Has the in situ right internal thoracic artery been overlooked? An angiographic study of the radial artery, internal thoracic arteries and saphenous vein graft patencies in symptomatic patients

Pallav J. Shah\textsuperscript{a}, Khoi Bui\textsuperscript{a}, Shane Blackmore\textsuperscript{a}, Ian Gordon\textsuperscript{b}, David L. Hare\textsuperscript{c}, John Fuller\textsuperscript{d}, Siven Seevanayagam\textsuperscript{a}, Brian F. Buxton\textsuperscript{a,}\textsuperscript{*}

\textsuperscript{a}Department of Cardiac Surgery, Austin Hospital, Melbourne, Vic., Australia
\textsuperscript{b}Statistical Consulting Centre, University of Melbourne, Parkville, Vic., Australia
\textsuperscript{c}University of Melbourne, Department of Cardiology, Austin Hospital, Melbourne, Vic., Australia
\textsuperscript{d}Epworth Medical Centre, Melbourne, Vic., Australia

Abstract

Objective: The right internal thoracic artery is being used infrequently despite favorable observational angiographic data. Conversely, the radial artery utilization has increased with only limited data available. The purpose of this paper is to re-evaluate the roles of the right internal thoracic artery and the radial artery grafts. Methods: We reviewed all ischemia-directed coronary angiographic procedures from January 1996 to December 2003. A total of 219 patients had primary coronary artery bypass grafting with an internal thoracic artery and a radial artery as two of the bypass grafts. Six hundred and seventy-nine (679) graft angiograms (45 saphenous vein, 363 radial artery, 54 right internal thoracic artery and 217 left internal thoracic artery) were studied. The mean period from operation to re-angiogram was 1104 ± 761 days. Angiographic outcomes were divided into groups as: (1) patent (<50% stenosis) or (2) failed (≥50% stenosis, string sign or occluded). A generalized linear mixed model was used to analyze predictors of graft patency. Turnbull’s estimates of cumulative patency were used to compare graft failure rates over time. Results: A total of 632/679 (93%) grafts were patent and 47/679 (7%) grafts had failed. Empirical saphenous vein graft patency was 40/45 (89%), radial artery patency 329/363 (91%), right internal thoracic artery patency 51/54 (94%) and left internal thoracic artery patency 212/217 (98%). Pairwise comparisons of patency from the generalized linear mixed model were: LITA > RITA, OR = 1.5 (P = 0.5); LITA > RA, OR = 5.7 (P < 0.001); LITA > SV, OR = 6.5 (P < 0.001); RITA > RA, OR = 3.9 (P = 0.01); RITA > SV, OR = 4.4 (P = 0.01); RA > SV, OR = 1.1 (P = 0.7). Five-year patency estimates from the Turnbull’s model were the left internal thoracic artery (95.9%), right internal thoracic artery (91.2%), the radial artery (90.6%) and the saphenous vein (81.8%). Conclusions: Consideration should be given to the routine use of both internal thoracic arteries for coronary artery bypass grafting. When additional grafts are required, there is no evidence to suggest that either the radial artery or saphenous vein is superior.

© 2005 Elsevier B.V. All rights reserved.

Keywords: CABG; Radial artery; Internal thoracic artery; Saphenous vein; Conduits

