Does grafting of the left anterior descending artery with the in situ right internal thoracic artery have an impact on late outcomes in the context of bilateral internal thoracic artery usage?

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**Background:** Despite their well-established advantages, bilateral internal thoracic arteries (BITA) are still largely underused. This is partly because of the technical complexities associated with the use of the right internal thoracic artery (RITA) to guarantee the universally accepted gold standard left internal thoracic artery (LITA) to left anterior descending artery (LAD) graft. The use of the in situ RITA for LAD grafting is a less technically demanding strategy. The impact of this strategy on early and late outcomes is investigated in the context of BITA usage.

**Methods:** Among 1667 patients undergoing first-time isolated coronary artery bypass grafting using BITA, in situ RITA for LAD grafting was used in 546 patients compared with in situ LITA to LAD in 1121 patients. Propensity score matching was carried out to investigate the impact of in situ RITA to LAD on early and late outcomes including mortality and need for repeat revascularization.

**Results:** A total of 546 propensity matched pairs were available for comparison. In the propensity matched cohort, the mean follow-up time was 7.8 ± 3.8 years. RITA to LAD did not increase the risk for late death (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.48-1.26), the need for repeat revascularization (HR, 0.83; 95% CI, 0.70-2.42), and the composite of death or repeat revascularization (HR, 0.81; 95% CI, 0.64-1.14).

**Conclusions:** Using in situ BITA with retrosternal in situ RITA for LAD grafting is a technically less demanding, safe, and effective strategy that can increase usage of BITA by avoiding a composite graft configuration or technically challenging retrocaval routing of in situ RITA through the transverse sinus. (J Thorac Cardiovasc Surg 2014;148:1275-81)

A large body of evidence supports the clinical superiority of bilateral internal thoracic arteries (BITA) over conventional use of a single left internal thoracic artery (LITA) in coronary artery bypass grafting (CABG). As the in situ LITA to LAD graft is universally accepted as the gold standard in CABG, BITA usage predominantly involves LITA for LAD grafting and the right internal thoracic artery (RITA) to bypass the branches of the circumflex artery either as an in situ graft routed through the transverse sinus or as a composite Y-graft. However, these strategies are technically demanding resulting in under use of BITA.

The use of the in situ RITA for grafting the LAD and in situ LITA to bypass the target vessels on the lateral aspect of the heart represents a less technically demanding and easily reproducible alternative when performing BITA grafting because it avoids complex graft configurations. However, this strategy has not yet gained popularity among cardiac surgeons. This is largely due to the common perception that using LITA to graft non-LAD territories might jeopardize late results after CABG. However, the superiority of LITA over RITA for grafting the LAD has not been demonstrated, and whether the alternative strategy of in situ RITA to LAD is as effective as the well-established gold standard in situ LITA to LAD remains to be established.

Therefore, we investigated the impact of using in situ RITA instead of LITA for grafting the LAD on early and late outcomes in the context of BITA usage.

**METHODS**

**Study Population**

The study was conducted in accordance with the principles of the Declaration of Helsinki. Prospectively collected data from the institutional surgical and interventional database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) was retrospectively analyzed. The PATS database captures detailed information on a wide range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients.
undergoing CABG in our institution. The data are collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain & Ireland database criteria. The database is maintained by a team of full-time clinical information analysts, who are responsible for continuous prospective data collection as part of a continuous audit process. Data collection is validated regularly. Information about death from any cause is obtained regularly from the General Register Office approximately 1 week after the event. Data on the need for reintervention were obtained from local institutional surgical and interventional databases, which are updated regularly.

Data for all patients who underwent isolated first-time CABG from April 2001 to May 2013 were analyzed. Inclusion criteria were as follows: CABG using MITA in situ ITA (left or right) grafted to the LAD; additional arterial or saphenous vein grafts if required to complete revascularization. Patients receiving in situ RITA to LAD with in situ LITA for bypassing the branches of the circumflex artery were considered as the treatment group and patients receiving in situ LITA to LAD with RITA either as in situ graft routed through the transverse sinus or as a composite Y-graft were considered as the control group. Patients receiving an ITA on the right coronary system were excluded from the present analysis (n = 77) because this strategy remains questionable.7

Surgical Technique
The operative technique has been described previously in detail.7,10,11 All interventions were performed via a midline sternotomy either on- or off-pump. Left and right ITAs were harvested with minimal trauma as pedicles or skeletonized grafts, based on the surgeon’s preference, and treated with papaverine solution before use. The great saphenous vein was harvested or skeletonized grafts, based on the surgeon’s preference, and treated with papaverine solution before use. The radial artery was harvested using an open or endoscopic technique. The radial artery was harvested or skeletonized grafts, based on the surgeon’s preference, and treated with papaverine solution before use. The great saphenous vein was harvested or skeletonized grafts, based on the surgeon’s preference, and treated with papaverine solution before use. The radial artery was harvested using an open or endoscopic technique.

