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# What is the best choice for third conduit when using bilateral internal mammary arteries for coronary artery bypass grafting—radial artery or saphenous vein graft?

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## Abstract

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was 'What is the best choice for third conduit when using bilateral internal mammary arteries for coronary artery bypass grafting—radial artery or saphenous vein graft?'. Altogether >525 papers were found using the reported search, of which **7** 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. Overall, there was no survival benefit demonstrated with the use of a radial artery over the use of a saphenous vein graft as a choice of third conduit following bilateral internal mammary artery grafts for coronary artery bypass grafting. The main limitation of the current evidence available is the restricted follow-up periods and the high attrition rates with small sample sizes affecting the strength of conclusions that can be drawn beyond 10 years of follow-up. We conclude that despite previous evidence supporting improved long-term patency of radial arterial grafts, there is no strong evidence that the use of a radial artery, over a saphenous vein graft, has any survival benefit when used as the third conduit following bilateral internal mammary artery grafts.

**Keywords:** Review • Coronary artery bypass grafts • Bilateral internal mammary artery • Bilateral internal thoracic artery • Radial artery • Saphenous vein graft

## 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 artery bypass grafting with use of bilateral internal mammary arteries] is [use of a radial artery graft] compared [to use of a saphenous vein graft as choice for third conduit] associated with a significant survival benefit.

## CLINICAL SCENARIO

A 50-year-old male patient requires coronary artery bypass grafting (CABG) for the management of significant triple vessel coronary artery disease. He is non-diabetic and has no increased risk

factors for sternal wound complication and you wish to use bilateral internal mammary artery (BIMA) for his grafts. A colleague suggests that there is no benefit to use of a radial artery (RA) over use of a saphenous vein graft (SVG) for the third choice of conduit in his operation. You decide to check the available evidence to clarify if there is any benefit to be gained in use of a radial artery over use of a saphenous vein in this case.

## SEARCH STRATEGY

The literature search was performed in Medline from 1946 to June 2021 using the Ovid interface.

[Coronary Artery Bypass OR Bilateral Internal Mammary Artery OR Bilateral Internal Thoracic Artery] AND [Radial Artery OR Arterial Conduit OR Arterial Revascularisation OR Arterial graft\$] AND [Randomized Controlled Trial OR Controlled Clinical Trial OR Randomized OR Placebo OR Drug Therapy OR Randomly OR Trial OR Groups] NOT [exp animals/not humans].

## SEARCH OUTCOME

A total of 525 papers were found using the reported search. From these, 4 papers were identified that provided the best evidence to answer the question and an additional 3 papers were identified from review of the references. One meta-analysis addressing the same question was located and is discussed below. These are presented in Table 1.

## RESULTS

Formica *et al.* [2] retrospectively analysed 660 patients with triple vessel disease undergoing CABG with either BIMA and RA ( $n=206$ ) or BIMA and SVG ( $n=454$ ), with propensity score matching used to obtain 190 matched pairs. The median follow-up time was 9.2 years (interquartile range 5.6–13 years). They found that there was no significant difference between in-hospital mortality or in long-term survival between the 2 groups at 5, 10 or 15 years following their operation. For the BIMA and RA group, the survival at 5, 10 and 15 years was  $94.8 \pm 1.7\%$ ,  $83.7 \pm 3.1\%$  and  $78.6 \pm 3.9\%$ , respectively. This compares the BIMA and SVG that had survival at 5, 10 and 15 years of  $96.2 \pm 1.4\%$ ,  $85.1 \pm 2.9\%$  and  $80.4 \pm 3.6\%$ , respectively. This trial has a relatively small sample size and with a median follow-up time of only 9.2 years, concerns of attrition affecting the validity of the 15-year survival must be noted. Overall, this study demonstrated no survival benefit from use of RA over SVG as third conduit following BIMA.

