCBs) and nitrates. In particular, the combined use of verapamil and nitroglycerine is favoured and is more effective at RA vasospasm prevention than when each agent is used individually. A verapamil/nitroglycerine solution better preserves RA endothelial function than does papaverine.¹²⁰ For an RA bath including papaverine, a buffered solution such as Ringer's lactate, or heparinized blood at 37° may be used.³⁴ The phosphodiesterase inhibitor milrinone has a potent vasodilatory effect on the RA and may be used topically in heparinized arterial blood.^{32,34}

Post-operative protocols

Patients with RA grafts commonly receive oral antispasm therapy postoperatively, and the CCBs amlodipine and diltiazem are

used most frequently¹²¹ (Table 2). However, the evidence on the effect of CCB on the RA is inconsistent. A small RCT that assigned 100 patients to either receive or not receive diltiazem for 1 year starting in the early postoperative period showed no difference in clinical or angiographic outcomes at 1 year.¹³² Similarly, a *post hoc* analysis of the Radial Artery Patency Study found that among 440 patients with RA grafts, the incidence of string sign (the highest degree of RA spasm) was not associated with patients' compliance with the prescribed post-operative CCB therapy.¹³³ In a *post hoc* analysis of the RADIAL database that included 732 patients with RA grafts, CCB therapy was associated with a significantly lower risk of major adverse cardiac events (MACE) (HR, 0.52; 95% CI, 0.31-0.89; $P = .02$) and RA occlusion (HR, 0.20; 95% CI, 0.08-0.49; $P < .001$).¹³⁴ Calcium channel blocker therapy for 1 year was associated with a greater reduction in the risk of MACE ($P < .001$) and RA occlusion ($P = .006$) than a shorter duration of CCB therapy. A benefit of a longer duration of CCB therapy was not demonstrated ($P = .08$), although the numbers of patients on prolonged CCB therapy was small. After implantation in the coronary circulation, RA grafts undergo remodelling of the vessel wall with a progressive reduction in the muscular component of the media and thus a reduction in the propensity for spasm.¹³⁵ This process is completed 1 year post-operatively,¹³⁵ suggesting that in clinical practice, the duration of CCB therapy may be limited to the first post-operative year.

It is unclear whether there is a difference in the antispasm efficacy on the RA between amlodipine and diltiazem. In the *post hoc* analysis of RADIAL, use of amlodipine (HR, 0.30; 95% CI, 0.12-0.74; $P = .009$) and diltiazem (HR, 0.20; 95% CI, 0.07-0.51; $P < .001$) was associated with a similar protective effect on the risk of RA occlusion when compared with non-use of CCBs.¹³⁴

It should be noted that chronic CCB use has side effects including headache, tachycardia, flushing, and peripheral oedema. In addition, use of CCB therapy due to its hypotensive effect may preclude the use of secondary preventive medications such as beta-blockers or renin-angiotensin-aldosterone system inhibitors.

An RCT that compared a strategy of 24 h i.v. infusion of nitroglycerine with diltiazem, followed by 6-month treatment with a daily oral dose of isosorbide mononitrate or diltiazem, found no differences in clinical outcomes.¹³⁶ Tachyphylaxis may render oral nitrates less effective for continued prevention of RA graft vasospasm, and no evidence exists evaluating their post-operative use with regard to graft patency.

Best practice clinical consensus statements: antispasm prophylaxis	Strength of evidence
<ul style="list-style-type: none"> Consider oral calcium channel blockers (amlodipine or diltiazem) for 1 year post-operatively after RA grafting 	Non-randomized study ¹³⁴

Secondary prevention of graft failure

The mechanism of graft failure is distinctly different between arterial grafts and SVGs. Acute thrombosis and late atherosclerosis are observed predominantly in SVGs, and pharmacological therapy is thus mainly aimed at preventing SVG failure (Table 2).

Table 1: Summary of published internal thoracic artery and saphenous vein segment vascular reactivity testing in women and men

Author, year	Conduit evaluated	Vascular reactivity results	Patient age	Endothelium dependent	Cyclooxygenase dependent	NO dependent
Dignan, 1992 ¹⁰⁶	IMA segments	<ul style="list-style-type: none"> • Serotonin (women greater strength contraction) • Norepinephrine (women weaker contraction) • Nitroprusside (women equal relaxation) 	50–76 years			
Akar, 2007 ¹¹¹	IMA segments	<ul style="list-style-type: none"> • Noradrenaline (no difference) • Vasodilatory effects of levosimendan (K_{ATP} channel opener) greater in men vs. women • Levosimendan vasodilatory effect in men inhibited by blockade of K_{ATP} and K_{Ca} channels in men but not women 	Men 44–73 years Women 46–73 years			
Muir, 2010 ¹¹²	IMA and SV segments	<ul style="list-style-type: none"> • Acetylcholine (endothelium dependent) relaxation greater in men vs. women • Nitroprusside (endothelium independent) no difference 	Men 29–82 years Women 44–79 years; all post-menopausal			
Mannacio, 2012 ¹⁰⁷	IMA segments	<ul style="list-style-type: none"> • Acetylcholine (women lower maximal relaxation response vs. men) 	Men 62 ± 4 years Women 62 ± 4 years; all post-menopausal			
Lamin, 2018 ¹⁰⁹	IMA segments	<ul style="list-style-type: none"> • Serotonin (women increased sensitivity vs. men) • Thromboxane A₂ (no difference) • Nitroprusside (no difference) 	Men 66.8 ± 10.4 SD Women 66.6 ± 12.2 SD	Yes—serotonin response	Yes—serotonin response	No—serotonin response
Riedel, 2019 ¹¹³	IMA segments	<ul style="list-style-type: none"> • Norepinephrine (constriction less in women vs. men) • Isoprenaline (women more relaxation vs. men) 	Men and Women 48–55 years	Yes—norepinephrine, isoprenaline		Yes—norepinephrine, isoprenaline
Jaghoori, 2020 ¹¹⁰	IMA and SV segments	<ul style="list-style-type: none"> • Phenylephrine (IMA and SV hypersensitive in women vs. men) • Endothelin-1 (no difference) 	Men 67.7 ± 10.5 SD Women 69 ± 10.1 SD; all post-menopausal	Yes—phenylephrine	Yes—phenylephrine	No—phenylephrine

K_{ATP}, adenosine triphosphate-sensitive potassium channel; K_{Ca}, calcium-activated potassium channel; IMA, internal thoracic artery; SV, saphenous vein; NO, nitric oxide.

The role of pharmacological therapies in optimizing the late patency of arterial grafts is not well characterized.

Antithrombotic therapy Aspirin

The routine use of aspirin is based on decades-old RCTs demonstrating the benefit of aspirin compared with placebo to prevent SVG occlusion.^{122–124} Goldman *et al.*¹²² in the largest RCT with angiographic follow-up including 772 patients (Veterans Administration Cooperative Study) found that aspirin significantly decreased SVG occlusion vs. placebo early and at 1 year after CABG (15.8% vs. 22.6%, $P = .029$).¹³⁷ A meta-analysis of 17 RCTs that included 1443 patients showed that a low (100 mg) to

medium (325 mg) daily aspirin dose initiated within 6 h post-CABG is most effective, without an increase in post-operative bleeding.^{124,138} Randomized clinical trials of delayed (>24 h post-operatively) initiation of aspirin did not find a benefit on^{138,139} SVG patency. Low-dose aspirin (75–100 mg daily) appears sufficient as maintenance therapy as it exceeds the minimal effective dose required for platelet thromboxane A₂ suppression and overcomes interindividual variability in drug response.¹⁴⁰ More than once-daily dosing may be considered in the immediate post-operative phase after on-pump CABG. Use of cardiopulmonary bypass promotes postoperative platelet turnover leading to increased synthesis of thromboxane and may reduce early post-operative aspirin efficacy. However,

Table 2: Therapeutic strategies for preventing arterial graft spasm and graft atherogenesis after coronary artery bypass grafting

Agent	Mechanisms of action	Time of initiation after CABG and treatment duration	Main study findings	Strength of evidence
Vasospasm prevention				
Amlodipin, diltiazem	Calcium channel antagonist	Treatment duration 1 year	↓ incidence of RA occlusion	Observational ³²
Inhibition of platelet aggregation				
Aspirin	Cyclooxygenase inhibition	Within 24 h (ideally with 6 h) after CABG and continued indefinitely	↓ incidence of SVG occlusion	Multiple RCTs and MAs of RCTs ¹²²⁻¹²⁴
Clopidogrel	Irreversible P2Y12 receptor inhibitor	Variable timing of post-operative initiation; treatment duration 3-12 months	↓ incidence of SVG failure or occlusion Conflicting findings with regard to incidence of major bleeding	Several study-level MA of small RCTs and observational studies ¹²⁵⁻¹²⁷
Ticagrelor	Reversible P2Y12 receptor inhibitor Pleiotropic effects including attenuation of ischaemia-reperfusion injury, inflammation, and atherosclerosis ¹²⁸	Within 48 h after CABG and continued for 1 year	↓ incidence of SVG failure ↑ incidence of BARC types 2, 3, 5 bleeding, no difference in incidence of BARC types 3 and 5 bleeding compared with aspirin alone	Single RCT of 500 patients, ¹²⁹ study-level MA of RCTs, ¹²⁵ IPD-MA of RCTs ¹³⁰
LDL-C-lowering				
Statins	HMG-CoA reductase inhibition Pleiotropic effect on inflammation	Continued peri-operative treatment to LDL-C target level	↓ progression of graft atherosclerosis	One large RCT ¹³¹

