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Does the use of bilateral mammary artery grafts compared with the use of a single mammary artery graft offer a long-term survival benefit in patients undergoing coronary artery bypass surgery?

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Abstract

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was: 'Does the use of bilateral mammary artery grafts compared with the use of a single mammary artery graft offer a long-term survival benefit in patients undergoing coronary artery bypass surgery?' Altogether 214 papers were found using the reported search, of which 13 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. All the included studies were follow-up studies; eight studies used prospective data collection, and five studies collected the study data retrospectively. No randomized controlled trials were found. Nine of the 13 included papers used a propensity-score-matched comparison of the survival of bilateral mammary artery graft [or, bilateral internal thoracic artery (BITA) graft] patients vs single mammary artery graft [or, single internal thoracic artery (SITA) graft] patients. These studies consistently showed an enhanced survival of BITA patients compared with propensity-score-matched SITA patients. Three of the 13 included papers used Cox proportional hazards regression analysis to compare survival of BITA vs SITA patients; one larger study showed better crude survival of BITA patients, but did not identify BITA grafts as independent predictor of enhanced survival. The remaining two studies also did not identify BITA grafts as independent predictor of enhanced survival. One study only presented crude survival estimates of BITA vs SITA patients and therefore was of limited informative value. We conclude that the use of BITA grafts seems to offer a long-term survival benefit compared with a SITA graft for patients undergoing coronary artery bypass grafting surgery. Although randomized evidence is lacking, observational evidence supporting this hypothesis is mounting.

Keywords: Review • Coronary artery bypass grafting • Bilateral internal mammary artery • Survival

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in the ICVTS [1].

THREE-PART QUESTION

In patients undergoing coronary bypass grafting surgery, is the use of bilateral mammary artery bypass grafts superior to the use of a single mammary artery bypass graft in terms of long-term survival?

CLINICAL SCENARIO

You are scheduled to perform an elective coronary bypass grafting procedure and discuss the case with your resident the night before. You plan to revascularize the anterior wall with the left internal mammary artery (LIMA), and discuss the possibilities of revascularization of the lateral and inferior wall with your resident. He suggests using a second mammary artery graft. You ask him to do a literature search on the latest research on long-term survival of this procedure compared with the use of a saphenous vein graft (SVG).

SEARCH STRATEGY

Medline (PubMed interface) was searched from 1950 until January 2013, using the following criteria: 'Coronary Artery Bypass'[Mesh] AND 'bilateral mammary artery' AND 'Mortality'.

