Should Radial Arteries Be Used Routinely for Coronary Artery Bypass Grafting?

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Case Presentation: Mr P is a 57-year-old construction worker who has had Canadian Cardiovascular Society class III angina for the past 3 months. He has multiple cardiovascular risk factors including smoking, hypertension, dyslipidemia, and diabetes. He is obese and has had a previous laparotomy for a perforated bowel. Coronary angiography revealed triple vessel disease involving the left anterior descending artery (LAD), the first obtuse marginal branch, and the right coronary artery (RCA), and an akinetic inferior wall with an estimated ejection fraction of 40%. The patient was referred for consideration of coronary artery bypass graft (CABG) surgery. Is Mr P a candidate for CABG and, if so, which vascular conduits should be used?

CABG is the standard surgical procedure for the treatment of advanced coronary artery disease. Since the first successful results reported by Favaloro,1 CABG surgery has been demonstrated to improve symptoms and, in specific subgroups of patients, to prolong life.2 Despite its success, the long-term outcome of coronary bypass surgery is strongly influenced by the fate of the vascular conduits used. Five to 7 years after surgery, patients are at increased risk of suffering from ischemic complications coincident with graft failure.2 Furthermore, as patients undergoing CABG surgery become older with more preoperative risk factors, and treated patients are living longer and therefore requiring reoperation, the optimal selection of vascular grafts for bypass is essential.

Conduits Used in Bypass Surgery

Conventional CABG surgery utilizes a combination of arterial and venous grafts. Saphenous vein (SV) grafts, the first vascular conduits used in CABG, are still widely utilized, primarily to bypass vessels other than the LAD. Despite being readily accessible, of adequate length to access every vessel on the heart, and the correct diameter to facilitate coronary and aortic anastomoses, SV grafts are limited by poor long-term patency. Because of a combination of intimal hyperplasia and accelerated atherosclerosis, up to 15% of SV grafts are occluded within 1 year,3 and by 10 years postoperatively, at least 50% demonstrate significant disease.4,5 To bypass the LAD, most centers use the left internal thoracic (mammary) artery (LITA or LIMA). In contrast to SV grafts, the LITA displays excellent long-term patency, up to 90% after 10 years, which is associated with improved survival.5–9 The excellent results obtained with the LITA anastomosed to the LAD have added strength to the concept of complete arterial revascularization to improve clinical outcomes. Recently, a prospective randomized trial demonstrated that total arterial revascularization with composite grafts improved patient outcome in terms of freedom from cardiac events, angina recurrence, and the need for percutaneous transluminal coronary angioplasty reintervention when compared with conventional arterial and venous grafting.10 Additional arterial grafts are being increasingly used in place of the SV to avoid the late complications of vein graft atherosclerosis and restenosis.

The use of arterial conduits has expanded beyond the LITA to include the right internal thoracic artery (RITA), the right gastroepiploic artery (RGEA), the inferior epigastric artery (IEA), and the radial artery (RA). Bi-
lateral ITAs, using the RITA as a pedicled or free graft, have been demonstrated to have long-term patency exceeding SV grafts and result in improved patient survival. However, no randomized trials have been done. The use of bilateral ITAs is commonly avoided in elderly, obese, or diabetic patients, characteristics common to CABG patients, because of higher rates of sternal infection, dehiscence, and mediastinitis. The RGEA, primarily used as an in situ graft to bypass the RCA and its branches, has shown reasonable long-term patency that exceeds 90% up to 5 years postoperatively. Its use, however, has been limited because of the fragile quality of the artery, the small diameter of the vessel at the site of distal anastomosis, concerns regarding vessel twisting, increased operative time, and incisional discomfort with associated ileus. The IEAs, used in composite arterial conduits or as free grafts, are limited primarily by their short usable length, only making them suitable as grafts to diagonal or intermediate branches. The principle adverse events associated with IEA harvesting are related to wound complications such as abdominal wall hematoma or infection, and relative contraindications to their use include obesity, lower abdominal surgery, or coexisting illness potentially requiring abdominal surgery. Thus, despite improved graft patency, multiple arterial conduits have not gained wider acceptance for myocardial revascularization because of increased operative time, limited access to distal coronary sites because of graft length, and patient factors that preclude their use. The final arterial conduit used, the radial artery, which is the focus of this review, overcomes many of these disadvantages.