BARC, Bleeding Academic Research Consortium; CABG, coronary artery bypass grafting; HMG-CoA, hydroxy-methylglutaryl coenzyme A; MA, meta-analysis; RA, radial artery; RCT, randomized clinical trial; SVG, saphenous vein graft.

more frequent aspirin dosing must be balanced with an increased risk of bleeding. Based on an association between aspirin dosing and outcomes in a *post hoc* analysis of the Platelet Inhibition and Patient Outcomes Study, low-dose aspirin should be used in patients treated with ticagrelor.¹⁴¹

Current clinical practice is to continue antiplatelet therapy life-long after CABG, but evidence in support of a clinical benefit is limited. There is in fact little evidence to support a clinical benefit, as opposed to a graft patency benefit, from aspirin use after CABG.^{142,143} Most studies showed no effect on mortality, or even a trend to excess mortality,^{124,144} but they were underpowered for small to moderate differences in clinical outcomes and, in particular, in mortality.^{125,137,145} However, a pooled analysis of 7 contemporary RCTs with systematic graft imaging (4413 patients, 13 163 grafts) showed that graft failure is strongly associated with adverse cardiac events (adjusted OR 3.98, 95% CI 3.54-4.47, $P < .001$) and mortality after CABG (adjusted OR 2.79, 95% CI 2.01-3.89, $P < .001$),² indirectly supporting a potential clinical benefit of aspirin. On the other hand, 1 trial randomized 213 patients 1 year after CABG to continue aspirin 325 mg/day or switch to placebo for the following 2 years and found no difference in the rate of graft occlusion, MI, or death (although the trial was not formally powered and the described power limitations apply).¹⁴⁵

Dual antiplatelet therapy

Evidence from RCTs and observational studies supports a strategy of dual antiplatelet therapy (DAPT) after CABG to reduce SVG failure. An early meta-analysis of 11 studies (5 RCTs, 6 observational studies) and 25 728 patients showed that aspirin +

clopidogrel compared with aspirin was associated with a significantly lower risk of SVG occlusion (RR 0.59, 95% CI 0.43-0.82, $P = .02$), but also with a higher risk of major bleeding events (RR 1.17, 95% CI 1.00-1.37, $P = .05$).¹²⁶ A sub-analysis that included 2 RCT (560 patients) showed that aspirin + clopidogrel was associated with a lower risk of SVG occlusion after off-pump CABG. Dual antiplatelet therapy compared with aspirin was associated with a lower risk of 30-day/in-hospital mortality (RR 0.38, 95% CI 0.26-0.57, $P < .001$); there was no difference between the treatment strategies in the risk of angina or MI (RR 0.60, 95% CI 0.31-1.14, $P = .12$).¹²⁶ Another meta-analysis of 5 RCTs and 958 patients that compared aspirin + clopidogrel with aspirin also showed an association between aspirin and the risk of SVG occlusion (OR 1.70, 95% CI 1.20-2.40) but not arterial graft occlusion (OR 1.17, 95% CI 0.54-2.56).¹⁴⁶ A network meta-analysis that included 20 RCTs (4803 patients) investigating 9 different antithrombotic strategies showed that the use of either aspirin + ticagrelor (2 RCTs, OR 0.50, 95% CI 0.31-0.79) or aspirin + clopidogrel (7 RCTs, OR 0.60, 95% CI 0.42-0.86) was associated with a lower risk of SVG failure compared with aspirin alone, without significant differences in major bleeding, MI, and death.¹²⁵ However, the analyses were likely underpowered to detect small to moderate differences in clinical outcomes. All these study-level meta-analyses were limited by heterogeneity with regard to type and duration of P2Y12 inhibitor treatment, duration of follow-up, and definitions of SVG failure and bleeding.

In an individual patient data meta-analysis of 4 RCTs (1316 patients) that used rigorous re-adjudication of outcomes, aspirin + ticagrelor was associated with a significantly lower incidence of SVG failure compared with aspirin (11.2% vs. 20%; OR 0.51, 95% CI 0.35-0.74; $P < .001$).¹³⁰

This finding was consistent for patients undergoing on- or off-pump CABG ($P_{\text{INT}} = .15$) and for SVG and arterial grafts (including ITA and RA grafts, $P_{\text{int}} = .93$). However, patients receiving aspirin + ticagrelor had a significantly increased risk of clinically important bleeding events [Bleeding Academic Research Consortium (BARC) types 2, 3, or 5 bleeding: 22.1% vs. 8.7%, OR 2.98, 95% CI 1.99–4.47; $P < .001$]. Of note, the median treatment duration with aspirin + ticagrelor was 1 year. The specific impact of DAPT on arterial graft patency, particularly in relation to different arterial graft types, has not yet been studied in detail.

These findings highlight the importance of a DAPT strategy after CABG that reduces bleeding risk while retaining its efficacy in reducing SVG failure. Platelet-driven thrombosis is the predominant mechanism of early SVG failure and typically occurs during the first month after surgery,¹⁴⁷ providing a biological rationale for intensified antiplatelet therapy in the first month after CABG. The 1-month DAPT with ticagrelor in coronary artery bypass graft patients (ODIN) trial (NCT05997693) is an investigator-initiated prospective, randomized, international, multicentre trial that is designed to compare the effect of treatment with ticagrelor in addition to low-dose aspirin for 1 month vs. aspirin alone on the 1-year incidence of ischaemic events and graft failure among patients with chronic coronary syndromes undergoing CABG.¹⁴⁸ ODIN will also inform whether short-term DAPT provides a net clinical benefit in this patient population. The Ticagrelor-based De-escalation of Dual Antiplatelet Therapy after Coronary Artery Bypass Grafting (TOP-CABG) trial (NCT05380063) will investigate whether de-escalation of DAPT (ticagrelor + aspirin) to aspirin monotherapy after 3 months is non-inferior to DAPT for 12 months in reducing SVG occlusion and superior in reducing bleeding events.

No randomized head-to-head comparison of ticagrelor vs. clopidogrel (on a background of aspirin) for SVG patency exists. Ticagrelor has a rapid onset and offset of action and provides faster, more powerful, and predictable platelet inhibition than clopidogrel.¹⁴⁹ Clopidogrel has a variable interindividual response, with approximately one-third of patients having inadequate platelet inhibitory effects. Importantly, such patients who continue to have high platelet reactivity despite use of clopidogrel are at increased risk of thrombotic events.¹⁵⁰ Clopidogrel may be preferred when ticagrelor is not available, not tolerated or contraindicated, and in patients at high bleeding risk.

P2Y12 inhibitor monotherapy and anticoagulant therapy

Current evidence does not support P2Y12 inhibitor monotherapy as an alternative to aspirin after CABG.^{129,151,152} When pooling individual patient data from the two RCTs investigating the effect of ticagrelor monotherapy, ticagrelor was not associated with a significant difference in the risk of SVG failure compared with aspirin, although the point estimate favoured ticagrelor monotherapy (OR 0.86, 95% CI 0.58–1.27).¹³⁰ In a sub-study of the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial, the factor Xa inhibitor rivaroxaban either alone or in combination with aspirin did not reduce the 1-year incidence of graft failure compared with aspirin alone (rivaroxaban vs. aspirin: 7.8% vs. 8.0%; OR: 0.95, 95% CI: 0.67–1.33; $P = .75$; rivaroxaban + aspirin vs. aspirin: 9.1% vs. 8.0%; OR: 1.13, 95% CI 0.82–1.57; $P = .45$).¹⁵³

Lipid-lowering therapy

In patients with clinical atherosclerotic cardiovascular disease (ASCVD), including those with a history of CABG, high-intensity statin therapy is guidelines recommended with the aim of achieving a >50% reduction in LDL cholesterol (LDL-C) to reduce the risk of cardiovascular events.¹⁵⁴ The magnitude of the benefit of high-intensity statins is similar among women and men,^{155,156} although high-intensity statins remain underused in women. Elevated LDL-C levels are associated with atherosclerotic plaque progression in SVGs.¹⁵⁷ In addition to lowering LDL-C, statins are also known to have pleiotropic effects, improving endothelial function, NO levels, and antioxidant function, as well as inhibiting inflammatory response, vasoconstriction, thrombosis, and platelet aggregation.¹⁵⁸ Several studies have examined the effect of statins on graft patency.^{131,159,160} The Post Coronary Artery Bypass Graft (Post CABG) trial showed that aggressive (target LDL-C < 85 mg/dL) compared with moderate (target LDL-C < 140 mg/dL) lowering of LDL-C using lovastatin decreased obstructive changes in CABG grafts by 31% at >4 years of follow-up.¹³¹ In a non-randomized post hoc comparison of participants on statin therapy in the Clopidogrel after Surgery for Coronary Artery Disease trial, 12-month graft patency as assessed by coronary angiography was higher in those with LDL-C levels < 100 mg/dL than in those with LDL-C levels > 100 mg/dL (96.5% vs. 83.3%, $P = .03$).¹⁶¹ The ACTIVE trial, comparing a strategy of 10 mg (moderate-intensity) vs. 80 mg (high-intensity) atorvastatin, did not find a difference in the incidence of SVG occlusion at 1 year; however, the trial was limited by small sample size and high rate of protocol violations, with approximately one-third of patients in each arm discontinuing the assigned treatment over the course of the study.¹⁶⁰

More recently, circulating proprotein convertase subtilisin/kexin type 9 (PCSK9) has been shown to induce macrophage activation and vein graft lesion development via LDL receptor-independent mechanisms,¹⁶² representing a potential target for pharmacologic intervention. A small cross-sectional study from China (231 patients) showed a significant association between circulating PCSK9 levels and the presence of SVG disease at >1 year after CABG. The Effect of Evolocumab on Saphenous Vein Graft Patency Following Coronary Artery Bypass Surgery (NEWTON-CABG) trial (NCT03900026) will examine the effect of the PCSK9 inhibitor evolocumab vs. placebo in addition to statin therapy for 24 months on SVG disease (defined as significant stenosis > 50% or total occlusion) on protocol-specified CTA or earlier clinically indicated coronary angiography.