SEARCH OUTCOME

Two hundred and fourteen papers were found using the reported search. Two authors (T.S. and G.T.L.K.) independently assessed all the papers and selected 13 papers that provided the best evidence to answer the question. These are presented in Table 1. We used the meta-analysis performed in 2001 by Taggart et al. [2] as a starting point and thus excluded all papers that were published...
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<th>Author, date, journal and country</th>
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<tr>
<td>Grau et al. (2012), <em>Eur J Cardiothorac Surg</em> [3], USA</td>
<td>Prospective follow-up study</td>
<td>Elective CABG patients: BITA n = 1459, SITA (LIMA + SVG) n = 4854</td>
<td>15-year survival</td>
<td>BITA 79% vs SITA 61%, P &lt; 0.0001</td>
<td>Enhanced long-term survival of BITA patients, compared with propensity-score-matched SITA patients</td>
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<tr>
<td>Galbut et al. (2012), <em>J Thorac Cardiovasc Surg</em> [4], USA</td>
<td>Prospective follow-up study</td>
<td>Elective and non-elective CABG patients, stratified by LVEF: BITA n = 2197, SITA n = 2340</td>
<td>Long-term survival, LVEF &lt; 30%</td>
<td>BITA 51.7 ± 5.4% vs SITA 57.0 ± 5.3%</td>
<td>Enhanced long-term survival of BITA patients compared with propensity-score-matched SITA patients, with normal or reduced ejection fraction, but not in patients with EF &lt; 30%</td>
</tr>
<tr>
<td>Locker et al. (2012), <em>Circulation</em> [5], USA</td>
<td>Retrospective follow-up study</td>
<td>Isolated primary CABG patients</td>
<td>Multiple arterial grafts compared with SITA, propensity-score-matched survival</td>
<td>Multiple arterial grafts 83 and 70% vs SITA 80 and 60% at 10- and 15-year follow-up, respectively, P = 0.0025</td>
<td>BITA grafts conferred a survival benefit at 15 years compared with SITA grafts</td>
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<td>Kinoshita et al. (2012), Ann Thorac Surg [6], Japan</td>
<td>Prospective follow-up study</td>
<td>Isolated CABG patients ages 70 years or greater</td>
<td>Propensity-matched 5-year survival estimates</td>
<td>BITA 86.4 ± 3.2% vs SITA 73.5 ± 3.9% (P = 0.01)</td>
<td>In elderly patients, BITA grafting is associated with a lower 5-year mortality compared with SITA grafting</td>
</tr>
<tr>
<td>Kurlansky et al. (2010), Ann Thorac Surg [7], USA</td>
<td>Retrospective follow-up study</td>
<td>Isolated CABG patients</td>
<td>Crude survival estimates at 15 years</td>
<td>BITA 53.5 ± 1.2% vs SITA 37.5 ± 1.1% (P &lt; 0.001)</td>
<td>BITA grafting offers a long-term survival advantage over SITA grafting</td>
</tr>
<tr>
<td>Kieser et al. (2011), Ann Thorac Surg [8], Canada</td>
<td>Prospective follow-up study</td>
<td>Isolated CABG patients</td>
<td>1-year mortality</td>
<td>HR 0.46 (95% CI 0.37–0.57, P &lt; 0.0001)</td>
<td>Better crude survival for BITA patients. However, after adjustment not significant anymore. Maybe age is an effect modifier. BITA seems reasonable in patients &lt;70 years of age</td>
</tr>
<tr>
<td>Mohammadi et al. (2008), Eur J Cardiothorac Surg [9], Canada</td>
<td>Prospective follow-up study</td>
<td>Primary isolated CABG patients</td>
<td>Crude survival (at 5, 7 and 10 years, respectively)</td>
<td>98.4, 97.8 and 96.5% for BITA vs 96.6, 94.3 and 88.9% for SITA (P &lt; 0.0001)</td>
<td>Additional survival benefit of BITA compared with SITA. This survival benefit decreases gradually with age, and is lost after 60 years of age</td>
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Table 1: (Continued)

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<tr>
<td>Di Mauro et al. (2005), Ital Heart J [10], Italy</td>
<td>Prospective follow-up study</td>
<td>Primary CABG patients &lt;70 years of age</td>
<td>10-year survival</td>
<td>Propensity-score-matched groups: BITA n = 476, SITA n = 476</td>
<td>Mean follow-up 8.8 ± 4.0 years</td>
</tr>
<tr>
<td>Lytle et al. (2004), Ann Thorac Surg [11], USA</td>
<td>Prospective follow-up study</td>
<td>Primary CABG patients</td>
<td>Long-term survival</td>
<td>BITA vs SITA, 89 vs 87%, 81 vs 78%, 67 vs 58% and 50 vs 37% at 7-, 10-, 15- and 20-year follow-up, respectively, P &lt; 0.0001</td>
<td>BITA patients had better long-term survival compared with propensity-score-matched SITA patients</td>
</tr>
<tr>
<td>Calafiore et al. (2004), Eur J Cardiothorac Surg [12], Italy</td>
<td>Prospective follow-up study</td>
<td>Primary CABG patients &lt;75 years</td>
<td>Propensity-matched 10-year survival</td>
<td>BITA 90.5 ± 2.8 vs SITA 87.1 ± 1.6, P = 0.0696</td>
<td>No significant survival benefit in propensity-matched groups of BITA vs SITA patients. BITA patients had better long-term freedom from cardiac death, as well as freedom from events</td>
</tr>
<tr>
<td>Hirotani et al. (2003), Ann Thorac Surg [13], Japan</td>
<td>Retrospective follow-up study</td>
<td>Primary CABG in diabetic patients (both insulin dependent and non-insulin dependent)</td>
<td>Long-term survival</td>
<td>No differences in long-term survival between BITA and SITA</td>
<td>No difference in long-term mortality between BITA patients and SITA patients</td>
</tr>
</tbody>
</table>

These results should be interpreted with caution as only crude survival estimates were compared
before 2001. We included studies in which at least 100 patients in each arm were followed up at least for 4 years. The variables age, sex, ventricular function and diabetes status needed to be reported for each study arm separately.