Taggart *et al.* [3] reported results from the Arterial Revascularization Trial, a multicentre randomized control trial comparing survival benefit between BIMA and single left internal mammary artery. They have reported on a *post hoc* analysis of 5-year outcomes and offered subgroup analysis of BIMA and RA compared to BIMA and SVG. Because of the lack of randomization with regard to receiving an RA compared to SVG they have relied on propensity matching to perform their subgroup analysis. Of the total 3102 patients enrolled in the trial, 273 patients received BIMA and RA and 775 received BIMA and SVG, these have been propensity matched to the final of 272 patients. The results are reported in their supplemental data with no significant survival benefit demonstrated. These are not randomized groups and of note the follow-up is only at 5 years which is well within the expected patency period of SVG. The 5-year overall death rate was reported as 7.4% (95% CI 4.3–10.5) for the BIMA + RA group and 7.8% (95% CI 4.6–11.1) for the BIMA + SVG group. The 10-year follow-up of this trial [4] unfortunately does not report on the data from these subgroups and hence was not included in this BET. Overall, no survival benefit with use of a RA over SVG was demonstrated within the BIMA subgroup.

Mohammadi *et al.* [5] retrospectively analysed 1750 patients undergoing CABG with BIMA, with 255 having BIMA and RA and 1495 having BIMA and SVG. Propensity score matching yielded 249 pairs. There was no statistical difference in the 5-, 10- and 15-year survival rates between the matched groups ( $P=0.12$ ). For the BIMA and RA group, survival rates at 5, 10 and 15 years were 98.3%, 92.0% and 92.0%, respectively, compared to 96.5%, 93.0% and 87.0% in the BIMA and SVG group. Of note the median follow-up was only 8.1 years for the RA group and 7.9 years for the SVG group, potentially limiting the validity of the longer-term results. While there was a suggestion of a divergence emerging between the 2 groups at the 10-year mark favouring survival of

the BIMA and RA group, due to the significant attrition of patients beyond that point conclusions cannot be drawn. Overall, they showed no survival advantage with the use of RA over SVG in long-term follow-up.

Shi *et al.* [6] retrospectively analysed 1497 patients undergoing CABG with BIMA. They had 1037 patients with BIMA and RA and 460 patients with BIMA and SVG as third conduit. Propensity score matching yielded 262 matched pairs. The mean follow-up was  $12 \pm 5$  years. There was a broad variation within the radial group in terms of grafting targets with 131 patients having bilateral radials and targets including the circumflex, diagonal and right coronary artery. This may influence the results compared to other papers in this review as some have hypothesized the value of the radial compared to a saphenous vein is diminished when used as a 'third conduit' given it is going to the 'third territory' of importance, which has less long-term prognostic implications for the patient. At 15 years, they found BIMA and RA to have better risk-adjusted survival ( $P=0.021$ ). Survival in the BIMA and RA group at 15 years was  $82 \pm 5.2\%$  compared to  $72 \pm 6.0\%$  in the BIMA + SVG group. Overall, they found a survival benefit to the use of a radial artery as third conduit.

Benedetto *et al.* [7] retrospectively analysed 764 patients undergoing CABG with BIMA. They had 275 patients with BIMA and RA and 489 patients with BIMA and SVG, resulting in 275 matched pairs. The mean follow-up of  $10.6 \pm 4.8$  years. The BIMA and RA group had 5-, 10- and 15-year survivals of  $97.4 \pm 0.9\%$ ,  $90.3 \pm 2.0\%$ , and  $81.7 \pm 3.2\%$ , respectively, and the BIMA and SVG had 5-, 10- and 15-year survivals of  $97.0 \pm 1.0\%$ ,  $94.1 \pm 1.5\%$  and  $82.1 \pm 3.4\%$ , respectively. The matched BIMA and RA group were heterogenous including patients who had additional SVG; however, when analysis was restricted to only patients with total arterial revascularization, the survival was still comparable ( $P=0.34$ ). Overall, the addition of an RA to BIMA was not associated with improved long-term survival.

Grau *et al.* [8] retrospectively analysed 751 patients who underwent BIMA and RA and SVG ( $n=183$ ) or BIMA and SVG ( $n=568$ ) with propensity score matching, resulting in 183 matched pairs. They found no significant difference in survival between the 2 groups at 14 years; however, when splitting the groups at 10 years and performing a time segment analysis, they identified a trend of increased survival in the BIMA and SVG group prior to 10 years and increased survival in the BIMA and RA and SVG after 10 years, suggesting that the survival benefit of the addition of an RA is not appreciated until after the 10-year mark. Survival in the BIMA and RA group was 97.3%, 91.9% and 91.9% at 3-, 10- and 14-year follow-up, compared to 99.4%, 90.5% and 83.2% in the BIMA and SVG group. This article has a relatively small sample size. The inclusion of SVG into the RA group creates a heterogenous group and does not offer a reflection of total arterial revascularization strategy. Overall, no survival benefit was demonstrated with the use of RA over SVG.