Best practice clinical consensus statements: secondary prevention of graft failure	Strength of evidence
<ul style="list-style-type: none"> Initiate aspirin (100–325 mg once daily) within 6 h post-operatively to reduce the risk of SVG occlusion 	Meta-analysis of RCTs ¹²⁴
<ul style="list-style-type: none"> Consider clopidogrel or ticagrelor in addition to aspirin in the first post-operative year in patients who are not at high bleeding risk to reduce the risk of SVG failure, irrespective of the use of cardiopulmonary bypass 	Study-level and individual participant data meta-analyses of RCTs ^{125,130}
<ul style="list-style-type: none"> Use high-intensity or maximally tolerated statin therapy to reduce LDL-C and the risk of SVG disease progression 	Large RCT ¹³¹

Future research directions

Several gaps in our knowledge remain with respect to intra-operative and post-operative management of conduits, and further research is urgently needed to address these.

- Randomized studies are needed comparing skeletonized and pedicled ITA harvesting to determine how these techniques affect ITA graft patency and post-operative cardiac outcomes.
- Further studies are needed to evaluate the effect of ERAH on cardiovascular and patient-reported outcomes, given that the majority of randomized trials demonstrating superiority of the RA over the SVG have used ORAH.
- Further research is needed to investigate potential relative clinical benefits of available storage solutions and address cost-effectiveness.
- The role of oestrogen in arterial graft physiology remains unclear. Outcomes following CABG are worse in women (pre- and postmenopausal) compared with men and have been noted to be significantly worse in younger women.¹⁶⁴ Clarification of pathways that are influenced by the levels of oestrogen will be important for future therapeutics. Sex-specific management of arterial conduits should be a focus of future research.
- Randomized studies are needed to evaluate the efficacy of continued oral antispasm therapy in patients with RA grafts.
- Low-grade systemic inflammation is a more powerful determinant of recurrent cardiovascular events and death than LDL-C in patients with stable ASCVD.¹⁶⁵ The clinical benefit of targeted inflammation inhibition has been shown in particular for low-dose colchicine.¹⁶⁶ Given the pro-inflammatory mechanisms implicated in graft failure subsequent to endothelial injury, further studies are needed to determine whether patients after CABG would benefit from the addition of these pharmacotherapies to reduce the risk of graft failure.

SUMMARY

Preserving the structural and functional integrity of the conduit during graft harvesting and storage, prevention and treatment of vasospasm, and attenuating atherogenesis are integral to graft patency and the clinical benefits of CABG. The best practice clinical consensus statements outlined in this document provide a comprehensive, evidence-based approach to the intra-operative and post-operative management of conduits for CABG surgery. These strategies can serve as a valuable resource for multidisciplinary heart teams, facilitating more informed and effective treatment planning tailored to individual patient needs and local practices.

DECLARATIONS

Disclosure of Interest

This document is submitted following review and approval by the ESC Scientific Documents Committee (SDoC). The

declarations of interests review is handled by the respective oversight body according to the section 6.3.3 'DOI review' of the ESC Scientific Documents policy.

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No data were generated or analysed for this manuscript.

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REFERENCES

- [1] Gaudino M, Di Franco A, Bhatt DL, Alexander JH, Abbate A, Azzalini L, *et al.* The association between coronary graft patency and clinical status in patients with coronary artery disease. *Eur Heart J* 2021;42:1433–41. <https://doi.org/10.1093/eurheartj/ehab096>
- [2] Gaudino M, Sandner S, An KR, Dimagli A, Di Franco A, Audisio K, *et al.* Graft failure after coronary artery bypass grafting and its association with patient characteristics and clinical events: a pooled individual patient data analysis of clinical trials with imaging follow-up. *Circulation* 2023;148:1305–15. <https://doi.org/10.1161/CIRCULATIONAHA.123.064090>
- [3] Gaudino M, Antoniadis C, Benedetto U, Deb S, Di Franco A, Di Giammarco G, *et al.* Mechanisms, consequences, and prevention of coronary graft failure. *Circulation* 2017; 136:1749–64. <https://doi.org/10.1161/CIRCULATIONAHA.117.027597>
- [4] Antonopoulos AS, Ouditayo A, Oikonomou EK, Trivella M, Petrou M, Collins GS, *et al.* Development of a risk score for early saphenous vein graft failure: an individual patient data meta-analysis. *J Thorac Cardiovasc Surg* 2020;160:116–27.e4. <https://doi.org/10.1016/j.jtcvs.2019.07.086>
- [5] Wood A, Antonopoulos A, Chuaiphichai S, Kyriakou T, Diaz R, Al Hussaini A, *et al.* PHACTR1 modulates vascular compliance but not endothelial function: a translational study. *Cardiovasc Res* 2023;119:599–610. <https://doi.org/10.1093/cvr/cvac092>
- [6] Spadaccio C, Antoniadis C, Nenna A, Chung C, Will R, Chello M, *et al.* Preventing treatment failures in coronary artery disease: what can we learn from the biology of in-stent restenosis, vein graft failure, and internal thoracic arteries? *Cardiovasc Res* 2020;116:505–19. <https://doi.org/10.1093/cvr/cvz214>
- [7] Oikonomou EK, Antoniadis C. Immunometabolic regulation of vascular redox state: the role of adipose tissue. *Antioxid Redox Signal* 2018;29:313–36. <https://doi.org/10.1089/ars.2017.7017>
- [8] Akoumianakis I, Badi I, Douglas G, Chuaiphichai S, Herdman L, Akawi N, *et al.* Insulin-induced vascular redox dysregulation in human atherosclerosis is ameliorated by dipeptidyl peptidase 4 inhibition. *Sci Transl Med* 2020;12:eaav8824. <https://doi.org/10.1126/scitranslmed.aav8824>
- [9] Antoniadis C, Bakogiannis C, Tousoulis D, Reilly S, Zhang MH, Paschalis A, *et al.* Preoperative atorvastatin treatment in CABG patients rapidly improves vein graft redox state by inhibition of Rac1 and NADPH-oxidase activity. *Circulation* 2010;122: S66–73. <https://doi.org/10.1161/CIRCULATIONAHA.109.927376>
- [10] Antoniadis C, Shirodaria C, Crabtree M, Rinze R, Alp N, Cunningham C, *et al.* Altered plasma versus vascular biopterins in human atherosclerosis reveal relationships between endothelial nitric oxide synthase coupling, endothelial function, and inflammation. *Circulation* 2007;116:2851–9. <https://doi.org/10.1161/CIRCULATIONAHA.107.704155>
- [11] Akoumianakis I, Polkinghorne M, Antoniadis C. Non-canonical WNT signalling in cardiovascular disease: mechanisms and therapeutic implications. *Nat Rev Cardiol* 2022;19: 783–97. <https://doi.org/10.1038/s41569-022-00718-5>
- [12] Desai ND, Naylor CD, Kiss A, Cohen EA, Feder-Elituv R, Miwa S, *et al.* Impact of patient and target-vessel characteristics on arterial and venous bypass graft patency: insight from a randomized trial. *Circulation* 2007; 115:684–91. <https://doi.org/10.1161/CIRCULATIONAHA.105.567495>
- [13] Saito T, Kurazumi H, Suzuki R, Matsunaga K, Tsubone S, Lv B, *et al.* Perivascular adipose tissue is a major source of nitric oxide in saphenous vein grafts harvested via the no-touch technique. *J Am Heart Assoc* 2022;11:e020637. <https://doi.org/10.1161/JAHA.120.020637>