Postoperative Management
All patients received an intravenous nitroglycerin (0.1-8 μg/kg/min) infusion for the first 24 hours unless hypotensive (systolic blood pressure <90 mm Hg). The choice of inotropic agents was dictated by the hemodynamic data. Other routine medications included daily aspirin and resumption of cholesterol-lowering agents and β-blockers. Clindogrel use in addition to aspirin was dictated by the surgeon’s preference.

Study End Points
The primary study end point was all-cause late mortality. Secondary end points were the need for repeat revascularization (percutaneous coronary intervention [PCI] or CABG) and composite of death or repeat revascularization. Early outcomes were also investigated including 30-day mortality, reexploration for bleeding, reintubation, postoperative cerebrovascular accident (CVA, transient or permanent deficit), postoperative renal replacement therapy (RRT), need for postoperative intra-aortic balloon pump (IABP), postoperative atrial fibrillation (POAF), deep sternal wound infection (SWI) defined by the Centers for Disease Control and Prevention as the presence of one of the following criteria: (1) an organism isolated from a culture of mediastinal tissue or fluid; (2) evidence of mediastinitis seen during the operation; (3) presence of either chest pain, sternal instability, or fever >38°C and either purulent drainage from the mediastinum, isolation of an organism present in a blood culture, or culture of the mediastinal area), and length of hospital stay.

Statistical Analysis
For the baseline characteristics, variables are summarized as the mean ± standard deviation for continuous variables and number and percentage for categorical variables.

Variables of interest included age, gender, diabetes mellitus, diabetics on insulin, hypertension, hypercholesterolemia, obesity (defined as a body mass index [BMI] ≥30 kg/m²), current smoking, renal impairment defined as a baseline serum creatinine level of 200 mmol/L or higher, previous myocardial infarction, previous PCI, chronic obstructive pulmonary disease, functional New York Heart Association (NYHA) class III or IV, reduced left ventricular ejection fraction (<50%), poor left ventricular function (<30%), history of CVA, peripheral vascular disease (PVD), preoperative atrial fibrillation (AF), neurologic dysfunction, elective indication for surgery, use of cardiopulmonary bypass (CPB), number of diseased vessels, number of grafts received, incidence of incomplete revascularization, and rate of total arterial grafting.

Because of the significant imbalances in baseline covariates between the 2 groups, we used propensity score matching. A propensity score representing the probability of having in situ RITA to LAD graft as opposed to an in situ LITA to LAD graft was calculated for each patient by using a nonparsimonious logistic regression model including all baseline risk factors. Pairs of patients receiving in situ RITA to LAD or in situ LITA to LAD were derived using greedy 1:1 matching with calipers of width 0.2 standard deviations (SDs) of the logit of the propensity score. Covariate balance was measured using the standardized differences; an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance (Figure 1). Generalized linear mixed models as appropriate were used to estimate the effect of in situ RITA to LAD over in situ LITA to LAD on early outcomes.

Kaplan-Meier estimates were used to plot the rates of long-term adverse events (all-cause death, repeat revascularization, and composite of death or repeat revascularization) and differences between risk curves were assessed using the Klein-Moeschberger test for matched pairs12 to adjust for differences in mean follow-up between the 2 groups. For each adverse long-term outcome, the hazard ratio (HR) of RITA to LAD versus LITA to LAD was estimated using Cox proportional hazard models with robust standard errors, to account for clustering in matched pairs.

