Saphenous vein was the conduit used in the first series of coronary surgery, and, with the exception of revascularization of the left anterior descending coronary artery, it remains the most commonly used conduit. There are several reasons for this. First, because of its relatively large diameter and wall characteristics, it is technically easy to use; second, it is plentiful, and therefore can be used to perform multiple grafts; third, it is long and can reach any coronary artery; and fourth, it is easily harvested. However, its durability and longevity are not ideal. One year after coronary surgery, 10% to 20% of saphenous vein grafts fail. From 1 to 5 years, an additional 5% to 10% fail, and from 6 to 10 years, an additional 20% to 25% fail. At 10 years, only about half of saphenous vein grafts are patent, and of those, only half are free of angiographic arteriosclerosis.

Mural thrombi and intimal hyperplasia are the early stages responsible for further saphenous vein graft failure. After adhering to the intima, platelets release mitogenic proteins, stimulating smooth muscle cell migration, resulting in intimal proliferation and hyperplasia. After a year from surgery, arteriosclerosis is responsible for further saphenous vein graft failure. Mural thrombi and intimal hyperplasia are the early stages of vein graft arteriosclerosis. With time, lipid becomes incorporated in these areas of intimal hyperplasia, resulting in arteriosclerotic plaque, and eventual graft stenosis or occlusion.

### Study

In the current issue of *Circulation*, Mehta and colleagues compared 1-year saphenous vein graft failure (defined as ≥75% angiographic stenosis or occlusion) and 5-year clinical events (composite of death, myocardial infarction, or repeat revascularization) among patients in the Project of Ex-Vivo Vein Graft Engineering via Transfection (PREVENT) IV randomized trial who received saphenous vein grafts with either single or multiple distal anastomoses during coronary artery bypass surgery. Principal findings were (1) saphenous vein grafts with multiple distal anastomoses were more likely to fail at 1 year, and (2) the 5-year clinical event rate was higher in patients receiving saphenous vein grafts with multiple distal anastomoses. The authors conclude that, whenever possible, saphenous vein grafts should be performed with single distal anastomoses.

This study has several strengths. First, angiography was performed systematically, independent of clinical status. Most studies comparing coronary artery bypass graft patency are observational and opportunistic. Graft patency data from these studies are obtained from patients undergoing angiography for clinical indications, usually recurrent ischemia. This will bias graft patency rates lower. Second, the study was a large multicenter one, with graft data from >107 US sites. Most graft patency reports are obtained from small, single-center studies. Third, a large number of patients returned for angiography at 12 to 18 months; and fourth, a high proportion of patients who were scheduled to undergo follow-up angiography actually returned for it.

The findings of this study make surgical sense. Technical failure is a known cause of early bypass graft failure, and saphenous vein grafts with multiple distal anastomoses present more opportunity for technical misadventure. Each anastomosis must be done perfectly, and the length and lie of the saphenous vein graft between each distal anastomosis must be estimated correctly to prevent graft failure. Getting this length and lie right can be difficult because of changes in heart size and saphenous vein graft length. During on-pump arrested-heart surgery, the heart is flaccid and empty for the construction of the distal anastomoses. The vein is also unpressurized and contracted. After being weaned from cardiopulmonary bypass, the full heart increases in size and the pressurized saphenous vein graft increases in length. These changes must be taken into account to prevent the kinking (if the graft is too long) or flattening (if the graft is too short) of the saphenous vein graft. Although getting the graft length correct for saphenous vein grafts with single anastomoses is also critical, the relatively long length of graft between the aortic proximal anastomoses and distal coronary anastomoses allows for a wider margin of error in length before graft kinking or flattening. The shorter distances between distal anastomoses in saphenous vein grafts with multiple distal anastomoses result in much less tolerance to errors in estimation of graft length.

It is also consistent that the clinical event rate of death, myocardial infarction, or repeat revascularization was higher in patients having saphenous vein grafts with multiple distal anastomoses. The effectiveness of coronary artery bypass surgery is related directly to graft patency. Because graft failure was higher in saphenous vein grafts with multiple distal anastomoses, clinical outcomes would be expected to...
be worse in patients with saphenous vein grafts with multiple distal anastomoses.

This study also has several weaknesses. Although the angiographic and clinical results come from patients enrolled in the randomized PREVENT IV study, this substudy is observational. The decision regarding whether a single saphenous vein graft was used to revascularize one coronary artery or multiple coronary arteries was left to the discretion of the surgeon. Patients were not randomly assigned to receive saphenous vein grafts with either single or multiple distal anastomoses. A limited multivariate analysis was used to account for differences in patient factors that may have accounted for differences in the 2 groups; however, many factors are difficult to adjust for, and some would likely influence a surgeon’s decision regarding whether to perform single or multiple distal anastomoses with a single saphenous vein graft.