1. Introduction

Since the early 1980s, the use of the left internal thoracic artery (LITA) for grafting of the left arterial descending (LAD) became the standard of care based on reports of superior graft patency, reduced cardiac events, decreased need for further intervention and enhanced long-term survival when compared with patients receiving only venous conduits [1–4]. The widely accepted success of the LITA has led to the use of both internal thoracic arteries (ITA), although the right internal thoracic artery (RITA), used as an in situ or free graft, has never become popular, despite convincing observational data [5]. The development of surgical strategies to achieve total arterial revascularization has led to the search of other arterial conduits, especially the radial artery (RA). The use of the RA for coronary artery bypass grafting was first introduced by Carpentier et al. [6] in 1971. At that time, the study was conducted in a limited number of patients with use of mechanical dilation, diathermy for harvesting and no vasodilator treatment post-operatively. This strategy resulted in a high rate of graft failure and its use as a conduit was abandoned after 1976. Late angiography of some patients from the earlier series found patent and disease-free RA conduits which previously had been considered occluded [7]. This led to
the revival of interest in the RA with improved patency [8,9]. Recently, however, the reputation of the RA as a bypass graft has been questioned by Khot et al. [10]. Along with these developments, recent information suggests that late patency of saphenous vein (SV) grafts may have improved [11]. The purpose of this study is to analyze angiographic results in patients who presented with symptoms and signs of ischemia from 1996 to 2003 and to compare the patencies with the LITA, RITA, RA and SV conduits to redefine their roles as bypass conduits.

2. Materials and methods

2.1. Study population

The study population consisted of 219 patients who had undergone primary coronary artery bypass surgery between 1996 and 2003, had received at least one ITA and one RA graft and later presented with recurrence of symptoms or evidence of ischemia requiring coronary angiography. A total of 6456 patients underwent primary coronary artery bypass surgery during this period. 4782 (74%) patients receiving a RA graft. The study population of 219 patients accounted for 5% of patients who had received a RA graft during this period.

The preoperative patient characteristics and intraoperative variables were recorded prospectively. A total of 679 graft angiograms were studied in these 219 patients. The preoperative patient characteristics and intraoperative variables are described in Table 1. The type and distribution of grafts and target coronary arteries are described in Table 2.

The mean interval (Fig. 1) from operation to re-angiogram was 1104±761 days (mean±SD). Aspirin and lipid lowering agents were routinely given in post-operative patients. Calcium channel blockers were given to all patients for 6 months.

2.2. Angiographic analysis

The native coronary artery and graft angiograms were performed using selective catherization. In patients who had two or more post-operative angiograms, the last angiogram was used for analytical purposes. A cardiologist and a surgeon read the angiograms. The method of reporting was uniform. All grafts were described in detail, together with the degree of stenosis and target coronary artery grafted.

A graft was considered patent when it had <50% stenosis after visualization of the entire course of the graft, including proximal and distal anastomoses and distal target coronary artery. In sequential grafts and Y-grafts, each segment was analyzed as a separate graft, defined by the number of distal anastomoses. Grafts were considered to have failed if they had ≥50% stenosis, had a string sign or were occluded.

2.3. Statistical analysis

Continuous variables were expressed as mean±SD. We used a generalized linear mixed model to compare and analyse the patency of the four graft conduits. The variables accounted for were: subject (a random effect), graft type (RA, SVG, RITA, LITA), target artery system: LAD (left anterior descending and diagonal), circumflex (intermediate and obtuse marginal) or RCA (right coronary, posterior descending artery and posterolateral branch) and target artery stenosis. A generalized linear mixed model was fitted to the binary variable defined as 1 if the graft was ≥50% patent.
stenosed or occluded and 0 otherwise. This is an extension of logistic regression that allows for two levels of variation that are present in the data. Some variables are constant for all grafts from a given patient, for example, age, sex, year of operation and interval to angiogram. Other variables pertain to individual grafts and therefore take different values for grafts from the same patient, for example, the coronary artery to which the graft is anastomosed. Unlike standard logistic regression, the analysis allows for incorporation of these two levels of variation [12]. The model is multivariable in the usual sense that each variable’s effect is adjusted for the effects of other variables considered. The model was fitted using S-Plus [13] and the MASS [14] library of additional functions.

In addition, we have obtained univariable estimates of the cumulative patency by graft type, allowing for the interval censoring that is present in the data: if a graft failure is observed, our knowledge of its timing is limited to the interval between the operation and the angiogram. The method used is that of Turnbull [15] who derived an efficient algorithm from the theory developed by Peto [16].