All statistical analyses were performed using R, version 2.15.2 (R Core Team. R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org), the nonrandom package (Susanne Stampf, Nonrandom: Stratification and Matching by the Propensity Score: R Package Version 1.4. Q3; http://cran.r-project.org/package=nonrandom%20), and the survival package (Terry Therneau, A Package for Survival Analysis in S. R package version 2.36-14; http://cran.r-project.org/web/packages/survival) were used.
patients receiving an in situ RITA to LAD graft, in situ LITA was used to graft circumflex branches in 425 cases and diagonal branches in the remaining cases. Among patients receiving in situ LITA to LAD graft, RITA was used to graft circumflex artery branches in 419 cases and diagonal branches in 137 cases. A Y-graft configuration was used in 423 cases and an in situ graft routed through the transverse sinus in the remaining cases. Patient characteristics before and after matching are shown in Table 1.

Early Outcomes
Table 2 summarizes the postoperative outcomes for matched cohorts. In the matched sample, 18 of 1092 (1.6%) patients died within 30 days of the index procedure with a significant trend toward increased mortality for the control group (14 of 546, 2.5% vs 4 of 546, 0.7%; \( P = .02 \)). The incidence of reexploration for bleeding was significantly higher in the control group (30 of 546, 5.4% vs 15 of 546, 2.7%; \( P = .02 \)). No differences were observed for the incidence of postoperative CVA (\( P = .9 \)), RRT (\( P = .8 \)), reintubation (\( P = .13 \)), POAF (\( P = .5 \)), postoperative IABP usage (\( P = .09 \)), and deep SWI (\( P = .2 \)). Mean length of hospital stay was also similar for the 2 groups (9.4 ± 1.2 days vs 8.9 ± 0.9 days; \( P = .4 \)).

Follow-up and Late Outcomes
Follow-up times for the propensity matched cohorts ranged from 0 to 12.1 years. The mean follow-up time was 7.8 ± 3.8 years with a trend toward longer follow-up for the control group (2270 days; range, 0-4446 days vs 1890 days; range, 3-4432 days). A total of 42 and 25 patients died in the control and treatment groups, respectively (Klein-Moeschberger test; \( P = .32 \)). Survival for the control group was 97.7 ± 0.6 versus 98.0 ± 0.8 for treatment group at the 1-year follow-up, 92.1 ± 1.3 versus 93.4 ± 1.1 at the 5-year follow-up, and 83.8 ± 1.3 versus 86.1 ± 0.3 at the 10-year follow-up (Figure 2). Repeat revascularization was required in 22 and 20 patients in the control and treatment groups, respectively (Klein-Moeschberger test; \( P = .37 \)). Freedom from repeat revascularization was 98.6 ± 1.0 for the control group versus 98.7 ± 1.1 for the treatment group at the 1-year follow-up, 96.2 ± 1.5 versus 96.8 ± 2.0 at the 5-year follow-up, and 94.8 ± 1.8 versus 95.1 ± 1.0 at the 10-year follow-up (Figure 3). The incidence of the composite of death or repeat revascularization was 61 and 43 in the control and treatment groups, respectively (Klein-Moeschberger test; \( P = .81 \)). Freedom from the composite of death or repeat revascularization was 95.4 ± 0.8 for the control group versus 96.5 ± 0.8 versus for treatment group at the 1-year follow-up, 91.9 ± 1.2 versus 91.9 ± 1.3 at the 5-year follow-up, and 87.8 ± 1.5 versus 88.1 ± 1.9 at the 10-year follow-up (Figure 4).

The HRs using in situ RITA to LAD for outcomes of interest were as follows: late death (HR, 0.78; 95% CI, 0.48-1.26), need for repeat revascularization (HR, 0.83; 95% CI,
0.70-2.42), and the composite of death or repeat revascularization (HR, 0.81; 95% CI, 0.64-1.14).

**DISCUSSION**

The main finding of this single-center propensity score matched comparison is that CABG using BITA with in situ RITA to LAD and in situ LITA for circumflex territory showed long-term outcomes comparable with BITA with in situ LITA to LAD, and it was associated with reduced operative mortality and the need for reexploration for bleeding.