### RESULTS

Grau et al. [3] performed a prospective follow-up study of patients undergoing elective coronary artery bypass surgery (CABG), and made 928 propensity-score-matched pairs of bilateral internal thoracic artery (BITA) vs single internal thoracic artery (SITA) patients. During a mean follow-up of 9 years, BITA patients showed to have an enhanced 15-year survival compared with SITA patients. Although no separate analysis of BITA grafts (i.e. without patients receiving the combination SITA + RA) compared with propensity-score-matched SITA patients is presented, the crude survival estimates of BITA-only patients and BITA + SVG patients are both significantly better than SITA patients. Also, the Cox proportional hazards model showed that both the use of BITA-only and of BITA + SVG were associated with a significantly lower risk of early mortality compared with SITA.

Kinoshita et al. [6] performed a propensity-score-matched analysis in patients ≥70 years of age and showed that the use of BITA grafts is associated with significantly lower mortality at 5-years of follow-up in these patients.

Kurlansky et al. [7] performed a retrospective analysis of 2197 propensity-score-matched pairs of BITA and SITA patients and showed that BITA grafts offered a long-term survival benefit compared with SITA grafts at 15- and 25-years of follow-up.

Kieser et al. [8] performed a prospective follow-up study showing that crude mortality was lower in BITA patients compared

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<tr>
<td>Endo et al. (2003), Circulation [14], Japan</td>
<td>Primary CABG patients, studied in subgroups of diabetic patients and non-diabetic patients</td>
<td>Crude 10-year survival among diabetic patients</td>
<td>BITA 80.2 ± 3.8% vs SITA 75.4 ± 3.0%, P = 0.46</td>
<td>BITA grafting is not significantly better in reducing all-cause mortality than SITA grafting when assessing the Cox proportional hazards estimates</td>
</tr>
<tr>
<td>Retrospective follow-up study</td>
<td>Diabetic patients: BITA n = 190, SITA n = 277. Non-diabetic patients: SITA n = 411, BITA n = 253</td>
<td>10-year survival among diabetic patients with LVEF &gt; 40%</td>
<td>BITA 87.8 ± 3.5% vs SITA 75.2 ± 3.4%, P = 0.04</td>
<td></td>
</tr>
<tr>
<td>Adjustment for differences between groups by Cox model (level IIIa)</td>
<td>Median follow-up 8.1 years</td>
<td>Adjusted survival benefit BITA (Cox model) among diabetic patients</td>
<td>HR = 0.91 (95% CI 0.597–1.4, P = 0.6)</td>
<td></td>
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<tr>
<td>Endo et al. (2001), Circulation [15], Japan</td>
<td>Isolated CABG patients</td>
<td>7-year all death-free rate</td>
<td>BITA 88.7 ± 1.9% vs SITA 86.9 ± 1.4%, P = 0.6</td>
<td>No differences in mortality between BITA and SITA patients</td>
</tr>
<tr>
<td>Retrospective follow-up study</td>
<td>BITA n = 443, SITA n = 688</td>
<td>7-year re-CABG free rate</td>
<td>BITA 99.5% vs SITA 97.3%, P = 0.0256</td>
<td></td>
</tr>
<tr>
<td>Adjustment for differences between groups by Cox model (level IIIa)</td>
<td>Median follow-up 6.15 years</td>
<td>Adjusted survival benefit BITA vs SITA (Cox model)</td>
<td>HR = 0.95, 95% CI 0.67–1.35</td>
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Survival data are presented as Kaplan–Meier survival estimate ± standard error of the mean, or as Kaplan–Meier survival estimate with corresponding 95% CI. AMI: acute myocardial infarction; BITA: bilateral internal thoracic artery; CABG: coronary artery bypass grafting; CI: confidence interval; GEA: gastroepiploic artery; HR: hazard ratio; LITA: left internal thoracic artery; LVEF: left ventricular ejection fraction; SVG: saphenous vein graft; MI: myocardial infarction; RA: radial artery.
with SITA patients. However, the adjusted survival benefit was non-significant. Subanalyses of the data showed that age was a potential effect modifier and that BITA grafting might offer a survival benefit in patients <70 years of age.