2.4. Surgery

Coronary artery bypass grafting (CABG) was performed by eight surgeons using a similar protocol. All operations were performed on cardiopulmonary bypass with the use of antegrade/retrograde blood cardioplegia. LITA was harvested and used in situ in all patients. The RITA was employed predominately as an in situ 45/54 (83%) and less often as a free 9/54 (17%) graft. The RA was harvested with a no-touch technique and was semi-skeletonised. Veins were harvested by using a conventional open ‘no-touch’ technique. Veins were dilated to their naturally distended state avoiding overdilatation. Arterial grafts were pharmalogically dilated with an intraluminal solution (100 cm$^3$ solution containing equal parts of Ringers lactate and blood with 2 mM papaverine (80 mg) and 5000 U of heparin) at arterial pressure and stored in the same solution until use.

3. Results

3.1. Empirical graft patency

A total of 632/679 (93%) grafts were patent and 47/679 (7%) grafts had failed. Overall, SV graft patency was 40/45 (89%), RA patency 329/363 (91%), RITA patency 51/54 (94%) and LITA patency was 212/217 (98%) (Fig. 2).

3.2. Generalized linear mixed model

Using the generalized linear mixed model, the estimates of the effects on graft failure of conduit, target artery and target artery stenosis are shown in Table 3. Neither target artery nor target artery stenosis showed a significant association with graft failure. On the other hand, there were a number of statistically significant differences between conduits, discussed below.

3.3. Turnbull’s method

Univariable estimates of cumulative patency rates are shown in Fig. 3. The 5-year estimates of patencies were LITA (95.9%), RITA (91.2%), RA (90.6%) and SV (81.8%).

![Fig. 2](image-url)

4. Discussion

Re-angiography, for evidence of ischemia, at a mean interval of 3 years post-surgery, confirmed that the patency of the RITA and LITA grafts are not significantly different. Graft patencies of the right and left ITA are superior to those of the RA and the SV which are themselves not statistically significantly different. These results were adjusted for target artery and target artery stenosis. These findings suggest that the RITA has been underused and that wider application of the RITA might improve the results of coronary artery bypass surgery. These CABG patients are from a group of surgeons who have a philosophy of selecting ITA and RA in preference to the RITA and SV graft conduits; therefore, there are relatively few RITAs and SVs in this study. The RITA was employed only in a quarter of the patients, the majority of which were used as an in situ graft routed across the anterior aspect of the aorta to the left coronary system. Like many other surgeons, the ease of RA harvest may have resulted in the RA being used in preference to the RITA, despite the compelling evidence of the benefits of the RITA from a major observational study [5]. Implantation of high proportion diseased grafts may influence the outcome. Competitive flow, by grafting target arteries with a low-grade stenosis, has been recognized as cause of arterial graft failure [20]. However, Khot’s univariate analysis, and our own generalized linear mixed model, did not confirm the significant increase in graft failure when attached to arteries with low-grade lesions (<70%). However, there were few low-grade lesions grafted in our series. Differences in harvesting techniques, such as sharp dissection, electrocautery, ultrasound or videoscopic techniques, choice of vasodilator, storage medium, surgical techniques or type of statistical analyses may have contributed to their poor results [21].

Khot et al. [10] used univariable assessment, multivariable logistic regression analysis for the entire cohort and patients who had coronary artery bypass surgery during the study period and therefore, may not be truly representative. Furthermore there was no indication of the total number of RA grafts performed during the study period. There are a number of other considerations. Khot et al. included re-operations, which were excluded in our series. RAs harvested in this age group have a medial calcification rate of 10% and atherosclerosis in 5% of grafts [19]. Implantation of high proportion diseased grafts may influence the outcome. Competitive flow, by grafting target arteries with a low-grade stenosis, has been recognized as cause of arterial graft failure [20]. However, Khot’s univariate analysis, and our own generalized linear mixed model, did not confirm the significant increase in graft failure when attached to arteries with low-grade lesions (<70%). However, there were few low-grade lesions grafted in our series. Differences in harvesting techniques, such as sharp dissection, electrocautery, ultrasound or videoscopic techniques, choice of vasodilator, storage medium, surgical techniques or type of statistical analyses may have contributed to their poor results [21].