Di Mauro *et al.* [9] retrospectively analysed 1015 patients undergoing BIMA and arterial conduit ( $n=372$ ) or BIMA and SVG ( $n=643$ ) with propensity score matching used to identify 885 patients (295 with arterial conduit and 590 SVG). Of note the arterial conduit group was heterogenous and included use of right gastroepiploic artery ( $n=208$ ) and RA ( $n=87$ ). The follow-up period was 8 years. Survival at 8 years was  $91.9 \pm 2.9\%$  for the BIMA and RA group, compared to  $95.6 \pm 0.9\%$  in the BIMA and SVG group. Only subgroup analysis of the radial artery patients compared to SVG was used for this review. When divided into 3 groups (RA, REGA, SVG), there was no statistical difference found between the 3 groups; however, there was no direct propensity matching

**Table 1:** Best evidence papers

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Formica <i>et al.</i> (2019), J Thorac Cardiovasc Surg [2], Italy Cohort study (level III)	660 patients undergoing CABG - BIMA + RA ( <i>n</i> = 206) - BIMA + SVG ( <i>n</i> = 454) 190 matched pairs - Group A—BIMA + RA - Group B—BIMA + SVG	In-hospital mortality 5-Year survival 10-Year survival 15-Year survival	A—1.1% B—1.1% <i>P</i> > 0.99 A—94.8 ± 1.7% B—96.2 ± 1.4% A—83.7 ± 3.1% B—85.1 ± 2.9% A—78.6 ± 3.9% B—80.4 ± 3.6% Stratified log-rank <i>P</i> = 0.78	Nil significant long-term survival benefit found with addition of radial artery compared to SVG
Taggart <i>et al.</i> (2017), Circulation [3], UK RCT (level II)	1048 patients undergoing CABG - BIMA + RA ( <i>n</i> = 273) - BIMA + SVG ( <i>n</i> = 775) Data from supplemental table - Group A—BIMA + RA ( <i>n</i> = 273) - Group B—BIMA + SVG ( <i>n</i> = 276)	5-Year outcomes MI Repeat revascularization CV death CV death/MI/repeat revascularization Overall death	A—1.5% (95% CI 0.04–2.90) B—3.3% (95% CI 1.2–5.4) A—3.7% (95% CI 1.4–6.0) B—6.3% (95% CI 3.4–9.3) A—3.7% (95% CI 1.4–5.9) B—3.7% (95% CI 1.5–6.0) A—7.6% (95% CI 4.4–10.8) B—12.1% (95% CI 8.2–16.1) A—7.4% (95% CI 4.3–10.5) B—7.8% (95% CI 4.6–11.1)	Only a subgroup analysis, nil randomization between groups Nil benefit demonstrated at 5 years
Mohammadi <i>et al.</i> (2016), Ann Thorac Surg [5], Canada Cohort study (level III)	1750 patients undergoing CABG - BIMA + RA ( <i>n</i> = 255) - BIMA + SVG ( <i>n</i> = 1495) 249 matched pairs Group A—BIMA + RA Group B—BIMA + SVG	5-Year survival 10-Year survival 15-Year survival	A—98.3% B—96.5% A—92.0% B—93.0% A—92.0% B—87.0% <i>P</i> = 0.12	No additional survival benefit seen with addition of radial graft
Shi <i>et al.</i> (2016), Eur J Cardiothorac Surg [6], Australia Cohort study (level III)	1497 patients undergoing CABG - BIMA + RA ( <i>n</i> = 1037) - BIMA + SVG ( <i>n</i> = 460) 262 matched pairs Group A—BIMA + RA Group B—BIMA + SVG	30-Day mortality 15-Year survival	A—1.1% B—1.1% <i>P</i> > 0.99 A—82 ± 5.2% B—72 ± 6.0% <i>P</i> = 0.021	15-Year survival benefit seen with addition of radial artery graft
Benedetto <i>et al.</i> (2016), J Thorac Cardiovasc Surg [7], UK Cohort study (level III)	764 patients undergoing CABG BIMA + RA ( <i>n</i> = 275) BIMA + SVG ( <i>n</i> = 489) 275 matched pairs Group A (BIMA + RA) Group B (BIMA + SVG)	5-Year survival 10-Year survival 15-Year survival	A—97.4% ± 0.9% B—97.0% ± 1.0% A—90.3% ± 2.0% B—94.1% ± 1.5% A—81.7% ± 3.2% B—82.1% ± 3.4% Log-rank <i>P</i> = 0.54	Lack of survival benefit demonstrated with use of RA
Grau <i>et al.</i> (2015), Eur J Cardiothorac Surg [8], USA Cohort study (level III)	751 patients undergoing CABG - BIMA + RA + SVG ( <i>n</i> = 183) - BIMA + SVG ( <i>n</i> = 568) 183 matched pairs - Group A—BIMA + RA + SVG - Group B—BIMA + SVG	Length of stay 3-Year survival 10-Year survival 14-Year outcomes	A—6 days B—5 days <i>P</i> = 0.016 A—97.3% B—99.4% A—91.9% B—90.5% A—91.9% B—83.2% <i>P</i> = 0.252	No significant impact on long-term survival with addition of a radial graft
Di Mauro <i>et al.</i> (2009), J Thorac Cardiovasc Surg [9], Italy Cohort study (level III)	677 patients undergoing CABG - BIMA + RA ( <i>n</i> = 87) - BIMA + SVG ( <i>n</i> = 590) Subgroup—not directly propensity matched - Group A—BIMA + RA - Group B—BIMA + SVG	8-Year outcomes (% free from event) All-cause mortality Cardiac death Cardiac event	A—91.9 ± 2.9% B—95.6 ± 0.9% <i>P</i> = 0.129 A—97.6 ± 1.6% B—98.6 ± 0.5% <i>P</i> = 0.492 A—96.4 ± 2.0% B—95.9 ± 0.8% <i>P</i> = 0.793	RA and SVG comparison only a subgroup analysis—not directly propensity matched. Nil significant benefit in RA demonstrated over SVG