- [14] Gao YJ, Zeng ZH, Teoh K, Sharma AM, Abouzahr L, Cybulsky I, et al. Perivascular adipose tissue modulates vascular function in the human internal thoracic artery. *J Thorac Cardiovasc Surg* 2005;130:1130–6. <https://doi.org/10.1016/j.jtcvs.2005.05.028>
- [15] Akoumianakis I, Sanna F, Margaritis M, Badi I, Akawi N, Herdman L, et al. Adipose tissue-derived WNT5A regulates vascular redox signaling in obesity via USP17/RAC1-mediated activation of NADPH oxidases. *Sci Transl Med* 2019;11:eaav5055. <https://doi.org/10.1126/scitranslmed.aav5055>
- [16] Akawi N, Checa A, Antonopoulos AS, Akoumianakis I, Daskalaki E, Kotanidis CP, et al. Fat-secreted ceramides regulate vascular redox state and influence outcomes in patients with cardiovascular disease. *J Am Coll Cardiol* 2021;77:2494–513. <https://doi.org/10.1016/j.jacc.2021.03.314>
- [17] Deja MA, Wos S, Golba KS, Zurek P, Domaradzki W, Bachowski R, et al. Intraoperative and laboratory evaluation of skeletonized versus pedicled internal thoracic artery. *Ann Thorac Surg* 1999;68:2164–8. [https://doi.org/10.1016/S0003-4975\(99\)00820-6](https://doi.org/10.1016/S0003-4975(99)00820-6)
- [18] Wendler O, Tscholl D, Huang Q, Schafers HJ. Free flow capacity of skeletonized versus pedicled internal thoracic artery grafts in coronary artery bypass grafts. *Eur J Cardiothorac Surg* 1999;15:247–50. [https://doi.org/10.1016/S1010-7940\(99\)00012-3](https://doi.org/10.1016/S1010-7940(99)00012-3)
- [19] Kusu-Orkar TE, Kermali M, Masharani K, Noshirwani A, MacCarthy-Ofose B, Oguamanam N, et al. Skeletonized or pedicled harvesting of left internal mammary artery: a systematic review and meta-analysis. *Semin Thorac Cardiovasc Surg* 2021;33: 10–8. <https://doi.org/10.1053/j.semtcvs.2020.09.010>
- [20] Saso S, James D, Vecht JA, Kidher E, Kokotsakis J, Malinovsky V, et al. Effect of skeletonization of the internal thoracic artery for coronary revascularization on the incidence of sternal wound infection. *Ann Thorac Surg* 2010;89:661–70. <https://doi.org/10.1016/j.athoracsur.2009.08.018>
- [21] Dimagli A, Gemelli M, Kumar N, Mitra M, Sinha S, Fudulu D, et al. A systematic review and meta-analysis of internal thoracic artery harvesting techniques: skeletonized vs pedicled. *Int J Cardiol* 2024;395:131577. <https://doi.org/10.1016/j.ijcard.2023.131577>
- [22] Lamy A, Browne A, Sheth T, Zheng Z, Dagenais F, Noiseux N, et al. Skeletonized vs pedicled internal mammary artery graft harvesting in coronary artery bypass surgery: a post hoc analysis from the COMPASS trial. *JAMA Cardiol* 2021;6:1042–9. <https://doi.org/10.1001/jamacardio.2021.1686>
- [23] Gaudino M, Audisio K, Rahouma M, Chadow D, Cancelli G, Soletti GJ, et al. Comparison of long-term clinical outcomes of skeletonized vs pedicled internal thoracic artery harvesting techniques in the arterial revascularization trial. *JAMA Cardiol* 2021;6:1380–6. <https://doi.org/10.1001/jamacardio.2021.3866>
- [24] Taggart DP. How I deploy arterial grafts. *Ann Cardiothorac Surg* 2018;7: 690–7. <https://doi.org/10.21037/acs.2018.09.06>
- [25] Boodhwani M, Lam BK, Nathan HJ, Mesana TG, Ruel M, Zeng W, et al. Skeletonized internal thoracic artery harvest reduces pain and dysesthesia and improves sternal perfusion after coronary artery bypass surgery: a randomized, double-blind, within-patient comparison. *Circulation* 2006; 114:766–73. <https://doi.org/10.1161/CIRCULATIONAHA.106.615427>
- [26] Sa MP, Ferraz PE, Escobar RR, Vasconcelos FP, Ferraz AA, Braile DM, et al. Skeletonized versus pedicled internal thoracic artery and risk of sternal wound infection after coronary bypass surgery: meta-analysis and meta-regression of 4817 patients. *Interact Cardiovasc Thorac Surg* 2013;16:849–57. <https://doi.org/10.1093/icvts/ivt012>
- [27] Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Pawlaczyk R, et al. Pedicled and skeletonized single and bilateral internal thoracic artery grafts and the incidence of sternal wound complications: insights from the arterial revascularization trial. *J Thorac Cardiovasc Surg* 2016;152: 270–6. <https://doi.org/10.1016/j.jtcvs.2016.03.056>
- [28] Gaudino M, Audisio K, Rahouma M, Robinson NB, Soletti GJ, Cancelli G, et al. Association between sternal wound complications and 10-year mortality following coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2023;166:532–9.e4. <https://doi.org/10.1016/j.jtcvs.2021.10.067>
- [29] Perezgrovas-Olaria R, Audisio K, Cancelli G, Rahouma M, Ibrahim M, Soletti GJ, et al. Deep sternal wound infection and mortality in cardiac surgery: a meta-analysis. *Ann Thorac Surg* 2023;115:272–80. <https://doi.org/10.1016/j.athoracsur.2022.04.054>
- [30] Horii T, Suma H. Semiskeletonization of internal thoracic artery: alternative harvest technique. *Ann Thorac Surg* 1997;63:867–8. [https://doi.org/10.1016/S0003-4975\(96\)01123-X](https://doi.org/10.1016/S0003-4975(96)01123-X)
- [31] Maskell P, Berks M, Vibhishanan J, Harky A. In patients undergoing coronary artery bypass grafting is semi-skeletonization superior to pedicled harvesting of the left internal mammary artery? *Interact Cardiovasc Thorac Surg* 2021;33:362–6. <https://doi.org/10.1093/icvts/ivab103>
- [32] Gaudino M, Fremes S, Schwann TA, Tatoulis J, Wingo M, Tranbaugh RF. Technical aspects of the use of the radial artery in coronary artery bypass surgery. *Ann Thorac Surg* 2019;108:613–22. <https://doi.org/10.1016/j.athoracsur.2018.10.066>
- [33] Rukosujew A, Reichelt R, Fabricius AM, Drees G, Tjan TD, Rothenburger M, et al. Skeletonization versus pedicle preparation of the radial artery with and without the ultrasonic scalpel. *Ann Thorac Surg* 2004;77: 120–5. [https://doi.org/10.1016/S0003-4975\(03\)01488-7](https://doi.org/10.1016/S0003-4975(03)01488-7)
- [34] Tatoulis J. The radial artery: an important component of multiarterial coronary surgery and considerations for its optimal harvest. *JTCVS Tech* 2021;5:46–55. <https://doi.org/10.1016/j.jtc.2020.10.042>
- [35] Suma H, Tanabe H, Takahashi A, Horii T, Isomura T, Hirose H, et al. Twenty years experience with the gastroepiploic artery graft for CABG. *Circulation* 2007;116:1188–91. <https://doi.org/10.1161/CIRCULATIONAHA.106.678813>
- [36] Gagliardotto P, Coste P, Lazreg M, Dor V. Skeletonized right gastroepiploic artery used for coronary artery bypass grafting. *Ann Thorac Surg* 1998;66:240–2. [https://doi.org/10.1016/S0003-4975\(98\)00403-2](https://doi.org/10.1016/S0003-4975(98)00403-2)
- [37] Ali E, Saso S, Ashrafian H, Athanasiou T. Does a skeletonized or pedicled right gastroepiploic artery improve patency when used as a conduit in coronary artery bypass graft surgery? *Interact Cardiovasc Thorac Surg* 2010;10:293–8. <https://doi.org/10.1510/icvts.2009.221226>
- [38] Blake KL, Watt PA, Smith JM, De Souza AC, Spyt TJ, Thurston H. Randomized comparison of ultrasonic aspiration versus conventional electrocautery for dissection of the human internal thoracic artery. *J Thorac Cardiovasc Surg* 1996;111:1194–9. [https://doi.org/10.1016/S0022-5223\(96\)70221-0](https://doi.org/10.1016/S0022-5223(96)70221-0)
- [39] Lehtola A, Verkkala K, Jarvinen A. Is electrocautery safe for internal mammary artery (IMA) mobilization? A study using scanning electron microscopy (SEM). *Thorac Cardiovasc Surg* 1989;37:55–7. <https://doi.org/10.1055/s-2007-1013906>
- [40] Yoshida H, Wu MH, Kouchi Y, Onuki Y, Shi Q, Sauvage LR. Comparison of the effect of monopolar and bipolar cauterization on skeletonized, dissected internal thoracic arteries. *J Thorac Cardiovasc Surg* 1995;110: 504–10. [https://doi.org/10.1016/S0022-5223\(95\)70247-4](https://doi.org/10.1016/S0022-5223(95)70247-4)
- [41] Keeley SB. The skeletonized internal mammary artery. *Ann Thorac Surg* 1987;44:324–5. [https://doi.org/10.1016/S0003-4975\(10\)62088-7](https://doi.org/10.1016/S0003-4975(10)62088-7)
- [42] Lamm P, Juchem G, Weyrich P, Schutz A, Reichart B. The harmonic scalpel: optimizing the quality of mammary artery bypass grafts. *Ann Thorac Surg* 2000;69:1833–5. [https://doi.org/10.1016/S0003-4975\(00\)01288-1](https://doi.org/10.1016/S0003-4975(00)01288-1)
- [43] Isomura T, Suma H, Sato T, Horii T. Use of the harmonic scalpel for harvesting arterial conduits in coronary artery bypass. *Eur J Cardiothorac Surg* 1998;14:101–3. [https://doi.org/10.1016/S1010-7940\(98\)00146-8](https://doi.org/10.1016/S1010-7940(98)00146-8)
- [44] Urso S, Alvarez L, Sadaba R, Greco E. Skeletonization of the internal thoracic artery: a randomized comparison of harvesting methods. *Interact Cardiovasc Thorac Surg* 2008;7: 23–6. <https://doi.org/10.1510/icvts.2007.168831>
- [45] Kieser TM, Rose MS, Aluthman U, Narine K. Quicker yet safe: skeletonization of 1640 internal mammary arteries with harmonic technology in 965 patients. *Eur J Cardiothorac Surg* 2014;45:e142–50. <https://doi.org/10.1093/ejcts/ezu024>
- [46] Oz BS, Mataraci I, Iyem H, Kuralay E, Doganci S, Demirkilic U, et al. Comparison of ultrasonically activated scalpel and traditional technique in radial artery harvesting: clinical research. *Thorac Cardiovasc Surg* 2007;55:104–7. <https://doi.org/10.1055/s-2006-924504>
- [47] Brazio PS, Laird PC, Xu C, Gu J, Burris NS, Brown EN, et al. Harmonic scalpel versus electrocautery for harvest of radial artery conduits: reduced risk of spasm and intimal injury on optical coherence tomography. *J Thorac Cardiovasc Surg* 2008;136:1302–8. <https://doi.org/10.1016/j.jtcvs.2008.05.060>
- [48] Ferdinand FD, MacDonald JK, Balkhy HH, Bisleri G, Hwang HY, Northrup P, et al. Endoscopic conduit harvest in coronary artery bypass grafting surgery: an ISMICS systematic review and consensus conference statements. *Innovations (Phi/a)* 2017;12: 301–19. <https://doi.org/10.1097/imi.0000000000000410>
- [49] Perrault LP, Jeanmart H, Bilodeau L, Lesperance J, Tanguay JF, Bouchard D, et al. Early quantitative coronary angiography of saphenous vein grafts for coronary artery bypass grafting harvested by means of open versus endoscopic saphenectomy: a prospective randomized trial. *J Thorac Cardiovasc Surg* 2004;127:1402–7. <https://doi.org/10.1016/j.jtcvs.2003.10.040>
- [50] Yun KL, Wu Y, Aharonian V, Mansukhani P, Pfeffer TA, Sintek CF, et al. Randomized trial of endoscopic versus open vein harvest for coronary

