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REVIEW ARTICLE

Current role of saphenous vein graft in coronary artery bypass grafting

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Abstract

Saphenous vein was the conduit used in the first series of coronary artery bypass grafting (CABG), and, with the exception of surgical revascularization of the left anterior descending artery, it remains the most commonly used bypass conduit. However, its durability and longevity are not ideal. Arterial grafts have better patency than saphenous vein grafts and therefore should be preferred over them. However, in certain situations, like grafting right coronary arteries with lesser degree of proximal stenosis and higher competitive flow, or in certain patient populations, like those at very high risk of wound infections and octogenarians, arterial grafting may not be the best option and saphenous vein grafting should be considered instead.

Keywords Saphenous vein grafts · Surgical revascularization · Coronary surgery

Introduction

Coronary artery disease (CAD) is the most common cause of death worldwide making it one of the most important public health issues [1]. Treatment options include medical management, percutaneous coronary intervention (PCI), and CABG surgery. For patients with complex multivessel CAD, CABG is the treatment of choice, making it one of the most commonly performed surgeries in the world, with about 400,000 procedures performed in USA alone [2, 3]. The effectiveness of coronary surgery is directly related to bypass graft patency. Arterial grafts have better patency than vein grafts and thus are preferred conduits. However, in certain situations or patient populations, arterial grafting may not be the best option and saphenous vein grafting should be considered instead.

In this review, we have examined the role of saphenous vein as a bypass conduit, described mechanism and risk factors for its failure, identified strategies to improve its durability, and discussed its current role in coronary artery bypass grafting.

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Saphenous vein as bypass conduit

The commonly used grafts in surgical revascularization include internal thoracic artery (ITA), radial artery, gastroepiploic artery, and the saphenous vein [4]. Saphenous vein was the conduit used in the first series of CABG and except for the revascularization of the left anterior descending coronary artery (LAD), it remains the most commonly used bypass conduit [5]. This is because it is easily harvested and is technically easy to use due to its wall characteristics and large diameter. Also, because it is long and plentiful, it can reach any coronary artery and can be used to graft multiple vessels. However, its durability and longevity are not ideal. One year after CABG, 10 to 20% of saphenous vein grafts fail [6–8]. From 1 to 5 years, an additional 5 to 10% fail, and from 6 to 10 years, an additional 20 to 25% fail [9]. Ten years after surgery, only about half of saphenous vein grafts are patent, and of those, only half are free of stenosis [10].

Mechanism of saphenous vein graft failure

Early saphenous vein graft failure, occurring during first year of surgery, occurs due to technical errors, thrombosis, and intimal hyperplasia [11, 12]. During initial harvesting and preparation, venous conduits undergo a period of ischemia and distention from reperfusion resulting in increases in oxidation stress and damage to the endothelial lining of the lumen. Furthermore, initial exposure to arterial pressure also results in endothelial damage [13, 14]. This leads to platelet adherence which may result in graft thrombosis and acute occlusion. The adherence of platelets to the intima also serves as the initial event in the development of intimal hyperplasia. Platelets, after adhering to the intimal surface, release mitogenic proteins leading to smooth muscle cell migration which results in intimal proliferation and hyperplasia [15–18].

Late failure, occurring after a year from surgery, occurs due to arteriosclerosis [19, 20]. Mural thrombi and intimal hyperplasia are the early stages of arteriosclerosis [8, 19]. With time, lipid accumulates in the areas of intimal hyperplasia, resulting in arteriosclerotic plaque, and eventual graft stenosis or occlusion [16, 17, 20, 21].

Risk factors of saphenous vein graft failure

Saphenous vein graft failure can be due to both, patient-related and surgical factors. Patient-related factors include demographic and clinical factors such as Hispanic race, hyperlipidemia, hypertension, renal insufficiency, and current tobacco use [22, 23]. Female gender is also a risk factor and is largely attributable to smaller coronary vessel diameter [23, 24]. Surprisingly, diabetes is not a risk factor for saphenous vein graft occlusion. A recent study assessed 20,066 saphenous grafts and 7903 ITA grafts and found no influence of diabetes on ITA or saphenous vein graft patency over more than 20 years after CABG. ITA graft patency remained stable over time, whereas saphenous vein graft patency declined progressively for patients with and without diabetes. Because patients with diabetes have more severe coronary artery stenosis, one would expect that stenosis in their bypass grafts would also be more severe than in patients without diabetes, resulting in lower graft patency. However, this does not appear to be the case [25]. This is important because the proportion of patients undergoing CABG who have diabetes have increased over the last few decades and today, diabetic patients represent nearly 40 to 50% of all patients undergoing CABG [26, 27].