Abundant evidence validating the benefits of BITA grafting is available.\(^1\)\(^-\)\(^5\) Two meta-analyses have clearly shown long-term outcomes comparable with BITA with in situ RITA to LAD and in situ LITA to LAD, and it was associated with reduced operative mortality and the need for reexploration for bleeding. El Bardissi and colleagues\(^1\)\(^5\) recently reported current trends in isolated CABG in the United States. They studied 1,427,059 patients undergoing isolated primary CABG from the Society of Thoracic Surgeons Database from 2000 to 2009. Use of LITA increased from 83.7% in 2000 to only 4.1% in 2009; still low use of the RITA was not influenced by the use of the radial artery as an alternate graft; radial artery use was extremely low considering the mean age of the patients at 0.6%. RITA use as a single ITA graft remained constant from 2000 to 2009. Use of LITA increased from 83.7% to 94.6%. RITA use as a single ITA graft remained constant at 0.6%, and use of the RITA as part of a BITA procedure increased from 3.5% in 2000 to only 4.1% in 2009; still extremely low considering the mean age of the patients had reduced (66 years in 2000 vs 65 years in 2009). The low use of the RITA was not influenced by the use of the radial artery as an alternate graft; radial artery use was

### TABLE 2. Postoperative outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>LITA to LAD (%)</th>
<th>RITA to LAD (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-d mortality</td>
<td>2.5</td>
<td>0.7</td>
<td>.02</td>
</tr>
<tr>
<td>Reintubitation</td>
<td>2.9</td>
<td>2.7</td>
<td>.13</td>
</tr>
<tr>
<td>Postoperative CVA</td>
<td>0.73</td>
<td>0.7</td>
<td>.9</td>
</tr>
<tr>
<td>Postoperative RRT</td>
<td>2.3</td>
<td>2.2</td>
<td>.8</td>
</tr>
<tr>
<td>Need for postoperative IABP</td>
<td>3.09</td>
<td>1.49</td>
<td>.09</td>
</tr>
<tr>
<td>Reexploration for bleeding</td>
<td>5.5</td>
<td>2.7</td>
<td>.02</td>
</tr>
<tr>
<td>POAF</td>
<td>19.8</td>
<td>18.2</td>
<td>.5</td>
</tr>
<tr>
<td>Deep SWI</td>
<td>2.7</td>
<td>2.2</td>
<td>.2</td>
</tr>
<tr>
<td>Length of hospital stay, d ± SD</td>
<td>9.4 ± 1.2</td>
<td>8.9 ± 0.9</td>
<td>.47</td>
</tr>
</tbody>
</table>

_LITA, left internal thoracic artery; LAD, left anterior descending artery; RITA, right internal thoracic artery; CVA, cerebrovascular accident; RRT, renal replacement therapy; IABP, intra-aortic balloon pump; POAF, postoperative atrial fibrillation; SWI, sternal wound infection; SD, standard deviation._
10.8% in 2000, declining to 5.5% in 2009. The situation is no different globally.

Although the reason for the low use of the RITA/BITA is multifactorial, the technical complexity and unfamiliarity related to the RITA graft configuration and subsequent perceived concerns with perioperative results play an important role.

The optimal RITA configuration has not yet been established. Conventionally, the in situ RITA has been used for revascularizing the proximal branches of the circumflex system via the transverse sinus. Other strategies include retrocaval routing or construction of a Y-graft by anastomosing free RITA to in situ LITA. Unfortunately, these strategies are not without significant limitations that preclude the universal adoption of routine use of the RITA as a conduit for CABG.

Retrocaval and transverse sinus routing of the RITA results in the inability to control bleeding from retroaortic RITA branches, accidental clip removal as a result of aortic compression of the RITA, and compromised graft patency because of undetected kinks, graft overstrecthing, and rotation, which can also facilitate anastomotic site bleeding. On the other hand, the free RITA to the in situ LITA (Y-graft) configuration does not apply the principle of left ventricular revascularization from 2 different in situ sources, increasing the risk of hypoperfusion as well as potentially jeopardizing the patency of the gold standard conduit, the in situ LITA.