### Radial Arteries for CABG: Historical Perspective

The RA was first used for coronary revascularization by Carpentier and colleagues in 1971. However, 2 years later, its use was abandoned because of an occlusion rate that was greater than that observed in SV grafts. A combination of graft spasm and severe intimal hyperplasia, likely the result of endothelial denudation from mechanical dilation and trauma on skeletonized harvesting, was thought to contribute to the initial poor results obtained with RA grafting. The discovery of a patent RA graft 15 years postoperatively, which was initially thought to be occluded, prompted the revitalization of the RA as a bypass conduit.

In 1992, Acar and colleagues reported the results from 104 patients who received a RA graft as a bypass conduit since 1989. The study showed that the RA is a reasonable alternative to other types of conduits to complement the LITA. Notably, in contrast to initial attempts, early RA patency was 100% in this modern experience, likely because of modifications that reduced endothelial damage and graft spasm.

Three major modifications are now used to minimize RA spasm, the primary cause of early graft failure. First, the RA is harvested as a pedicle, including 2 satellite veins and the surrounding fatty tissue, using an atraumatic “no-touch” technique similar to that used in the harvest of other arterial conduits for coronary surgery (see the Figure). During harvesting, direct handling of the RA is avoided. Second, mechanical dilation of the graft has been replaced by pharmacological dilation with papaverine, a phosphodiesterase III inhibitor that enhances the nitric oxide pathway, minimizing endothelial damage and dysfunction. Third, in hopes of minimizing postoperative RA spasm, vasodilator therapy, most commonly with calcium channel blockers or nitrates, has been adopted, despite limited clinical outcome data to support this practice.
Potential Advantages of Radial Artery Use
The RA possesses several anatomical features that make it an excellent candidate for use in coronary revascularization.27 The average length of the RA, >20 cm, makes it suitable to bypass all coronary artery territories, and its inner diameter, which is between 2 to 3 mm, closely matches that of the coronary arteries. Both coronary and aortic anastomoses are technically less demanding to construct with the RA when compared with other arterial conduits because of its thick muscular wall. On a practical basis, harvesting of the RA may occur concurrently with harvesting of all other conduits, reducing the duration of the surgical procedure.26

When compared with other vascular conduits, the RA provides additional benefits. According to observational studies, relative to SV grafts, RAs can be harvested without interfering with ambulation and their use has been shown to be protective against both early and late mortality and morbidity,28 resulting in enhanced late survival.29 Also, unlike SV grafts, RA grafts are adapted to higher arterial pressures and have a homogeneous caliber free from internal valves, characteristics possibly contributing to the RA’s superior results. Compared with other arterial grafts, contraindications such as obesity, diabetes mellitus, or previous laparotomy do not apply to RA harvesting, allowing this conduit to be harvested in a majority of patients.

When comparing the RITA to the RA as a second arterial graft, patients receiving a RA have a lower incidence of sternal wound infection and decreased transfusion requirement, though there is no difference in perioperative or intermediate-term cardiac morbidity or mortality rates.30 Furthermore, RA use is safe in patients with moderate to severe left ventricular dysfunction31 and in patients over the age of 65.32 (see Table 1).

Potential Disadvantages of Radial Artery Use
Before harvesting the RA, it is mandatory to assess the adequacy of the ulnar collateral circulation to the hand to avoid ischemia. Methods to detect adequate forearm collateral flow include the Allen test, static and dynamic Doppler testing, direct digit pressure measurement during RA compression, and oxymetric plethysmography, together with the computation of a perfusion index.33 If concerns with the adequacy of the forearm collateral circulation are raised by the preoperative testing method, RA harvesting is contraindicated. Other contraindications to RA harvesting include a radial artery plaque on ultrasound, damage to the RA due to trauma or previous cannulation, the presence of an arteriovenous fistula for hemodialysis, vasculitis, or Raynaud’s disease.31,37 Other disadvantages of the RA include a slightly higher degree of atherosclerosis as compared with the LITA and its increased chance of being subject to previous iatrogenic vascular trauma.31,37 However, the inability to use the RA because of severe calcification or chronic dissection from prior cannulation is relatively rare, occurring in less than 2% of candidates for RA harvest34 (see Table 1).