Surgical factors associated with vein graft failure injury include injury to the graft during harvesting, preparation, and initial exposure to arterial pressures. Small target vessel diameter (≤ 1.5 mm) also plays a role [28]. In the Reduction in Graft Occlusion Rates (RIGOR) study population, this was a strong predictor of saphenous vein graft occlusion and was thought to be due to impaired distal run-off [23]. Low mean graft blood flow also plays a role in saphenous vein graft failure. A study by McLean et al. showed a 14% increase in the odds of saphenous vein graft occlusion for every 10 ml/min decrease in flow [23].

Strategies to reduce SV graft failure

Surgical strategies

Harvesting

Endothelial damage during vein graft harvesting is known to be an important cause of vein graft failure. Graft injury during harvesting can serve as an inciting event leading to a cascade of endothelial pathways ultimately resulting in atherosclerosis and graft failure. Therefore, efforts should be made to harvest the vein atraumatically. Endoscopic vein harvesting is an atraumatic procedure that involves harvesting a saphenous vein without direct contact or manipulation of the vein. This technique is beneficial in reducing wound-related complications and postoperative pain and morbidity compared with open vein harvest technique. However, the Randomized On/Off Bypass (ROOBY) trial showed that endoscopic vein harvesting was associated with lower 1-year SV graft patency and higher 1-year revascularization rates compared with open harvesting [29]. More recently, Hess et al. also reported higher rates of graft failure in patients who underwent endoscopic vein harvesting 12–18 months after CABG in the PREVENT IV trial [30]. The on-going Randomized Endo-Vein Graft Prospective (REGROUP) trial aims to compare endoscopic vein harvest with open harvest in terms of major adverse cardiac events and may provide definitive evidence in this regard [31]. It is important to note, however, that whether the procedure is performed via open vein harvesting or endoscopically, the key is to take the vein atraumatically, which requires a skilled operator. Due to the improved patient comfort and reduction in leg complications—which in previous years were pervasive and common—open vein harvesting may become obsolete someday. However, the proper operator training with endoscopic vein harvesting needs to occur.

An atraumatic, "no-touch" technique for harvesting the saphenous vein has also been developed. This involves harvesting the vein with a pedicle of surrounding tissue maintaining the vasa vasorae and the nerves in the adventitia. This protects the vein from spasm and prevents the need for distension. However, wound complications remain an important issue with the use of this technique [32]. A randomized trial from a single center in Sweden showed that use of SV grafts, harvested using no-touch technique compared to conventional technique, to non-LAD targets, can provide long-term patency comparable to that of left ITA to LAD [33].

Preservation

The graft preservation solutions used after procurement and before implantation are a relatively understudied and neglected area [34]. We now know that normal saline and blood-based media are not appropriate solutions for vein preservation. Buffered saline solutions should be used instead as they have shown to have lower vein graft failure rates and trend toward better long-term clinical outcomes compared with patients in which saline- or blood-based solutions are used for graft preservation [35].

External stenting of veins

Taggart et al. have recently shown that external stents have the potential to reduce the process of diffuse intimal hyperplasia in saphenous vein grafts 1 year after CABG [36]. They prevent saphenous vein graft distension when exposed to arterial pressures and hence prevent injury. In their study, 30 patients underwent on-pump multivessel CABG including a left ITA to the LAD and saphenous vein grafts to right and circumflex territories. Each patient received one external stent device to a single saphenous vein graft to either the right or the circumflex artery. Results showed that external stenting of saphenous vein graft had a significant reduction of intimal hyperplasia by approximately 15% and a reduction in intimal thickness. When comparing