- artery bypass grafting: six-month patency rates. *J Thorac Cardiovasc Surg* 2005;129:496–503. <https://doi.org/10.1016/j.jtcvs.2004.08.054>
- [51] Lopes RD, Hafley GE, Allen KB, Ferguson TB, Peterson ED, Harrington RA, *et al.* Endoscopic versus open vein-graft harvesting in coronary-artery bypass surgery. *N Engl J Med* 2009;361:235–44. <https://doi.org/10.1056/NEJMoa0900708>
- [52] Zenati MA, Shroyer AL, Collins JF, Hattler B, Ota T, Almassi GH, *et al.* Impact of endoscopic versus open saphenous vein harvest technique on late coronary artery bypass grafting patient outcomes in the ROOBY (Randomized On/Off Bypass) trial. *J Thorac Cardiovasc Surg* 2011;141:338–44. <https://doi.org/10.1016/j.jtcvs.2010.10.004>
- [53] Gaudino M, Bakaeen FG, Sandner S, Aldea GS, Arai H, Chikwe J, *et al.* Expert systematic review on the choice of conduits for coronary artery bypass grafting: endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and The Society of Thoracic Surgeons (STS). *Eur J Cardiothorac Surg* 2023;64:ezaad163. <https://doi.org/10.1093/ejcts/ezad163>
- [54] Kodia K, Patel S, Weber MP, Luc JGY, Choi JH, Maynes EJ, *et al.* Graft patency after open versus endoscopic saphenous vein harvest in coronary artery bypass grafting surgery: a systematic review and meta-analysis. *Ann Cardiothorac Surg* 2018;7:586–97. <https://doi.org/10.21037/acs.2018.07.05>
- [55] Li G, Zhang Y, Wu Z, Liu Z, Zheng J. Mid-term and long-term outcomes of endoscopic versus open vein harvesting for coronary artery bypass: a systematic review and meta-analysis. *Int J Surg* 2019;72:167–73. <https://doi.org/10.1016/j.ijsu.2019.11.003>
- [56] Zenati MA, Bhatt DL, Bakaeen FG, Stock EM, Biswas K, Gaziano JM, *et al.* Randomized trial of endoscopic or open vein-graft harvesting for coronary-artery bypass. *N Engl J Med* 2019;380:132–41. <https://doi.org/10.1056/NEJMoa1812390>
- [57] Zenati MA, Bhatt DL, Stock EM, Hattler B, Wagner TH, Bakaeen FG, *et al.* Intermediate-term outcomes of endoscopic or open vein harvesting for coronary artery bypass grafting: the REGROUP randomized clinical trial. *JAMA Netw Open* 2021;4: e211439. <https://doi.org/10.1001/jamanetworkopen.2021.1439>
- [58] Desai P, Kiani S, Thiruvanthan N, Henkin S, Kurian D, Ziu P, *et al.* Impact of the learning curve for endoscopic vein harvest on conduit quality and early graft patency. *Ann Thorac Surg* 2011;91:1385–91. discussion 91–2. <https://doi.org/10.1016/j.athoracsur.2011.01.079>
- [59] Kiaii BB, Swinamer SA, Fox SA, Stitt L, Quantz MA, Novick RJ. A prospective randomized study of endoscopic versus conventional harvesting of the radial artery. *Innovations (Phi/a)* 2017;12:231–8. <https://doi.org/10.1097/imi.0000000000000386>
- [60] Shapira OM, Eskenazi BR, Anter E, Joseph L, Christensen TG, Hunter CT, *et al.* Endoscopic versus conventional radial artery harvest for coronary artery bypass grafting: functional and histologic assessment of the conduit. *J Thorac Cardiovasc Surg* 2006; 131:388–94. <https://doi.org/10.1016/j.jtcvs.2005.07.036>
- [61] Medalion B, Tobar A, Yosibash Z, Stamler A, Sharoni E, Snir E, *et al.* Vasoreactivity and histology of the radial artery: comparison of open versus endoscopic approaches. *Eur J Cardiothorac Surg* 2008;34:845–9. <https://doi.org/10.1016/j.ejcts.2008.06.015>
- [62] Gaudino MF, Lorusso R, Ohmes LB, Narula N, McIntire P, Gargiulo A, *et al.* Open radial artery harvesting better preserves endothelial function compared to the endoscopic approach. *Interact Cardiovasc Thorac Surg* 2019;29:561–7. <https://doi.org/10.1093/icvts/ivz129>
- [63] Cao C, Tian DH, Ang SC, Peeceeyen S, Allan J, Fu B, *et al.* A meta-analysis of endoscopic versus conventional open radial artery harvesting for coronary artery bypass graft surgery. *Innovations (Phi/a)* 2014;9:269–75. <https://doi.org/10.1097/imi.0000000000000087>
- [64] Rahoma M, Kamel M, Benedetto U, Ohmes LB, Di Franco A, Lau C, *et al.* Endoscopic versus open radial artery harvesting: a meta-analysis of randomized controlled and propensity matched studies. *J Card Surg* 2017;32:334–41. <https://doi.org/10.1111/jocs.13148>
- [65] Li FD, Eagle S, Brophy C, Hocking KM, Osgood M, Komalavilas P, *et al.* Pressure control during preparation of saphenous veins. *JAMA Surg* 2014;149:655–62. <https://doi.org/10.1001/jamasurg.2013.5067>
- [66] Angelini GD, Passani SL, Breckenridge IM, Newby AC. Nature and pressure dependence of damage induced by distension of human saphenous vein coronary artery bypass grafts. *Cardiovasc Res* 1987;21:902–7. <https://doi.org/10.1093/cvr/21.12.902>
- [67] Bush HL, Jr., McCabe ME, Nabseth DC. Functional injury of vein graft endothelium. Role of hypothermia and distension. *Arch Surg* 1984;119:770–4. <https://doi.org/10.1001/archsurg.1984.01390190014003>
- [68] Galea J, Armstrong J, Francis SE, Cooper G, Crossman DC, Holt CM. Alterations in c-fos expression, cell proliferation and apoptosis in pressure distended human saphenous vein. *Cardiovasc Res* 1999;44:436–48. [https://doi.org/10.1016/S0008-6363\(99\)00220-5](https://doi.org/10.1016/S0008-6363(99)00220-5)
- [69] Viaro F, Capellini VK, Celotto AC, Carlotti CG, Jr., Rodrigues AJ, Reis GS, *et al.* Immunohistochemical evaluation of three nitric oxide synthase isoforms in human saphenous vein exposed to different degrees of distension pressures. *Cardiovasc Pathol* 2010;19:e211–20. <https://doi.org/10.1016/j.carpath.2009.11.002>
- [70] Stigler R, Steger C, Schachner T, Holfeld J, Edlinger M, Grimm M, *et al.* The impact of distension pressure on acute endothelial cell loss and neointimal proliferation in saphenous vein grafts. *Eur J Cardiothorac Surg* 2012;42:e74–9. <https://doi.org/10.1093/ejcts/ezs402>
- [71] Ahmed SR, Johansson BL, Karlsson MG, Souza DS, Dashwood MR, Loesch A. Human saphenous vein and coronary bypass surgery: ultrastructural aspects of conventional and “no-touch” vein graft preparations. *Histo/Histopathol* 2004;19:421–33. <https://doi.org/10.14670/HH-19.421>
- [72] Dashwood MR, Savage K, Tsui JC, Dooley A, Shaw SG, Fernandez Alfonso MS, *et al.* 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;138:334–40. <https://doi.org/10.1016/j.jtcvs.2008.11.060>
- [73] Verma S, Lovren F, Pan Y, Yanagawa B, Deb S, Karkhanis R, *et al.* Pedicled no-touch saphenous vein graft harvest limits vascular smooth muscle cell activation: the PATENT saphenous vein graft study. *Eur J Cardiothorac Surg* 2014;45:717–25. <https://doi.org/10.1093/ejcts/ezt560>
- [74] Fernandez-Alfonso MS, Gil-Ortega M, Aranguiz I, Souza D, Dreifaldt M, Somoza B, *et al.* Role of PVAT in coronary atherosclerosis and vein graft patency: friend or foe? *Br J Pharmacol* 2017;174:3561–72. <https://doi.org/10.1111/bph.13734>
- [75] Mikami T, Furuhashi M, Sakai A, Numaguchi R, Harada R, Naraoka S, *et al.* Antiatherosclerotic phenotype of perivascular adipose tissue surrounding the saphenous vein in coronary artery bypass grafting. *J Am Heart Assoc* 2021;10:e018905. <https://doi.org/10.1161/JAHA.120.018905>
- [76] Dreifaldt M, Souza DS, Loesch A, Muddle JR, Karlsson MG, Filbey D, *et al.* The “no-touch” harvesting technique for vein grafts in coronary artery bypass surgery preserves an intact vasa vasorum. *J Thorac Cardiovasc Surg* 2011;141:145–50. <https://doi.org/10.1016/j.jtcvs.2010.02.005>
- [77] Deng MX, Lia H, Lee G, Rahoma M, Di Franco A, Demetres M, *et al.* Angiographic patency of coronary artery bypass conduits: an updated network meta-analysis of randomized trials. *Braz J Cardiovasc Surg* 2022;37:7–31. <https://doi.org/10.21470/1678-9741-2022-0142>
- [78] Tian M, Wang X, Sun H, Feng W, Song Y, Lu F, *et al.* No-touch versus conventional vein harvesting techniques at 12 months after coronary artery bypass grafting surgery: multicenter randomized, controlled trial. *Circulation* 2021;144:1120–9. <https://doi.org/10.1161/CIRCULATIONAHA.121.055525>
- [79] Ragnarsson S, Janiec M, Modrau IS, Dreifaldt M, Ericsson A, Holmgren A, *et al.* No-touch saphenous vein grafts in coronary artery surgery (SWDEGRAFT): rationale and design of a multicenter, prospective, registry-based randomized clinical trial. *Am Heart J* 2020;224:17–24. <https://doi.org/10.1016/j.ahj.2020.03.009>
- [80] Hayashi I, Kashima I, Yoshikawa E. The endoscopic no-touch saphenous vein harvesting technique. *Mu/timed Man Cardiothorac Surg* 2020; 2020. <https://doi.org/10.1510/mmcts.2020.049>
- [81] Hayashi I, Kashima I, Yoshikawa E. Use of the no-touch saphenous vein harvesting technique via small incisions. *Innovations (Phi/a)* 2020;15:81–4. <https://doi.org/10.1177/1556984519886549>
- [82] Yoshino K, Abe K, Suzuki K, Tamaki R, Mitsuishi A, Yamasaki M, *et al.* A novel technique of endoscopic vein harvesting with preserved perivascular tissue. *Innovations (Phi/a)* 2020;15:475–7. <https://doi.org/10.1177/1556984520948139>
- [83] Williams JB, Harskamp RE, Bose S, Lawson JH, Alexander JH, Smith PK, *et al.* The preservation and handling of vein grafts in current surgical practice: findings of a survey among cardiovascular surgeons of top-ranked US hospitals. *JAMA Surg* 2015;150: 681–3. <https://doi.org/10.1001/jamasurg.2015.0404>
- [84] Gundry SR, Jones M, Ishihara T, Ferrans VJ. Optimal preparation techniques for human saphenous vein grafts. *Surgery* 1980;88:785–94.
- [85] Wilbring M, Tugtekin SM, Zatschler B, Ebner A, Reichenspurner H, Matschke K, *et al.* Even short-time storage in physiological saline solution impairs endothelial vascular function of saphenous vein grafts. *Eur J Cardiothorac Surg* 2011;40:811–5. <https://doi.org/10.1016/j.ejcts.2011.01.024>