The major disadvantage, which may affect long-term performance, is the propensity of the RA to go into spasm. RA graft spasm is more intense and more difficult to reverse compared with spasm of the internal thoracic artery.36 Basic science investigations have elucidated the mechanism by which RA spasm is mediated. Although nonreceptor-mediated spasm in response to surgical trauma and local tissue acidity is important, it is the receptor-mediated response to catecholamines and platelet-derived factors, induced by endothelial damage and platelet aggregation, which should be abrogated in the setting of a coronary bypass graft. Endothelial function of the RA, in terms of the release of endothelium-derived relaxing factors such as nitric oxide, is similar to that of other arteries, as is its sensitivity to vasoconstricting agents.38 Thus, the propensity for the RA to go into spasm is likely due to the higher density of muscle cells in the media of this vessel that are organized into multiple tight layers, whereas the internal thoracic, gastroepiploic, and epigastric arteries have fewer muscle cells that are less organized.37 Because of the more muscular nature of the RA, a significantly

<table>
<thead>
<tr>
<th>TABLE 1. The Advantages and Disadvantages of Using the RA as a Bypass Conduit</th>
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<tbody>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td><strong>Anatomical</strong></td>
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<tr>
<td>Length (~20 cm)</td>
</tr>
<tr>
<td>Luminal diameter (2 to 3 mm)</td>
</tr>
<tr>
<td>Thick muscular wall/easy to work with</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>Excellent short-, mid-, and long-term patency</td>
</tr>
<tr>
<td>Obesity, diabetes, and previous laparotomy are not contraindications</td>
</tr>
<tr>
<td>Decreased transfusion requirement</td>
</tr>
<tr>
<td>Lower rate of sternal wound infection</td>
</tr>
<tr>
<td><strong>Practical</strong></td>
</tr>
<tr>
<td>Decreased operating time since harvested concurrently with other grafts</td>
</tr>
</tbody>
</table>
higher maximal contractile force can result in response to vasoconstricting agents, such as norepinephrine, serotonin, endothelin I, and angiotensin II, generated in response to endothelial damage and dysfunction. Thus, use of the RA as a bypass conduit in patients at high risk of needing postoperative vasopressor support should be avoided. Currently, the propensity of the RA to spasm has been greatly reduced by minimal touch harvesting, pharmacological dilation, and the use of both topical and systemic vasodilators, including calcium channel blockers, papaverine, the phosphodiesterase inhibitor milrinone, intravenous nitroglycerin, and α-adrenergic receptor blockers. Finally, studies suggest that the RA should be limited to grafting native vessels with a high degree of stenosis (>70%) because of graft sensitivity to competitive flow and its increased propensity to spasm.

**Patency Rates of Radial Artery Conduits**

The long-term success of CABG depends largely on graft patency. Based on the perceived advantages from arterial revascularization, the RA was increasingly used in the 1990s, either as a separate graft or in composite grafts. Several angiographic observational studies have shown that the RA achieves excellent short-, mid-, and long-term patency when used as a conduit for revascularization (see Table 2). Patency rates exceed that of the LITA, displays favorable short- and long-term patency. This was less than that of the SV, supporting its proposed role as a complementary arterial conduit for myocardial revascularization. Although these results are encouraging, there are few long-term studies assessing the patency rates of RA grafts in symptom-free patients in a randomized, controlled setting. To address this concern, there are 3 ongoing randomized trials comparing angiographic patency of RA grafts versus other vascular conduits. These are the Radial Artery Patency and Clinical Outcome (RAPCO) study, the Radial Artery Patency Study (RAPS), and the VA Comparative Study.