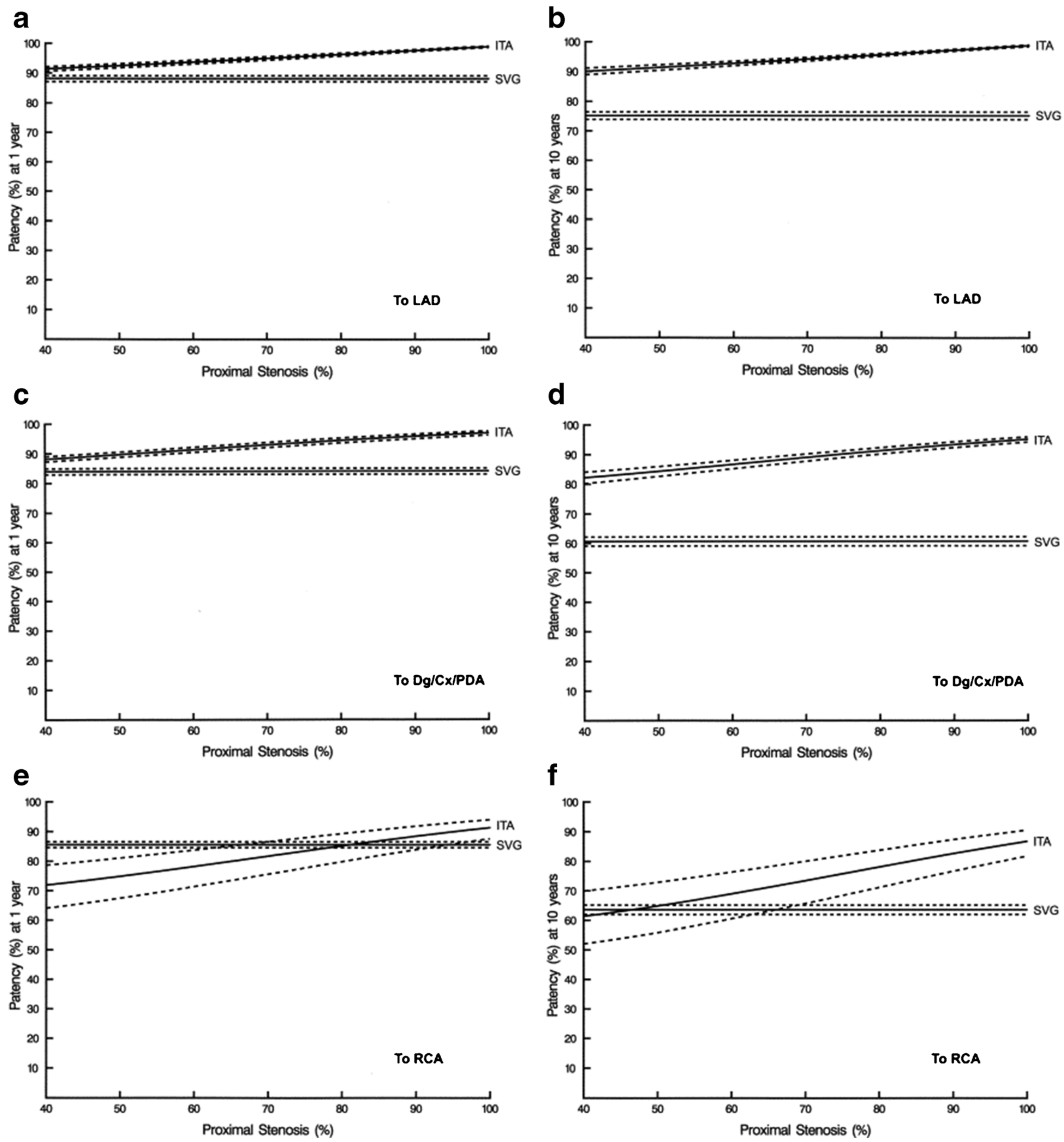

Fig. 1. Estimates of 1- and 10-year ITA and SVG patency according to coronary artery grafted and degree of proximal coronary stenosis. Solid lines are point estimates; dashed lines are 70% confidence intervals. Graphs depict a 65-year-old male non-diabetic undergoing CABG in 1974. **a** Grafts to the LAD 1 year after CABG. **b** Grafts to the LAD 10 years after CABG. **c** Grafts to the Dg, Cx, and PDA 1 year after CABG. **d** Grafts to the Dg, Cx, and PDA 10 years after CABG. **e** Grafts to the RCA 1 year after CABG. **f** Grafts to the RCA 10 years after CABG. Cx circumflex marginals, Dg diagonals, ITA internal thoracic artery, LAD left anterior descending coronary artery, PDA posterior descending artery, RCA right coronary artery, SVG saphenous vein graft. Reproduced with permission from Elsevier from reference 6

stented versus non-stented saphenous vein grafts, ligating saphenous vein side branches with sutures rather than metallic clips was associated with a reduction in both plaque area and thickness. The sutures also resulted in more uniform saphenous vein graft lumen in the stented group.