Because of these disadvantages, in situ RITA to the LAD and in situ LITA for the other graftable left-sided targets has been proposed. This represents an easily reproducible and technically less demanding strategy compared with previously described configurations. The RITA is biologically identical to the LITA and excellent angiographic results have been reported for RITA to LAD grafts. Tatoulis and colleagues reported a 95% 10-year patency rate for 149 RITA to LAD grafts and this result was comparable with LITA to LAD grafts (96%). Similarly, Shah and colleagues reported an in situ RITA to LAD graft patency rate of 94.6% that remained stable over time. Despite the available evidence on its excellent angiographic results, RITA to LAD grafting has not gained popularity and LITA continues to be the preferred conduit for LAD grafting in surgical series reporting BITA usage. In the cohort from Shah and colleagues, RITA was used to graft the LAD in 93 cases only compared with LITA to LAD grafting, which was used in 1193 cases. On the other hand, RITA to LAD grafting is considered a valuable strategy in redo CABG with failed LITA to LAD graft.
To the best of our knowledge, this study represents the largest experience of in situ RITA to LAD grafting in the context of first-time CABG using BITA. In our experience, this is a safe and effective strategy for grafting the LAD and has become the default strategy since 2007. Our analysis has shown a significant advantage of in situ RITA to LAD in terms of reexploration for bleeding and operative mortality, which was particularly low (0.7%). We can speculate that the difference in early mortality can be attributed to the aforementioned concerns associated with the use of the RITA for grafting left-sided targets other than the LAD. In particular, the increased rate of reexploration for bleeding seen in the control group may account for the increased operative mortality observed. Reexploration for bleeding is a well-recognized risk factor for increased operative mortality and morbidity including blood transfusion, need for inotropes, longer postoperative intensive care unit stay, and longer overall hospital stay.23

In the present series, the overall 4.1% incidence of reexploration for bleeding compares well with incidences of 2% to 6% mentioned in the literature.23 However, patients receiving RITA to non-LAD targets had a 5.5% reexploration rate compared with 2.7% for the RITA to LAD group. Inability to control bleeding from branches of the retrocaval and retroaortic routed RITA, which are in spasm at the time of closure and bleed later because of vasodilatation, as well as an increased number of potential bleeding sites due to construction of the Y-graft are some of the plausible reasons for this finding. All these technical pitfalls are avoided using in situ RITA to LAD and in situ LITA to lateral wall targets. In addition, the nonsignificant trend toward an increased need for postoperative IABP in the present series might suggest a role of perioperative myocardial hypoperfusion related to graft configurations that do not apply the principle of left ventricular revascularization from 2 different in situ sources.19

The most important objection to the retrosternal in situ RITA crossover routing is the potential risk of RITA damage during resternotomy. However, it should be taken into account that in the current PCI era, the rate of redo CABG is low and it becomes extremely low in the presence of a patent ITA to LAD graft. In addition BITA are expected to significantly enhance freedom from repeat revascularization13,14 because of their excellent patency rate. On the other hand, rapid advances in percutaneous options for treating both aortic as well as mitral valvular pathologies will almost preclude the need for resternotomy in patients with well-functioning BITA grafts and late presentation of degenerative valvular disease. Moreover, alternative surgical approaches are always possible to undertake repeat surgical revascularization24 or valvular intervention.25,26

The perceived increased risk for SWI continues to be a major reason for BITA underutilization.7 However, the impact of BITA harvesting on deep SWI is still debated. Recently published data from the New York State Department of Health Data Registry showed that BITA use was not associated with increased risk for SWI compared with single ITA; an overall rate for deep SWI has been reported as 1.8%.27 The overall rate of deep SWI in the present surgical cohort was 2.2% and 2.7% in the treatment and control groups, respectively, which is similar to the values reported in the literature,5,28,29 and the reduced rate for reexploration for bleeding might account for the better trend in the treatment group.

The primary limitation of the study is its retrospective nature. Propensity score adjustment is no substitute for a properly designed, randomized, controlled trial. The retrospective nature of the study cannot account for the unknown variables affecting the outcome that are not correlated strongly with measured variables. In situ RITA to LAD grafting has become the default strategy since 2007, therefore the average but not the maximum follow-up time was longer for the control group. However, time-dependent estimate analyses that was implemented accounted for these differences. When year of operation was forced into the propensity matched model, the final estimates did not significantly change but matched pairs showed residual unbalancing. Specific cause of death was not available in the present analysis and we could not investigate the impact of different strategies on cardiac-related death. However, all-cause death, which was used as the primary outcome, represents the most robust and unbiased index event in cardiovascular diseases because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments.30 Similarly, information about specific cause of bleeding for patients who were reexplored was not available. This study is a single-center experience thus its conclusions might not be generalizable to other experiences, populations, and current practices.

In conclusion, in situ RITA to LAD is a valid and easily reproducible alternative to in situ LITA to LAD when performing CABG using BITA. Using in situ BITA with retrosternal in situ RITA for LAD grafting is a technically less demanding strategy that can increase usage of BITA by avoiding a composite graft configuration or technically challenging routing of in situ RITA through the transverse sinus, which might potentially affect operative outcomes.

References