<table>
<thead>
<tr>
<th>Study</th>
<th>Timing</th>
<th>RA</th>
<th>LITA</th>
<th>RITA</th>
<th>FITA</th>
<th>RGEA</th>
<th>IEA</th>
<th>SVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acar et al</td>
<td>early</td>
<td>56/56 (100%)</td>
<td>48/48 (100%)</td>
<td>11/11 (100%)</td>
<td>16/18 (89.9%)</td>
<td>…</td>
<td>…</td>
<td>8/9 (88%)</td>
</tr>
<tr>
<td>Calafiore et al</td>
<td>early</td>
<td>26/26 (100%)</td>
<td>43/43 (100%)</td>
<td>35/35 (100%)</td>
<td>…</td>
<td>5/5 (100%)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Calafiore et al</td>
<td>early</td>
<td>75/76 (98.7%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>67/70 (95.7%)</td>
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<td>…</td>
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<tr>
<td>Chen et al</td>
<td>early</td>
<td>90/94 (95.7%)</td>
<td>62/62 (100%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>24/26 (92.3%)</td>
<td>…</td>
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<tr>
<td>da Costa et al</td>
<td>early</td>
<td>59/61 (96.7%)</td>
<td>31/32 (96.8%)</td>
<td>12/13 (92.3%)</td>
<td>…</td>
<td>1/1 (100%)</td>
<td>…</td>
<td>13/14 (92.8%)</td>
</tr>
<tr>
<td>Buxton et al</td>
<td>group 1</td>
<td>late</td>
<td>86/90 (95.5%)</td>
<td>…</td>
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<td>…</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Amano et al</td>
<td>early</td>
<td>137/139 (98.6%)</td>
<td>99/100 (99%)</td>
<td>27/27 (100%)</td>
<td>…</td>
<td>48/50 (96.0%)</td>
<td>…</td>
<td>34/38 (89.5%)</td>
</tr>
<tr>
<td>Acar et al</td>
<td>mid</td>
<td>29/31 (93.5%)</td>
<td>28/28 (100%)</td>
<td>9/9 (100%)</td>
<td>11/13 (84.6%)</td>
<td>…</td>
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<td>…</td>
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<tr>
<td>Calafiore et al</td>
<td>mid</td>
<td>16/17 (94.1%)</td>
<td>31/31 (100%)</td>
<td>22/23 (95.6%)</td>
<td>…</td>
<td>2/2 (100%)</td>
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<tr>
<td>Calafiore et al</td>
<td>mid</td>
<td>33/35 (99.3%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>25/25 (100%)</td>
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<td>…</td>
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<tr>
<td>Manasse et al</td>
<td>late</td>
<td>43/49 (87.8%)</td>
<td>45/47 (95.8%)</td>
<td>1/2 (50%)</td>
<td>2/4 (50%)</td>
<td>5/5 (100%)</td>
<td>…</td>
<td>35/46 (76.1%)</td>
</tr>
<tr>
<td>Tatoulis et al</td>
<td>mid</td>
<td>21/22 (95.7%)</td>
<td>16/16 (100%)</td>
<td>…</td>
<td>1/1 (100%)</td>
<td>…</td>
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<tr>
<td>Bhan et al</td>
<td>mid</td>
<td>60/62 (98.6%)</td>
<td>56/57 (98.2%)</td>
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<tr>
<td>Amano et al</td>
<td>mid</td>
<td>213/229 (93.0%)</td>
<td>142/149 (95.3%)</td>
<td>27/27 (100%)</td>
<td>…</td>
<td>75/82 (91.4%)</td>
<td>…</td>
<td>71/79 (89.8%)</td>
</tr>
<tr>
<td>Acar et al</td>
<td>late</td>
<td>54/64 (84.4%)</td>
<td>44/47 (93.6%)</td>
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</tr>
<tr>
<td>Possati et al</td>
<td>late</td>
<td>57/61 (91.9%)</td>
<td>58/60 (96.7%)</td>
<td>3/4 (75%)</td>
<td>9/10 (90%)</td>
<td>…</td>
<td>43/58 (74.1%)</td>
<td>…</td>
</tr>
<tr>
<td>Buxton et al</td>
<td>group 1</td>
<td>late</td>
<td>38/39 (95%)</td>
<td>…</td>
<td>…</td>
<td>29/29 (100%)</td>
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</tr>
<tr>
<td>Buxton et al</td>
<td>group 2</td>
<td>late</td>
<td>21/24 (86%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>21/22 (95%)</td>
<td>…</td>
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<tr>
<td>Possati et al</td>
<td>late</td>
<td>74/84 (88%)</td>
<td>79/82 (96.3%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>39/73 (53.4%)</td>
<td>…</td>
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<tr>
<td>Totals:</td>
<td>early</td>
<td>529/542 (97.6%)</td>
<td>283/285 (99.3%)</td>
<td>…</td>
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<tr>
<td></td>
<td>mid</td>
<td>415/445 (93.3%)</td>
<td>318/328 (97.0%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>…</td>
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<tr>
<td></td>
<td>late</td>
<td>244/272 (89.7%)</td>
<td>181/189 (95.8%)</td>
<td>…</td>
<td>…</td>
<td>…</td>
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</table>

Early indicates a mean follow-up of <6 months; mid, a mean follow-up of 6 to 36 months; late, a mean follow-up exceeding 36 months; and SVG, saphenous vein graft.