Pharmacological strategy after CABG

Antiplatelet and lipid-lowering therapies are clinically proven to prevent vein graft failure. Dual antiplatelet therapy with aspirin and clopidogrel after CABG has shown to improve early saphenous vein graft patency and is traditionally used [37, 38]. However, the Platelet Inhibition and Patient Outcomes (PLATO) study showed that tricagrelor may be more effective in preventing recurrent cardiovascular events compared to clopidogrel in patients with prior coronary artery bypass graft surgery [39]. Lipid-lowering agents such as statins are also recommended. The Post Coronary Artery Bypass Graft Trial compared the effects of two lipid-lowering regimens on patients who had undergone bypass surgery and reported that aggressive lowering of low-density lipoprotein (LDL) cholesterol levels to < 100 mg/dL compared with moderate reduction to 132 to 136 mg/dL delayed atherosclerosis progression in grafts [40].

When to do saphenous vein grafting?

The effectiveness of coronary surgery is directly related to coronary artery bypass graft patency. Therefore, for best outcomes, it is important to choose the best conduit for a given patient and a coronary target. The best conduit is the one that is most likely to remain patient. In most situations, arterial grafts have the best patency. However, one of the most important factors that influence arterial graft patency is competitive flow [6, 41]. As competitive flow increases, arterial graft patency decreases. A study evaluating the patency of ITA and saphenous vein grafts across a range of proximal stenosis by coronary system found that ITA grafts have better patency than saphenous vein grafts across all degrees of proximal stenosis in the left-sided coronary arteries and posterior descending artery [6]. For main right coronary artery (RCA), however, early (< 5 years) after operation, saphenous vein grafts were found to have equivalent or better patency than ITA grafts. At 10 years postoperatively, ITA grafts were more likely to be patent in RCA with 70% stenosis or greater (Fig. 1). Therefore, when bypassing RCA with less than 70% stenosis, an ITA graft may not be the best choice and saphenous vein grafting should be considered instead.

Radial artery grafts and gastroepiploic artery too are affected by competitive flow but probably to a much greater degree than ITAs. A study by Di Mauro et al. showed that in patients undergoing bilateral ITA grafting of left-sided coronary arteries, long-term freedom from cardiac mortality was lower in patients with right gastroepiploic artery grafted onto the RCA when the stenosis was less than 80% compared to a saphenous graft. This difference disappeared when RCA stenosis was at least 80% [42]. Similarly, a study by Maniar et al. showed that the patency of