- [86] Biswas KS, Thatte HS, Najjar SF, Rhee JH, Birjiniuk V, Crittenden MD, et al. Multi-photon microscopy in the evaluation of human saphenous vein. *J Surg Res* 2001;95:37–43. <https://doi.org/10.1006/jsre.2000.6019>
- [87] Catinella FP, Cunningham JN, Jr., Srungaram RK, Baumann FG, Nathan IM, Glassman EA, et al. The factors influencing early patency of coronary artery bypass vein grafts: correlation of angiographic and ultrastructural findings. *J Thorac Cardiovasc Surg* 1982;83:686–700. [https://doi.org/10.1016/S0022-5223\(19\)37208-3](https://doi.org/10.1016/S0022-5223(19)37208-3)
- [88] Lawrie GM, Weilbacher DE, Henry PD. Endothelium-dependent relaxation in human saphenous vein grafts. Effects of preparation and clinicopathologic correlations. *J Thorac Cardiovasc Surg* 1990;100:612–20. [https://doi.org/10.1016/S0022-5223\(19\)35507-2](https://doi.org/10.1016/S0022-5223(19)35507-2)
- [89] Wilbring M, Ebner A, Schoenemann K, Knaut M, Tugtekin SM, Zatschler B, et al. Heparinized blood better preserves cellular energy charge and vascular functions of in- traoperatively stored saphenous vein grafts in comparison to isotonic sodium-chloride- solution. *Clin Hemorheol Microcirc* 2013;55:445–55. <https://doi.org/10.3233/CH-131781>
- [90] Zerkowski HR, Knocks M, Konerding MA, Doetsch N, Roth G, Hakim K, et al. Endothelial damage of the venous graft in CABG. Influence of solutions used for storage and rinsing on endothelial function. *Eur J Cardiothorac Surg* 1993;7:376–82. [https://doi.org/10.1016/1010-7940\(93\)90070-R](https://doi.org/10.1016/1010-7940(93)90070-R)
- [91] Chong WC, Ong PJ, Hayward C, Moat N, Collins P. Effects of storage solutions on in vitro vasoreactivity of radial artery conduits. *J Thorac Cardiovasc Surg* 2001;122:470–5. <https://doi.org/10.1067/mtc.2001.115921>
- [92] Ben Ali W, Bouhout I, Perrault LP. The effect of storage solutions, gene therapy, and antiproliferative agents on endothelial function and saphenous vein graft patency. *J Card Surg* 2018;33:2352. <https://doi.org/10.1111/jocs.13608>
- [93] Harskamp RE, Alexander JH, Schulte PJ, Brophy CM, Mack MJ, Peterson ED, et al. Vein graft preservation solutions, patency, and outcomes after coronary artery bypass graft surgery: follow-up from the PREVENT IV randomized clinical trial. *JAMA Surg* 2014; 149:798–805. <https://doi.org/10.1001/jamasurg.2014.87>
- [94] Tatoulis J, Jiang GC, Moffatt JD, Cocks TM. Storage of radial artery grafts in blood increases vessel reactivity to vasoconstrictors in vitro. *Ann Thorac Surg* 1999;68:2191–5. [https://doi.org/10.1016/S0003-4975\(99\)01065-6](https://doi.org/10.1016/S0003-4975(99)01065-6)
- [95] Thatte HS, Biswas KS, Najjar SF, Birjiniuk V, Crittenden MD, Michel T, et al. Multi-photon microscopic evaluation of saphenous vein endothelium and its preservation with a new solution, GALA. *Ann Thorac Surg* 2003;75:1145–52; discussion 52. [https://doi.org/10.1016/S0003-4975\(02\)04705-7](https://doi.org/10.1016/S0003-4975(02)04705-7)
- [96] Perrault LP, Carrier M, Voisine P, Olsen PS, Noiseux N, Jeanmart H, et al. Sequential multidetector computed tomography assessments after venous graft treatment solution in coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2021;161:96–106.e2. <https://doi.org/10.1016/j.jtcvs.2019.10.115>
- [97] Tekin I, Demir M, Ozdem S. Effect of different storage solutions on oxidative stress in human saphenous vein grafts. *J Cardiothorac Surg* 2022; 17:7. <https://doi.org/10.1186/s13019-022-01752-7>
- [98] Nazari-Shafti TZ, Thau H, Zacharova E, Beez CM, Exarchos V, Neuber S, et al. Endothelial damage inhibitor preserves the integrity of venous endothelial cells from patients undergoing coronary bypass surgery. *Eur J Cardiothorac Surg* 2023;64: ezad327. <https://doi.org/10.1093/ejcts/ezad327>
- [99] Aschacher T, Baranyi U, Aschacher O, Eichmair E, Messner B, Zimpfer D, et al. A novel endothelial damage inhibitor reduces oxidative stress and improves cellular integrity in radial artery grafts for coronary artery bypass. *Front Cardiovasc Med* 2021;8:736503. <https://doi.org/10.3389/fcvm.2021.736503>
- [100] <https://www.nice.org.uk/advice/mib184/chapter/The-technology>
- [101] He GW, Taggart DP. Spasm in arterial grafts in coronary artery bypass grafting surgery. *Ann Thorac Surg* 2016;101:1222–9. <https://doi.org/10.1016/j.athoracsur.2015.09.071>
- [102] He GW. Contractility of the human internal mammary artery at the distal section increases toward the end. Emphasis on not using the end of the internal mammary artery for grafting. *J Thorac Cardiovasc Surg* 1993;106:406–11. [https://doi.org/10.1016/S0022-5223\(19\)34072-3](https://doi.org/10.1016/S0022-5223(19)34072-3)
- [103] Davie AP, Love MP, McMurray JJ. Even low-dose aspirin inhibits arachidonic acid- induced vasodilation in heart failure. *Clin Pharmacol Ther* 2000;67:530–7. <https://doi.org/10.1067/mcp.2000.106290>
- [104] Lawton JS, Barner HB, Bailey MS, Guthrie TJ, Moazami N, Pasque MK, et al. Radial artery grafts in women: utilization and results. *Ann Thorac Surg* 2005;80:559–63. <https://doi.org/10.1016/j.athoracsur.2005.02.055>
- [105] Joannides R, Costentin A, Iacob M, Compagnon P, Lahary A, Thuillez C. Influence of vascular dimension on gender difference in flow-dependent dilatation of peripheral conduit arteries. *Am J Physiol Heart Circ Physiol* 2002;282:H1262–9. <https://doi.org/10.1152/ajpheart.00209.2001>
- [106] Dignan RJ, Yeh T, Jr., Dyke CM, Lutz HA, Jr., Wechsler AS. The influence of age and sex on human internal mammary artery size and reactivity. *Ann Thorac Surg* 1992;53: 792–7. [https://doi.org/10.1016/0003-4975\(92\)91438-F](https://doi.org/10.1016/0003-4975(92)91438-F)
- [107] Mannacio V, Di Tommaso L, Antignano A, De Amicis V, Stassano P, Pinna GB, et al. Endothelial nitric oxide synthase expression in postmenopausal women: a sex-specific risk factor in coronary surgery. *Ann Thorac Surg* 2012;94:1934–9. <https://doi.org/10.1016/j.athoracsur.2012.06.040>
- [108] Huxley VH, Kemp SS. Sex-specific characteristics of the microcirculation. *Adv Exp Med Biol* 2018;1065:307–28. https://doi.org/10.1007/978-3-319-77932-4_20
- [109] Lamin V, Jaghoori A, Jakobczak R, Stafford I, Heresztyn T, Worthington M, et al. Mechanisms responsible for serotonin vascular reactivity sex differences in the internal mammary artery. *J Am Heart Assoc* 2018;7: e007126. <https://doi.org/10.1161/JAHA.117.007126>
- [110] Jaghoori A, Lamin V, Jakobczak R, Worthington M, Edwards J, Viana F, et al. Sex differences in vascular reactivity of coronary artery bypass graft conduits. *Heart Vessels* 2020;35:422–31. <https://doi.org/10.1007/s00380-019-01508-9>
- [111] Akar F, Manavbasi Y, Parlar AI, Ulus AT, Katircioglu SF. The gender differences in the relaxation to levosimendan of human internal mammary artery. *Cardiovasc Drugs Ther* 2007;21:331–8. <https://doi.org/10.1007/s10557-007-6047-x>
- [112] Muir AD, McKeown PP, Bayraktutan U. Role of gender, smoking profile, hypertension, and diabetes on saphenous vein and internal mammary artery endothelial relaxation in patients with coronary artery bypass grafting. *Oxid Med Cell Longev* 2010;3:199–205. <https://doi.org/10.4161/oxim.3.3.11757>
- [113] Riedel K, Deussen AJ, Tolkmitt J, Weber S, Schlinkert P, Zatschler B, et al. Estrogen determines sex differences in adrenergic vessel tone by regulation of endothelial beta-adrenoceptor expression. *Am J Physiol Heart Circ Physiol* 2019;317:H243–54. <https://doi.org/10.1152/ajpheart.00456.2018>
- [114] Masroor M, Zhou K, Chen C, Fu X, Zhao Y. All we need to know about internal thoracic artery harvesting and preparation for myocardial revascularization: a systematic review. *J Cardiothorac Surg* 2021;16:354. <https://doi.org/10.1186/s13019-021-01733-2>
- [115] Formica F, Ferro O, Brustia M, Corti F, Colagrande L, Bosisio E, et al. Effects of papaverine and glycerylnitrate-verapamil solution as topical and intraluminal vasodilators for internal thoracic artery. *Ann Thorac Surg* 2006;81:120–4. <https://doi.org/10.1016/j.athoracsur.2005.06.037>
- [116] Dregelid E, Heldal K, Resch F, Stangeland L, Breivik K, Svendsen E. Dilation of the internal mammary artery by external and intraluminal papaverine application. *J Thorac Cardiovasc Surg* 1995;110:697–703. [https://doi.org/10.1016/S0022-5223\(95\)70101-X](https://doi.org/10.1016/S0022-5223(95)70101-X)
- [117] Mayranpaa M, Simpanen J, Hess MW, Werkkala K, Kovanen PT. Arterial endothelial denudation by intraluminal use of papaverine-NaCl solution in coronary bypass surgery. *Eur J Cardiothorac Surg* 2004;25:560–6. <https://doi.org/10.1016/j.ejcts.2004.01.006>
- [118] Cooper GJ, Wilkinson GA, Angelini GD. Overcoming perioperative spasm of the internal mammary artery: which is the best vasodilator? *J Thorac Cardiovasc Surg* 1992;104:465–8. [https://doi.org/10.1016/S0022-5223\(19\)34805-6](https://doi.org/10.1016/S0022-5223(19)34805-6)
- [119] He GW, Taggart DP. Antispastic management in arterial grafts in coronary artery bypass grafting surgery. *Ann Thorac Surg* 2016;102:659–68. <https://doi.org/10.1016/j.athoracsur.2016.03.017>
- [120] He GW. Verapamil plus nitroglycerin solution maximally preserves endothelial function of the radial artery: comparison with papaverine solution. *J Thorac Cardiovasc Surg* 1998;115:1321–7. [https://doi.org/10.1016/S0022-5223\(98\)70215-6](https://doi.org/10.1016/S0022-5223(98)70215-6)
- [121] Robinson NB, Audisio K, Cancelli G, Masterson Creber RM, Fremes SE, Gelijns AC, et al. Current practice patterns for use of the radial artery for coronary surgery in dedicated centers. *J Thorac Cardiovasc Surg* 2022; 163:e251–2. <https://doi.org/10.1016/j.jtcvs.2021.09.035>
- [122] Goldman S, Copeland J, Mortiz T, Henderson W, Zadina K, Ovitt T, et al. Improvement in early saphenous vein graft patency after coronary artery bypass surgery with antiplatelet therapy: results of a veterans administration cooperative study. *Circulation* 1988;77:1324–32. <https://doi.org/10.1161/01.CIR.77.6.1324>
- [123] Lorenz RL, Schacky CV, Weber M, Meister W, Kotzur J, Reichardt B, et al. Improved aortocoronary bypass patency by low-dose aspirin (100 mg daily). Effects on platelet aggregation and thromboxane formation. *Lancet* 1984;1:1261–4. [https://doi.org/10.1016/S0140-6736\(84\)92446-2](https://doi.org/10.1016/S0140-6736(84)92446-2)