The long-term success of CABG depends largely on graft patency. Based on the perceived advantages from arterial revascularization, the RA was increasingly used in the 1990s, either as a separate graft or in composite grafts. Several angiographic observational studies have shown that the RA achieves excellent short-, mid-, and long-term patency when used as a conduit for revascularization (see Table 2). Patency rates exceed that of the LITA, displays favorable short- and long-term patency. This was less than that of the SV, supporting its proposed role as a complementary arterial conduit for myocardial revascularization. Although these results are encouraging, there are few long-term studies assessing the patency rates of RA grafts in symptom-free patients in a randomized, controlled setting. To address this concern, there are 3 ongoing randomized trials comparing angiographic patency of RA grafts versus other vascular conduits. These are the Radial Artery Patency and Clinical Outcome (RAPCO) study, the Radial Artery Patency Study (RAPS), and the VA Comparative Study.
The RAPCO study was undertaken to compare elective angiographic patency and cardiac event-free survival of the RA graft with that of the free RITA or SV during a 10-year period after primary CABG surgery. The RA was compared with the free RITA in a younger patient group (n=285, age <70 years) and with the SV in an older patient group (n=153, age ≥75 years). Patients were randomly assigned to receive either the RA, RITA, or SV grafted to the largest available coronary artery other than the LAD. The 5-year interim results of this prospective, randomized, single-center trial were recently reported.45 Buxton and colleagues45 report that in the first 5 years after surgery, there were no differences in the angiographic failure rates and major clinical outcomes, namely survival and cardiac event-free survival, of the RA compared with the RITA or SV. However, these results were based on only a small proportion of the expected angiographic results. Furthermore, in their study,45 SV graft patency rates were much better than those previously recorded or the non-study SVs. Also, the 5-year time point may be too short to assess the true difference in patency as SV grafts begin to display accelerated graft atherosclerosis and increasing rates of graft failure between 5 and 10 years postoperatively. Thus, the final results obtained after 10 years of follow-up should help clarify the long-term RA patency rates and whether the use of this graft in CABG is superior to the RITA or SV.

The results of the second trial, RAPS,46 were reported at the 2003 American Heart Association Scientific Sessions.57 RAPS was a prospective, multicenter, randomized clinical trial comparing RA patency with that of the SV when randomly allocated as the graft to the right or circumflex coronary arteries. The primary objective of the study was to determine the 8- to 12-month angiographic patency of the RA relative to the SV, with each patient serving as his or her own control. The long-term patency (5 to 10 years) of the RA relative to SV grafts will be assessed in follow-up studies. A total of 561 patients were enrolled, of whom 440 underwent follow-up angiography. Graft patency was greater in RA grafts (91.8%) than in SV grafts (86.4%, P=0.01; graft occlusion odds ratio =0.53, 95% confidence interval 0.31 to 0.85). Perfect graft patency, defined as grafts with Thrombolysis In Myocardial Infarction (TIMI) 3 flow, was similar (87.7% versus 85.7%, P=0.37). Perfect patency of the radial artery was highly dependent on the severity of the proximal native coronary artery stenosis (70% to 89% coronary stenosis: 81.7%; ≥90% coronary stenosis: 91.5%). Patency of the RA graft was similar in the RCA and circumflex territories.

The Future of the Radial Artery as a Vascular Conduit

The RA is becoming increasingly popular as a third arterial conduit in association with the LITA and RITA, or as the second in patients with contraindications to bilateral ITA harvesting. With the movement toward complete arterial revascularization and more frequent off-pump surgery to avoid aortic manipulation, the use of the RA to form composite arterial grafts to the LITA will become more common.58,59 Techniques simplifying the construction of anastomoses between vessels and the aorta, by use of aortic connectors, may be extended to RA grafts.60 New pharmacological agents or gene therapy strategies64 will be developed to further decrease the potential for RA spasm, which remains a problem that may be most relevant in patients who require postoperative vasopressor support. Furthermore, minimally invasive approaches for the harvesting of the RA are being developed, providing desirable clinical and cosmetic outcomes.65 Finally, as more patients require reoperation, the RA will be one of the few conduits still available for use.

Mr P was deemed eligible for CABG. Because of his age, the use of arterial grafts was preferred. However, his obesity, diabetes, and previous laparotomy prompted the surgeons to avoid harvesting the RITA, IEA, and RGEA. His right Allen test was sluggish; however, it was normal on the left. Therefore, Mr P underwent CABG with a LITA to the LAD, a left radial artery graft to the distal RCA, and a SV graft to the first obtuse marginal branch, similar to the procedure illustrated in the Figure. His perioperative course was unremarkable and he was discharged from hospital 5 days after surgery.

Note Added in Proof

During the review process, an important article on radial arteries was published by Zacharias et al.63 The authors evaluated 6-year outcomes in propensity-matched CABG-LITA-LAD patients (925 each) divided into those with one radial graft and those with vein-only grafting. Perioperative outcomes, including death, were similar, although cumulative survival was better for patients receiving the radial artery graft. Angiography data in re-studied symptomatic patients showed a trend for greater radial artery graft patency. Furthermore, the extent of vein graft failure was significantly worse than that of radial graft failure. These data would support the use of radial arteries as a second arterial conduit in CABG-LITA-LAD as opposed to vein grafting.

References

4. Bourassa MG, Fisher LD, Campeau L, et al. Long-term fate of bypass grafts: the Coronary Artery Surgery Study (CASS) and...


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