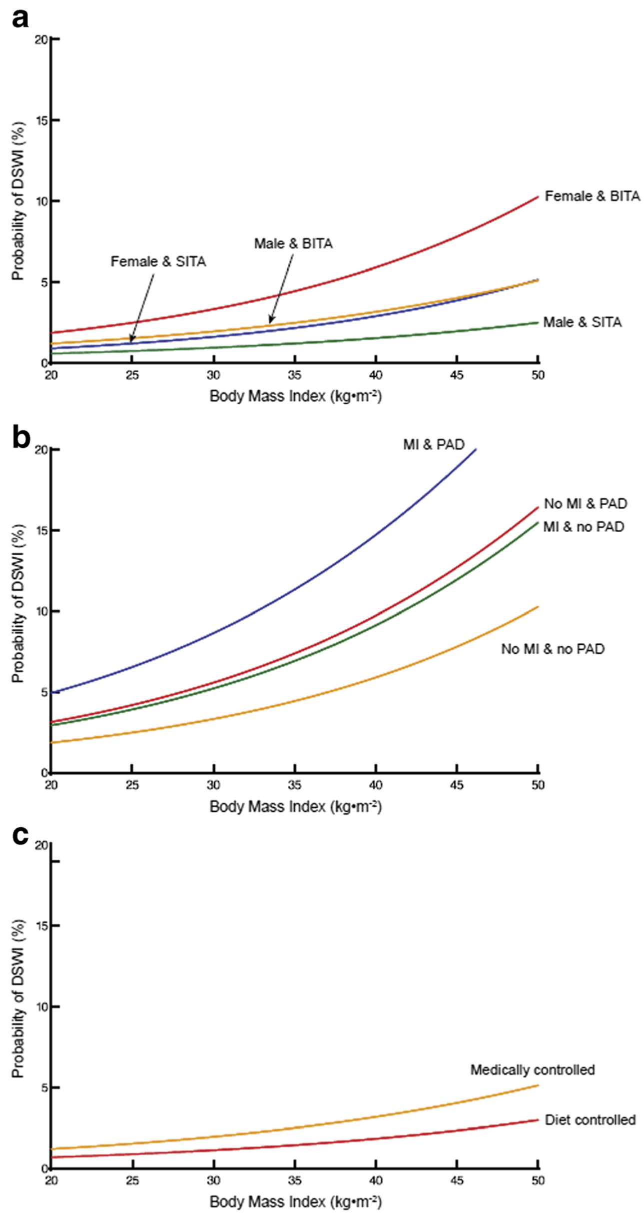

Fig. 2 Effect of risk factors on probability of deep sternal wound infection (*DSWI*) across a range of body mass indexes. Simulations were based on the logistic regression model for a patient undergoing coronary artery bypass grafting with cardiopulmonary bypass, in the past decade, with complete revascularization. Other factors are listed for the individual depictions. **a** Effect of female sex after bilateral (*BITA*) and single (*SITA*) internal thoracic artery grafting. Simulations are based on an insulin-treated patient with no history of peripheral arterial disease (*PAD*) or myocardial infarction (*MI*). **b** Effect of PAD and MI after BITA grafting. Simulations are based on an insulin-treated woman. **c** Effect of diet-controlled versus medically treated diabetes. Simulations are based on a man with no history of PAD or MI undergoing CABG with BITA grafting. Reproduced with permission from Elsevier from reference 44

radial arteries is worst if grafted to a moderately stenosed RCA [43]. Therefore, if a radial artery or gastroepiploic artery is being used to graft a RCA, it is important to make sure that the RCA is either critically stenosed or occluded, because the effect of competitive flow is more pronounced in the RCA system than the left. In patients with moderately stenosed RCA, saphenous vein grafting may result in best outcomes as its patency is not affected by competitive flow.

Another situation in which saphenous vein grafting may be a reasonable choice for revascularization of non-LAD targets is in patients who are not candidates for total arterial or bilateral ITA grafting. These include patients whose risk of deep sternal wound infection is too high or who are too old to derive benefit from multiple arterial grafting. Studies have shown that obese diabetic females with diffuse atherosclerotic burden are at the greatest risk of developing wound infections (Fig. 2) [44]. Therefore, it may be best to avoid use of bilateral ITA grafts in these patients and instead radial artery or saphenous vein grafting should be considered for revascularization of non-LAD lesions. Similarly, it may be best to avoid bilateral ITA grafting in octogenarians as they, due to their lower life expectancy, less likely derive survival benefit from use of multiple arterial grafts.

Conclusions

Saphenous vein remains the most commonly used bypass graft for non-LAD targets. To maximize the benefits of coronary surgery, it is important to identify and adopt strategies that improve the durability and longevity of vein grafts. The choice of graft should be tailored to the patient coronary anatomy for best outcomes.

Compliance with ethical standards

Being a review article, Ethical statements, Human and Animal Rights, Informed consent not required.

Conflict of interest Dr. Joseph F. Sabik, III: North American principal investigator for the Abbott Laboratories–sponsored left main coronary disease randomized trial (EXCEL). Society of Thoracic Surgeons board of directors. Scientific advisory board of Medtronic.