Mohammadi et al. [9] performed a prospective follow-up study of 1277 BITA patients and 9566 SITA patients. BITA grafting was associated with a significantly lower risk of early mortality, and this survival benefit seemed to be lost in patients older than 60 years of age.

Di Mauro et al. [10] showed in a prospective manner that BITA patients had a significant better 10-year survival compared with propensity-score-matched SITA patients.

Lytle et al. [11] studied 1152 propensity-score-matched pairs of BITA vs SITA patients over a mean period of 16.2 years and found that survival was significantly better among BITA patients compared with SITA patients.

Calafiore et al. [12] found no significant survival benefit of BITA grafting at 10-year follow-up.

Hirotani et al. [13] found no difference in long-term mortality between BITA and SITA patients with diabetes. However, this analysis has the limitation that only crude mortality rates were assessed in a small group of patients (BITA n = 179 vs SITA n = 124).

Endo et al. [14] performed a retrospective analysis among diabetic CABG patients. The data were stratified according to left-ventricular ejection fraction. At 7-years of follow-up, crude mortality rates were similar between BITA and SITA patients. Cox proportional hazards analysis showed a non-significant benefit of BITA grafts when assessing all-cause mortality. However, BITA grafts conferred a benefit when assessing the composite endpoint of death, redo coronary surgery or myocardial infarction.

In 2001, Endo et al. [15] found no survival benefit of BITA grafting among more than 1000 patients undergoing CABG.

CLINICAL BOTTOM LINE

Although methodological issues make head-to-head comparison difficult, observational studies suggest that the use of BITA grafts seems to offer a long-term survival benefit compared with SITA for patients undergoing CABG surgery. Although randomized evidence is currently lacking, observational evidence supporting this hypothesis is mounting.

Conflict of interest: none declared.

REFERENCES


eComment. Two internal mammary artery grafts are better than one

Author: Jamil Haji-Chahine
Department of Cardio-Thoracic surgery, University Hospital of Poitiers, Poitiers, France
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We read with great interest the paper by Smith et al. regarding the long-term survival benefit of the usage of bilateral internal mammary artery (BIMA) grafts in coronary revascularization surgery [1]. They included in their results 13 follow-up studies published after 2001. However, we found one additional relevant article investigating the long-term outcomes associated with BIMA grafting compared with single internal mammary artery (SIMA) among diabetic patients [2]. We would like to take this opportunity to briefly extract the relevant information from the above-mentioned study and to add a short comment on this salient subject.

Puskas et al. [2] conducted a retrospective cohort analysis by extracting data from the Society of Thoracic Surgeons database at a single referral academic centre. They included a total of 3527 coronary artery bypass grafting procedures (BIMA n = 812; SIMA n = 2715). After adjustment for differences between groups by the Cox model, BIMA grafting portended a 35% reduction in the hazard of long-term death at 8 years of follow-up (adjusted hazard ratio, 0.65; 95% CI, 0.48 to 0.88; P = 0.006). The authors concluded that the usage of BIMA grafting provides significant benefit in late survival compared with SIMA grafting in both diabetic and non-diabetic patients. BIMA grafting should be performed whenever patient risk factors and comorbidities allow an acceptable risk of deep sternal wound infection.

As rightly outlined by the authors, all these studies are follow-up studies. However, only one randomized trial comparing these two techniques (ART Arterial Revascularization Trial) [3] is currently under way in Europe that can broaden our understanding. ART primary outcome is survival at 10 years, therefore the results should be available by 2018. Until that date the debate will continue. This uncertainty has been reflected in the rate of adoption of BIMA grafting, the rate of use of the technique varies from 4% in North America to 10% in Europe [4]. The major reasons for not using BIMA grafts are the lack of solid evidence of benefits and the increased rate of sternal wound infection, particularly in diabetics. Of note, in the SYNTAX study [5], BIMA grafting was used in a relatively higher percentage of 28% of patients.