- [124] Fremes SE, Levinton C, Naylor CD, Chen E, Christakis GT, Goldman BS. Optimal antithrombotic therapy following aortocoronary bypass: a meta-analysis. *Eur J Cardiothorac Surg* 1993;7:169–80. [https://doi.org/10.1016/1010-7940\(93\)90155-5](https://doi.org/10.1016/1010-7940(93)90155-5)
- [125] Solo K, Lavi S, Kabali C, Levine GN, Kulik A, John-Baptiste AA, *et al.* Antithrombotic treatment after coronary artery bypass graft surgery: systematic review and network meta-analysis. *BMJ* 2019;367:15476. <https://doi.org/10.1136/bmj.15476>
- [126] Deo SV, Dunlay SM, Shah IK, Altarabsheh SE, Enwin PJ, Boilson BA, *et al.* Dual anti-platelet therapy after coronary artery bypass grafting: is there any benefit? A systematic review and meta-analysis. *J Card Surg* 2013; 28:109–16. <https://doi.org/10.1111/jocs.12074>
- [127] Cardoso R, Knijnik L, Whelton SP, Rivera M, Gluckman TJ, Metkus TS, *et al.* Dual versus single antiplatelet therapy after coronary artery bypass graft surgery: an updated meta-analysis. *Int J Cardiol* 2018;269:80–8. <https://doi.org/10.1016/j.ijcard.2018.07.083>
- [128] Triska J, Maitra N, Deshotels MR, Haddadin F, Angiolillo DJ, Vilahur G, *et al.* A comprehensive review of the pleiotropic effects of ticagrelor. *Cardiovasc Drugs Ther* 2022;38: 775–97. <https://doi.org/10.1007/s10557-022-07373-5>
- [129] Zhao Q, Zhu Y, Xu Z, Cheng Z, Mei J, Chen X, *et al.* Effect of ticagrelor plus aspirin, ticagrelor alone, or aspirin alone on saphenous vein graft patency 1 year after coronary artery bypass grafting: a randomized clinical trial. *JAMA* 2018;319:1677–86. <https://doi.org/10.1001/jama.2018.3197>
- [130] Sandner S, Redfors B, Angiolillo DJ, Audisio K, Fremes SE, Janssen PWA, *et al.* Association of dual antiplatelet therapy with ticagrelor with vein graft failure after coronary artery bypass graft surgery: a systematic review and meta-analysis. *JAMA* 2022; 328:554–62. <https://doi.org/10.1001/jama.2022.11966>
- [131] Post Coronary Artery Bypass Graft Trial I. The effect of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation on obstructive changes in saphenous-vein coronary-artery bypass grafts. *N Engl J Med* 1997;336: 153–62. <https://doi.org/10.1056/NEJM199701163360301>
- [132] Gaudino M, Luciani N, Nasso G, Salica A, Canosa C, Possati G. Is postoperative calcium channel blocker therapy needed in patients with radial artery grafts? *J Thorac Cardiovasc Surg* 2005;129:532–5. <https://doi.org/10.1016/j.jtcvs.2004.07.054>
- [133] Miwa S, Desai N, Koyama T, Chan E, Cohen EA, Fremes SE, *et al.* Radial artery angiograph-ic string sign: clinical consequences and the role of pharmacologic therapy. *Ann Thorac Surg* 2006;81:112–8; discussion 9. <https://doi.org/10.1016/j.athoracsur.2005.06.076>
- [134] Gaudino M, Benedetto U, Fremes SE, Hare DL, Hayward P, Moat N, *et al.* Effect of calcium-channel blocker therapy on radial artery grafts after coronary bypass surgery. *J Am Coll Cardiol* 2019;73:2299–306. <https://doi.org/10.1016/j.jacc.2019.02.054>
- [135] Gaudino M, Prati F, Caradonna E, Trani C, Burzotta F, Schiavoni G, *et al.* Implantation in coronary circulation induces morphofunctional transformation of radial grafts from muscular to elastomuscular. *Circulation* 2005; 112:1208–11. <https://doi.org/10.1161/CIRCULATIONAHA.104.512889>
- [136] Shapira OM, Alkon JD, Macron DS, Keaney JF, Jr., Vita JA, Aldea GS, *et al.* Nitroglycerin is preferable to diltiazem for prevention of coronary bypass conduit spasm. *Ann Thorac Surg* 2000;70:883–8. [https://doi.org/10.1016/S0003-4975\(00\)01628-3](https://doi.org/10.1016/S0003-4975(00)01628-3)
- [137] Goldman S, Copeland J, Moritz T, Henderson W, Zadina K, Ovitt T, *et al.* Saphenous vein graft patency 1 year after coronary artery bypass surgery and effects of antiplatelet therapy. Results of a veterans administration cooperative study. *Circulation* 1989; 80:1190–7. <https://doi.org/10.1161/01.CIR.80.5.1190>
- [138] Musleh G, Dunning J. Does aspirin 6 h after coronary artery bypass grafting optimise graft patency? *Interact Cardiovasc Thorac Surg* 2003;2: 413–5. [https://doi.org/10.1016/S1569-9293\(03\)00181-6](https://doi.org/10.1016/S1569-9293(03)00181-6)
- [139] Sharma GV, Khuri SF, Josa M, Folland ED, Parisi AF. The effect of antiplatelet therapy on saphenous vein coronary artery bypass graft patency. *Circulation* 1983;68:11218–21.
- [140] Patrono C, Garcia Rodriguez LA, Landolfi R, Baigent C. Low-dose aspirin for the prevention of atherothrombosis. *N Engl J Med* 2005;353: 2373–83. <https://doi.org/10.1056/NEJMra052717>
- [141] Mahaffey KW, Held C, Wojdyla DM, James SK, Katus HA, Husted S, *et al.* Ticagrelor effects on myocardial infarction and the impact of event adjudication in the PLATO (Platelet Inhibition and Patient Outcomes) trial. *J Am Coll Cardiol* 2014;63:1493–9. <https://doi.org/10.1016/j.jacc.2014.01.038>
- [142] Mangano DT; Multicenter study of perioperative ischemia research G. Aspirin and mortality from coronary bypass surgery. *N Engl J Med* 2002; 347:1309–17. <https://doi.org/10.1056/NEJMoa020798>
- [143] Cleland JGF. Aspirin for primary and secondary prevention of cardiovascular disease: time to stop? *Thromb Haemost* 2022;122:311. <https://doi.org/10.1055/s-0041-1740639>
- [144] Hastings S, Myles P, McIlroy D. Aspirin and coronary artery surgery: a systematic review and meta-analysis. *Br J Anaesth* 2015;115:376–85. <https://doi.org/10.1093/bja/aev164>
- [145] Goldman S, Copeland J, Moritz T, Henderson W, Zadina K, Ovitt T, *et al.* Long-term graft patency (3 years) after coronary artery surgery: effects of aspirin: results of a VA cooperative study. *Circulation* 1994;89:11383. <https://doi.org/10.1161/01.CIR.89.3.1138>
- [146] Nocerino AG, Achenbach S, Taylor AJ. Meta-analysis of effect of single versus dual anti-platelet therapy on early patency of bypass conduits after coronary artery bypass grafting. *Am J Cardiol* 2013;112:1576–9. <https://doi.org/10.1016/j.amjcard.2013.07.017>
- [147] Harik L, Perezgrovas-Olaria R, Soletti G, Jr., Dimagli A, Alzghari T, An KR, *et al.* Graft thrombosis after coronary artery bypass surgery and current practice for prevention. *Front Cardiovasc Med* 2023;10:1125126. <https://doi.org/10.3389/fcvm.2023.1125126>
- [148] Sandner S, Gaudino M, Redfors B, Angiolillo DJ, Ben-Yehuda O, Bhatt DL, *et al.* One-month DAPT with ticagrelor and aspirin for patients undergoing coronary artery bypass grafting: rationale and design of the randomised, multicentre, double-blind, placebo-controlled ODIN trial. *EuroIntervention* 2024;20:e322–8. <https://doi.org/10.4244/EIJ-D-23-00699>
- [149] Calderone D, Capodanno D, Angiolillo DJ. An updated drug profile of ticagrelor with considerations on the treatment of patients with coronary artery disease and diabetes mellitus. *Expert Rev Cardiovasc Ther* 2020;18:449–64. <https://doi.org/10.1080/14779072.2020.1792293>
- [150] Sibbing D, Aradi D, Alexopoulos D, Ten Berg J, Bhatt DL, Bonello L, *et al.* Updated expert consensus statement on platelet function and genetic testing for guiding P2Y₁₂ receptor inhibitor treatment in percutaneous coronary intervention. *JACC Cardiovasc Interv* 2019;12:1521–37. <https://doi.org/10.1016/j.jcin.2019.03.034>
- [151] Gao C, Ren C, Li D, Li L. Clopidogrel and aspirin versus clopidogrel alone on graft patency after coronary artery bypass grafting. *Ann Thorac Surg* 2009;88:59–62. <https://doi.org/10.1016/j.athoracsur.2009.04.024>
- [152] Kulik A, Abreu AM, Boronat V, Kouchoukos NT, Ruel M. Ticagrelor versus aspirin and vein graft patency after coronary bypass: a randomized trial. *J Card Surg* 2022;37: 563–70. <https://doi.org/10.1111/jocs.16189>
- [153] Lamy A, Eikelboom J, Sheth T, Connolly S, Bosch J, Fox KAA, *et al.* Rivaroxaban, aspirin, or both to prevent early coronary bypass graft occlusion: the COMPASS- CABG study. *J Am Coll Cardiol* 2019;73:121–30. <https://doi.org/10.1016/j.jacc.2018.10.048>
- [154] Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, *et al.* 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2020;41: 111–88. <https://doi.org/10.1093/eurheartj/ehz455>
- [155] Kostis WJ, Cheng JQ, Dobrzynski JM, Cabrera J, Kostis JB. Meta-analysis of statin effects in women versus men. *J Am Coll Cardiol* 2012;59: 572–82. <https://doi.org/10.1016/j.jacc.2011.09.067>
- [156] Gaudino M, Di Franco A, Cao D, Giustino G, Bairey Merz CN, Fremes SE, *et al.* Sex-related outcomes of medical, percutaneous, and surgical interventions for coronary artery disease: JACC focus seminar 3/7. *J Am Coll Cardiol* 2022;79:1407–25. <https://doi.org/10.1016/j.jacc.2021.07.066>
- [157] Campeau L, Enjalbert M, Lesperance J, Bourassa MG, Kwitrovich P, Jr., Wacholder S, *et al.* The relation of risk factors to the development of atherosclerosis in saphenous-vein bypass grafts and the progression of disease in the native circulation. A study 10 years after aortocoronary bypass surgery. *N Engl J Med* 1984;311:1329–32. <https://doi.org/10.1056/NEJM198411223112101>
- [158] Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, *et al.* Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* 2017;38:2459–72. <https://doi.org/10.1093/eurheartj/ehx144>
- [159] Makuuchi H, Furuse A, Endo M, Nakamura H, Daida H, Watanabe M, *et al.* Effect of pravastatin on progression of coronary atherosclerosis in patients after coronary artery bypass surgery. *Circ J* 2005;69:636–43. <https://doi.org/10.1253/circj.69.636>
- [160] Kulik A, Abreu AM, Boronat V, Ruel M. Intensive versus moderate statin therapy and early graft occlusion after coronary bypass surgery: The