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References

1. Organization WHO. The Top 10 Causes of Death. 2017; Available from: http://www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death.
2. Alexander JH, Smith PK. Coronary-Artery Bypass Grafting. N Engl J Med. 2016;375:e22.
3. Roger VL, Go AS, Lloyd-Jones DM, et al. Executive summary: heart disease and stroke statistics–2012 update: a report from the American Heart Association. Circulation. 2012;125:188–97.
4. Martínez-González B, Reyes-Hernández CG, Quiroga-Garza A, et al. Conduits Used in Coronary Artery Bypass Grafting: A Review of Morphological Studies. Ann Thorac Cardiovasc Surg. 2017;23:55–65.
5. Favaloro RG, Effler DB, Groves LK, Sheldon WC, Riahi M. Direct myocardial revascularization with saphenous vein autograft. Clinical experience in 100 cases. Dis Chest. 1969;56:279–83.
6. Sabik JF 3rd, Lytle BW, Blackstone EH, Houghtaling PL, Cosgrove DM. Comparison of saphenous vein and internal thoracic artery graft patency by coronary system. Ann Thorac Surg. 2005;79:544–51.
7. Fitzgibbon GM, Kafka HP, Leach AJ, Keon WJ, Hooper GD, Burton JR. Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years. J Am Coll Cardiol. 1996;28:616–26.
8. Chesebro JH, Fuster V, Elveback LR, et al. Effect of dipyridamole and aspirin on late vein-graft patency after coronary bypass operations. N Engl J Med. 1984;310:209–14.
9. Bourassa MG, Fisher LD, Campeau L, Gillespie MJ, McConney M, Lespérance J. Long-term fate of bypass grafts: the Coronary Artery Surgery Study (CASS) and Montreal Heart Institute experiences. Circulation. 1985;72:V71–8.
10. Campeau L, Lespérance J, Hermann J, Corbara F, Grondin CM, Bourassa MG. Loss of the improvement of angina between 1 and 7 years after aortocoronary bypass surgery: correlations with changes in vein grafts and in coronary arteries. Circulation. 1979;60:1–5.
11. de Vries MR, Simons KH, Jukema JW, Braun J, Quax PH. Vein graft failure: from pathophysiology to clinical outcomes. Nat Rev Cardiol. 2016;13:451–70.
12. Motwani JG, Topol EJ. Aortocoronary saphenous vein graft disease: pathogenesis, predisposition, and prevention. Circulation. 1998;97:916–31.
13. 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.
14. Kennedy JH, Lever MJ, Addis BJ, Paneth M. Changes in vein interstitium following distension for aortocoronary bypass. J Cardiovasc Surg (Torino). 1989;30:992–5.
15. Unni KK, Kottke BA, Titus JL, Frye RL, Wallace RB, Brown AL. Pathologic changes in aortocoronary saphenous vein grafts. Am J Cardiol. 1974;34:526–32.
16. Bulkley BH, Hutchins GM. Accelerated "atherosclerosis". A morphologic study of 97 saphenous vein coronary artery bypass grafts. Circulation. 1977;55:163–9.
17. Barboriak JJ, Batayias GE, Pintar K, Tieu TM, Van Horn DL, Korns ME. Late lesions in aorta-coronary artery vein grafts. J Thorac Cardiovasc Surg. 1977;73:596–601.
18. Kern WH, Dermer GB, Lindesmith GG. The intimal proliferation in aortic-coronary saphenous vein grafts. Light and electron microscopic studies. Am Heart J. 1972;84:771–7.
19. Fuster V, Dewanjee MK, Kaye MP, Josa M, Metke MP, Chesebro JH. Noninvasive radioisotopic technique for detection of platelet deposition in coronary artery bypass grafts in dogs and its reduction with platelet inhibitors. Circulation. 1979;60:1508–12.
20. Chesebro JH, Clements IP, Fuster V, et al. A platelet-inhibitor-drug trial in coronary-artery bypass operations: benefit of perioperative dipyridamole and aspirin therapy on early postoperative vein-graft patency. N Engl J Med. 1982;307:73–8.
21. Griffith LS, Bulkley BH, Hutchins GM, Brawley RK. Occlusive changes at the coronary artery–bypass graft anastomosis. Morphologic study of 95 grafts. J Thorac Cardiovasc Surg. 1977;73:668–79.