BIMA: bilateral internal mammary artery; CABG: coronary artery bypass grafting; CI: confidence interval; CV: cardiovascular; MI: myocardial infarction; RA: radial artery; RCT: randomised control trial; SVG: saphenous vein graft.

between RA and SVG groups. Relying on subgroup analysis has limited the sample size. Overall, there was no statistically significant difference between the BIMA and RA and BIMA and SVG in terms of all-cause mortality or cardiac event at their 8-year follow-up.

Formica *et al.* [10] published a meta-analysis addressing the same question as this BET. It included 6 papers, 5 of which are included in this BET [2, 5–8]. It has not included the papers by Taggart *et al.* [3] and Di Mauro *et al.* [9]. It included an additional paper by Yoshida *et al.* [11] which presents a comparison of results between the use of SVG and RA. While the paper makes reference to BIMAs and their value, it does not actually present any subgroup analysis of BIMA patients. The paper specifies that most patients in the RA group received BIMA to their left coronary system, while in the SVG group, most patients received left internal mammary artery and RA to their left system. Propensity matching in this paper does not incorporate use of BIMA, its results have been misrepresented in this meta-analysis. This paper has incorrectly contributed 91 'BIMA + RA' and 91 'BIMA + SVG' patients to meta-analysis total of 1250 in each group, meaning that caution must be used when assessing their conclusion that the addition of an RA compared to SVG to BIMA conferred significant survival benefit. Given the additional paper is not in fact a BIMA comparison, it was not included in this BET.

## CLINICAL BOTTOM LINE

Despite previous evidence supporting improved long-term patency of radial arterial grafts, there is no strong evidence that the use of a radial artery, over a saphenous vein graft, has any survival benefit when used as the third conduit following bilateral internal mammary artery grafts.

## Reviewer information

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