- Aggressive Cholesterol Therapy to Inhibit Vein Graft Events randomized clinical trial. *J Thorac Cardiovasc Surg* 2019;157:151–61.e1. <https://doi.org/10.1016/j.jtcvs.2018.05.123>
- [161] Kulik A, Voisine P, Mathieu P, Masters RG, Mesana TG, Le May MR, *et al.* Statin therapy and saphenous vein graft disease after coronary bypass surgery: analysis from the CASCADE randomized trial. *Ann Thorac Surg* 2011;92:1284–91. <https://doi.org/10.1016/j.athoracsur.2011.04.107>
- [162] Katsuki S, Jha PK, Lupieri A, Nakano T, Passos LSA, Rogers MA, *et al.* Proprotein convertase subtilisin/kexin 9 (PCSK9) promotes macrophage activation via LDL receptor-independent mechanisms. *Circ Res* 2022; 131:873–89. <https://doi.org/10.1161/CIRCRESAHA.121.320056>
- [163] Gao J, Wang HB, Xiao JY, Ren M, Reilly KH, Li YM, *et al.* Association between proprotein convertase subtilisin/kexin type 9 and late saphenous vein graft disease after coronary artery bypass grafting: a cross-sectional study. *BMJ Open* 2018;8:e021951. <https://doi.org/10.1136/bmjopen-2018-021951>
- [164] Vaccarino V, Abramson JL, Veledar E, Weintraub WS. Sex differences in hospital mortality after coronary artery bypass surgery: evidence for a higher mortality in younger women. *Circulation* 2002;105:1176–81. <https://doi.org/10.1161/hc1002.105133>
- [165] Nelson K, Fuster V, Ridker PM. Low-dose colchicine for secondary prevention of coronary artery disease: JACC review topic of the week. *J Am Coll Cardiol* 2023;82:648–60. <https://doi.org/10.1016/j.jacc.2023.05.055>
- [166] Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, *et al.* Colchicine in patients with chronic coronary disease. *N Engl J Med* 2020;383:1838–47. <https://doi.org/10.1056/NEJMoa2021372>