22. Yanagawa B, Algarni KD, Singh SK, et al. Clinical, biochemical, and genetic predictors of coronary artery bypass graft failure. J Thorac Cardiovasc Surg. 2014;148:515–520.e2.
23. McLean RC, Nazarian SM, Gluckman TJ, et al. Relative importance of patient, procedural and anatomic risk factors for early vein graft thrombosis after coronary artery bypass graft surgery. J Cardiovasc Surg (Torino). 2011;52:877–85.
24. Ahmed JM, Dangas G, Lansky AJ, et al. Influence of gender on early and one-year clinical outcomes after saphenous vein graft stenting. Am J Cardiol. 2001;87:401–5.
25. Raza S, Blackstone EH, Houghtaling PL, et al. Influence of Diabetes on Long-Term Coronary Artery Bypass Graft Patency. J Am Coll Cardiol. 2017;70:515–24.
26. Raza S, Blackstone EH, Sabik JF. The diabetes epidemic and its effect on cardiac surgery practice. J Thorac Cardiovasc Surg. 2015;150:783–4.
27. Raza S, Sabik JF 3rd, Ainkaran P, Blackstone EH. Coronary artery bypass grafting in diabetics: A growing health care cost crisis. J Thorac Cardiovasc Surg. 2015;150:304–2.
28. Roth JA, Cukingnan RA, Brown BG, Gocka E, Carey JS. Factors influencing patency of saphenous vein grafts. Ann Thorac Surg. 1979;28:176–83.
29. Zenati MA, Shroyer AL, Collins JF, 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.
30. Hess CN, Lopes RD, Gibson CM, et al. Saphenous vein graft failure after coronary artery bypass surgery: insights from PREVENT IV. Circulation. 2014;130:1445–51.
31. Zenati MA, Gaziano JM, Collins JF, et al. Choice of vein-harvest technique for coronary artery bypass grafting: rationale and design of the REGROUP trial. Clin Cardiol. 2014;37:325–30.
32. Kopjar T, Dashwood MR. Endoscopic Versus "No-Touch" Saphenous Vein Harvesting for Coronary Artery Bypass Grafting: A Trade-Off Between Wound Healing and Graft Patency. Angiology. 2016;67-121-32.
33. Samano N, Geijer H, Liden M, Fremes S, Bodin L, Souza D. The no-touch saphenous vein for coronary artery bypass grafting maintains a patency, after 16 years, comparable to the left internal thoracic artery: A randomized trial. J Thorac Cardiovasc Surg. 2015;150:880–8.
34. Winkler B, Reineke D, Heinisch PP, et al. Graft preservation solutions in cardiovascular surgery. Interact Cardiovasc Thorac Surg. 2016;23:300–9.
35. Harskamp RE, Alexander JH, Schulte PJ, 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.
36. Taggart DP, Ben Gal Y, Lees B, et al. A Randomized Trial of External Stenting for Saphenous Vein Grafts in Coronary Artery Bypass Grafting. Ann Thorac Surg. 2015;99:2039–45.
37. Deo SV, Dunlay SM, Shah IK, 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.
38. Belch JJ, Dormandy J, Biasi GM, et al. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. J Vasc Surg. 2010;52:825–33.
39. Brilakis ES, Held C, Meier B, et al. Effect of ticagrelor on the outcomes of patients with prior coronary artery bypass graft surgery: insights from the PLATelet inhibition and patient outcomes (PLATO) trial. Am Heart J. 2013;166:474–80.
40. Knatterud GL, Rosenberg Y, Campeau L, et al. Long-term effects on clinical outcomes of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation in the post coronary artery bypass graft trial. Post CABG Investigators. Circulation. 2000;102:157–65.
41. Sabik JF 3rd, Lytle BW, Blackstone EH, Khan M, Houghtaling PL, Cosgrove DM. Does competitive flow reduce internal thoracic artery graft patency? Ann Thorac Surg. 2003;76:1490–6.
42. Di Mauro M, Contini M, Iacò AL, et al. Bilateral internal thoracic artery on the left side: a propensity score-matched study of impact of the third conduit on the right side. J Thorac Cardiovasc Surg. 2009;137:869–74.
43. Maniar HS, Sundt TM, Barner HB, et al. Effect of target stenosis and location on radial artery graft patency. J Thorac Cardiovasc Surg. 2002;123:45–52.
44. Raza S, Sabik JF 3rd, Masabni K, Ainkaran P, Lytle BW, Blackstone EH. Surgical revascularization techniques that minimize surgical risk and maximize late survival after coronary artery bypass grafting in patients with diabetes mellitus. J Thorac Cardiovasc Surg. 2014;148:1257–64.