Two situations in which single saphenous vein grafts are preferentially used with multiple distal anastomoses are when there is limited saphenous vein and when there are poor distal coronary artery targets. Saphenous vein is often limited and of poor quality in patients with either large varicose or small sclerosed saphenous veins. In these patients, although most of their vein is not suitable, it is possible to find segments that are usable. In these situations, it may be necessary to perform multiple distal anastomoses with the best segments of saphenous vein. Although this vein is usable, it is often not ideal. These less than ideal veins are prone to graft failure, and this practice would be expected to bias against the patency of saphenous vein grafts with multiple distal anastomoses.

Similarly, when the coronary arteries are small with poor runoff, to improve graft patency a surgeon will preferentially perform multiple distal anastomoses with a single graft. It is believed that, by sequencing multiple small coronary arteries with poor runoff, bypass graft blood flow can be maximized, resulting in a bypass graft that is more likely than individual grafts to remain open. This would also bias against saphenous vein grafts with multiple distal anastomoses, because bypass grafts to coronary arteries with poor runoff have lower patency.

Mehta and colleagues did adjust for target vessel and graft quality in the analysis and reported similar findings in the 2 groups. However, the surgical bias of using sequential grafts when conduit is limited and coronary artery targets are poor is unlikely to be completely adjusted for and probably contributed to some of the lower patency observed in saphenous vein grafts with multiple distal anastomoses. The higher clinical event rate at 5 years may also be due in part to the patient characteristics associated with surgeon bias for using grafts with multiple distal anastomoses.

An important factor influencing bypass graft patency is target coronary artery. Bypass grafts performed to the left anterior descending coronary artery have the best patency; those performed to diagonals, circumflex branches, and the posterior descending artery have an intermediate patency; and those performed to the main right coronary artery have the worst patency. Mehta and colleagues do not mention adjustment of graft patency by target vessel grafted. This may be due to the difficulty in adjudicating grafts with multiple distal anastomoses. Other important patient characteristics and factors not adjusted for in their graft failure analysis include sex, diabetes mellitus, patient age, surgeon, and institution. Females, patients with diabetes, and younger patients have been shown to have lower bypass graft patency, and individual surgeon or institution bias toward single or sequential saphenous vein grafting may have contributed to their findings.

In evaluating the patency of saphenous vein grafts with multiple distal anastomoses, it is important to consider the sequential grafting technique. It is believed that the best sequential graft patencies are obtained by placing the last distal anastomosis of the sequential graft to the coronary artery with the greatest runoff. Smaller coronary arteries with poor runoff are Anastomosed to the graft more proximally. This technique ensures the greatest amount of blood flow throughout the graft, therefore increasing the likelihood of the entire graft remaining open. This method is in contrast to one in which the small coronary arteries with poor runoff are Anastomosed at the distal end of the sequential graft. With this technique, blood flow distally will be low, increasing the likelihood of graft failure. In this study, there is no consideration of how these different techniques affect patency of saphenous vein grafts with multiple distal anastomoses. It would therefore be interesting, if the data permitted the authors to do it, to perform a hierarchical mixed-model analysis that started with individual distal anastomoses (coronary vessel, position of anastomosis in sequence—starting with terminal end-to-side and working backward along the conduit—quality of coronary vessel at anastomosis, and degree of stenosis at 1-year angiography). The next level in the hierarchy would be each conduit (single or multiple distals), then patient, then surgeon/institution. This analytic strategy would avoid penalizing an entire sequential graft for stenosis of, say, the first and smallest vessel of the sequence and would add important information to our understanding of sequential graft patency.

Clinical Inferences

This study by Mehta and colleagues, along with previous publications from the PREVENT IV trial, are a sobering reminder of the Achilles’ heel of saphenous vein grafts—less than ideal patency rate. In the present study, we are reminded of the necessity of doing technically perfect coronary artery bypass surgery. Whether saphenous vein grafts are performed with single or multiple distal anastomoses, they must be done technically perfectly, with care taken to get the anastomoses, graft lengths, and lies correct.

In addition, despite PREVENT IV being a contemporary trial with modern surgical techniques and medications, saphenous vein graft failure is among the highest ever reported, with 1-year failure of 40% to 50%. This is alarming and suggests that, in addition to technical excellence in bypass grafting, further progress must be made in preventing both intimal injury during vein harvesting and exposure to arterial pressure, and platelet adherence and its resulting influence on the development of intimal hyperplasia and arteriosclerosis.

These findings also underscore the overuse of saphenous vein grafts and underuse of arterial grafts in coronary surgery.
in the United States. Internal thoracic artery grafts were used in only 92% of patients in this trial, and in only 90% of those undergoing saphenous vein grafts with multiple distal anastomoses. This is despite the reported clinical benefits of single and bilateral internal thoracic artery grafting,\textsuperscript{19–21} a result of their superior patency compared with saphenous vein grafts.\textsuperscript{2,22} In the United States, 95% of patients undergoing primary coronary surgery receive single internal thoracic artery grafting, and only 4% receive bilateral internal thoracic artery grafts (Society of Thoracic Surgeons Database). To further improve the results of coronary surgery, more arterial grafting should be performed.

Disclosures
None.

References

Key Words: Editorials ■ anastomosis ■ bypass graft ■ CABG ■ outcomes ■ saphenous vein graft

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