Khot et al. [10] used univariable assessment, multivariable logistic regression analysis for the entire cohort and

Table 3
Multivariable generalised linear mixed model analysis: odds ratios for graft failure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comparison</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduit</td>
<td>RITA compared to LITA</td>
<td>1.5</td>
<td>0.4</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>RA compared to LITA</td>
<td>5.7</td>
<td>2.6</td>
<td>12.4</td>
</tr>
<tr>
<td></td>
<td>SV compared to LITA</td>
<td>6.5</td>
<td>2.5</td>
<td>16.7</td>
</tr>
<tr>
<td></td>
<td>RA compared to RITA</td>
<td>3.9</td>
<td>1.4</td>
<td>10.8</td>
</tr>
<tr>
<td></td>
<td>SV compared to RITA</td>
<td>4.4</td>
<td>1.4</td>
<td>14.2</td>
</tr>
<tr>
<td></td>
<td>SV compared to RA</td>
<td>1.1</td>
<td>0.6</td>
<td>2.2</td>
</tr>
<tr>
<td>Target artery</td>
<td>Circumflex compared to LAD/Diag</td>
<td>0.9</td>
<td>0.4</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>RCA compared to LAD/Diag</td>
<td>1.2</td>
<td>0.6</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>RCA compared to Circumflex</td>
<td>1.4</td>
<td>0.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Coronary stenosis*</td>
<td>One level (x compared to x–1)</td>
<td>0.8</td>
<td>0.6</td>
<td>1.1</td>
</tr>
</tbody>
</table>

* Target coronary artery stenosis grading: (1) 0–19%; (2) 20–39%; (3) 40–59%; (4) 60–70%; (5) 80–99%; (6) 100%. Based on 664 grafts; 15 grafts had missing coronary artery stenosis data.

Fig. 3. Turnbull cumulative patency rates according to type of bypass graft.
a multivariable proportion hazards model to analyse longitudinal patency of the RA grafts only. These models assume that the variables are independent, which is not correct. When there are two or more grafts per patient there are two levels of variables, those that are common to the patient, such as age and gender and those that are specific to the graft such as the target artery. To overcome this problem we have used a generalized linear mixed model. Kaplan-Meier estimates assume that graft failure has occurred at the time of angiography. Although the Kaplan-Meier technique is readily applied to a single defining event, such as death, this technique is not valid when assessing a non-fatal event, e.g. graft failure, which may have occurred at any time between implantation and angiography. The Kaplan-Meier method used in this way may overestimate graft failure. Kaplan-Meier estimates of other non-fatal events, such as structural prosthesis valve failure, have found to be high when compared with empirical results [22]. Turnbull’s cumulative incidence technique addresses the issue of graft failure before the time of assessment; that is at angiography, and calculates estimates using left- and right-censoring techniques. Turnbull’s technique, however, assumes independence of each observation and therefore, has a limited application when there are multiple grafts in a single patient.

All the statistical techniques have limitations estimating longitudinal graft patency rates. Repeated observations from the same patient with multislice CT scan and magnetic resonance imaging in the future will further clarify differences between conduits. Analyses of comprehensive data sets from randomized trials, which minimize the selection bias when compared with subsets of symptomatic patients, will provide a better opportunity to assess graft patency.

There are prospective randomized studies which compare the patency of RA and SV grafts. The Radial Artery Patency and Clinical Outcome study (RAPCO) [10] found no differences in the graft patency and major clinical outcomes in the interim 5-year study. In this study, the overall graft patency at 3 years was LITA 97% (n=87), free RITA 91% (n=22), RA 86% (n=49), SV 86% (n=102). The Complete Arterial Revascularization and Conventional Coronary Artery Surgery Study trial (CARACASS) [23] found 30-day patencies of LITA 99% (n=172), free RITA 96.2%, n=79), RA (94.05%, n=84) and SV (93.15%, n=146). Mureretto et al. [24] compared the clinical and angiographic results of total arterial revascularization with composite grafts and conventional coronary artery surgery. Angiography at a mean 12±4 months showed a significantly lower SV graft patency rate (89%) compared with RA (99%) and suggested that the use of composite ITA and RA Y-grafts might improve clinical and angiographic results. Comparison of protocol-directed (Trial) outcomes with symptom or ischemia-driven studies like RAPS [25] will determine whether these observational studies are representative of the CABG population.

5. Limitations

Retrospective studies of graft patency have clear limitations. The selection of patients with evidence of ischemia might underestimate the true graft patency of patients having coronary artery bypass grafting. Although bias cannot be determined for certain, it seems plausible that those patients, given their symptoms, are more likely to have failed grafts. This may be offset to some extent because the asymptomatic population will include some patients with silent graft occlusion. Our patient population with ischemia-directed angiography was only a small population (5%) of all patients undergoing surgery during that time. The follow-up period is too short to derive long-term conclusions.

6. Conclusion

Methods, by which graft patencies are compared, require refinement and standardization. Consideration should be given to the use of bilateral ITA grafts where possible. If additional conduits are required, there is no evidence to suggest that there is any difference between the SV and the RA in this 3-year observational study.

References

Dr. A. Royse (Melbourne, Australia): I have got two brief comments. One is that your internal mammary artery groups are both pedicled and to the left anterior descending artery territory, representing the best scenario for grafting. In comparison, your other two conduits are aorta-coronary-grafted to the other two territories, representing the worst scenario for grafting. So one would probably expect some patency differences on this issue alone.

The second, which I think probably pertains a lot more to your reference to the Circulation paper, and that is—with a symptom-directed angiography series, there is an inevitable bias. We should be somewhat cautious about interpreting the data too much compared to randomized studies or studies in asymptomatic patients.

Dr. Buxton: I agree with your second comment that you’d expect that symptom-directed angiography would produce inferior results.

Regarding your first comment, in our group of right internal thoracic arteries, our preference is to use crossover right in situ grafts mobilized high up. There were relatively few aortic connections.

Dr. Royse: Both mammary groups are pedicled to the LAD system and both radial arteries and vein grafts are to the other two coronary territories and are not pedicled, so one may expect some difference on that alone.

Dr. Buxton: Yes, I accept that.

Dr. M. Turina (Zurich, Switzerland): Several recent papers have shown that the degree of stenosis of the coronary artery to be bypassed is the major predictor for patency, especially of the radial artery which is prone to spasm in the first weeks or months after the implantation. In your material you definitely must have this data. Did you look at it in this way?

Having similar experience in the last years, our policy has been to put the radial artery only to 90% plus stenosis or to an obstructed artery. The second, which I think probably pertains a lot more to your reference to the Circulation paper, and that is—with a symptom-directed angiography series, there is an inevitable bias. We should be somewhat cautious about interpreting the data too much compared to randomized studies or studies in asymptomatic patients.

Dr. Buxton: We certainly share the same experience that when grafting vessels with a low-grade stenosis and competitive flow, the results are generally poor. The influence of native vessel stenosis was adjusted for in this multivariable equation.

Just one other comment, the collateral circulation depends on many things, one of which is the degree of native vessel stenosis. For example, you may have a 100% block in the LAD with a large PDA collateral, resulting in a highly competitive situation, even in the presence of a total occlusion. There are many factors we need to learn about the collateral circulation so that we can predict in which situations a radial artery graft will more likely fail.