

**Dr Pettinari:** I think that could be an option, but personally in our centre we prefer now to go for total arterial revascularization of selected patients because biologically the mammary artery is a better graft, so we strongly believe in its patency in the long term.

**Dr Khaliel:** My last question is regarding your analysis of comparison with the matched population. You have compared the effect of EDP and mitral regurgitation in both groups. The SITA group were sicker. But do you think that it affected the survival at 10 years or 5 to 7 years? Because it wasn't really defined in the manuscript.

**Dr Pettinari:** I feel mitral regurgitation could be a risk factor. But in all Cox regression analyses we have found only age, kidney function, and bilateral mammary artery to be predictors of 10-year survival.

**Dr Khaliel:** And the cause of death (more in SITA than BITA at 10 years) at that time?

**Dr Pettinari:** I cannot directly answer because I didn't make this analysis for this paper.

**Dr D. Taggart (Oxford, UK):** I really enjoyed your presentation on two accounts. First, about 10-15 years ago I did several debates with Dr Paul Sergeant about the benefits of a second mammary artery, when he assured me there was no additional benefit. I don't know if he's here, but I say 'Thanks, Paul.' I'm sorry, that's obviously a bit of a joke. So I am encouraged to see your data. But the second thing concerning the use of two mammary arteries in patients over 70 (the last speaker or questioner alluded to it) is the importance of a no-touch aortic technique. Revascularizing patients, octogenarians, on the basis of two mammary arteries, maybe with composite grafts, and doing them off-pump with a no-touch aortic technique, very dramatically reduces the risk of neurological injury. So I don't think it's just a survival benefit per se that

you're looking at in this elderly population but the potential to significantly minimize neurological injury.

**Dr Pettinari:** Our experience in off-pump effectively started in 2000 and this data also from three decades before, so from 1971. I didn't find OPCAB as a positive factor for survival in this group in my Cox analysis because there were a lot of patients that were operated on before our restructured programme. But for sure in the last part of our experience the rates of stroke, myocardial infarction, and complications are dramatically decreased in comparison with our practice before introducing off-pump.

**Dr R. Mohr (Tel-Aviv, Israel):** Our experience about the difference between single and bilateral ITA's is a little bit different. We have a series starting in 1996 which included more than 2000 patients above the age of 70, and in our experience (we just analysed our data), the benefits of BITA are clear. Also, the benefits of off-pump compared to on-pump are clear. But when we compared our composite T grafts, including radial arteries, with the results of BITA, there was no significant difference. So when you regard a radial artery as a SITA, the difference in survival is not significant.

BITA was our preferred method of revascularization and most of the radial cases were those in whom we didn't want to use BITA, such as in diabetic women and other patients with increased risk of sternal infection. So the only difference was found between single mammary with veins, and arterial grafts.

**Dr Pettinari:** In our centre the use of bilateral mammary artery also increased more and more in the last year. I think we now prefer to use bilateral internal mammary arteries in 80% of our patients. The choice that we made is based on the general quality of the patient and the life expectancy of the patient. If the life expectancy of the patient is more than 5-7 years, then we opt for a bilateral mammary artery. That is what we believe from our data.

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## EDITORIAL COMMENT

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# Bilateral internal thoracic artery use: will another retrospective study ever strengthen the prospect?

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Since the introduction of coronary artery bypass grafting (CABG) 50 years ago [1], the conduit choice to bypass coronary artery stenosis continues to be a debate [2]. Already in the early years, CABG was performed using internal thoracic arteries (ITAs). However, it took several decades before evidence supported the use of ITAs, when Loop *et al.* showed that the left ITA (LITA) to the left anterior descending (LAD) artery prolonged long-term survival when compared with a saphenous vein graft [3]. Several research groups went even further by claiming that bilateral ITA (BITA) grafting was superior to the use of a single ITA (SITA). Although these initial studies were merely retrospective, the use

of the LITA to the LAD became widely accepted with >90% of patients receiving this construction in contemporary CABG practice [4]. The fate of BITA grafting has been less fortunate.

Over the past 25 years, a staggering number of retrospective and prospective observational studies have published long-term results of BITA versus SITA use. The majority of studies concluded that BITA grafting either reduced mortality or showed to have comparable results with SITA grafting. In a recent meta-analysis that exclusively included studies with long-term follow-up of at least a mean of 9 years ( $n = 9$  studies comprising 15 583 patients with nearly 200 000 patient-years of follow-up), BITA versus SITA grafting significantly

**Table 1:** Observational studies of BITA versus SITA grafting and the effect of age

Author, year	Number of patients (SITA:BITA)	Age cut-off used for inclusion	Analysis	Mean follow-up	Outcome	Results SITA versus BITA
Studies comparing SITA versus BITA above an age cut-off						
Galbut <i>et al.</i> [9]	736:731	≥65 years	Unadjusted	3.6 years	Survival	60.7 vs 67.9% at 8 years ( $P < 0.028$ )
Jones <i>et al.</i> [10]	338:172	>65 years	Multivariate model	5.0 years	Survival	Hazard ratio: $P = 0.031$
Hirovani <i>et al.</i> [11]	108:138	≥65 years	Unadjusted	-	Survival and cardiac events	Significant at 10 years: $P < 0.05$
Kinoshita <i>et al.</i> [12]	219:219	≥70 years	Propensity-matched	4.3 years	Survival	73.5 vs 86.4% at 5 years ( $P = 0.01$ ) Multivariate HR 0.56, 95% CI 0.31–0.99; $P = 0.04$
Studies determining an age cut-off						
Mohammadi <i>et al.</i> [13]	9566:1388	No cut-off	Adjusted	5.7 years	Cardiac survival	BITA superior to SITA up to 60 years of age
Kieser <i>et al.</i> [14]	4029:1038	No cut-off	Adjusted	7.1 years	Survival	BITA superior to SITA up to 70 years of age

BITA: bilateral internal thoracic artery; HR: hazard ratio; SITA: single internal thoracic artery.

reduced mortality with a hazard ratio of 0.79, 95% confidence interval (CI) 0.75–0.84 [5]. Despite these encouraging results, BITA use remains remarkably low. Among patients who underwent CABG in the SYNTAX trial and registry, BITA grafting was performed in 10% in the USA and 25% in Europe [6]. Another ‘real-world’ analysis of 541 368 patients receiving CABG in the USA showed that the rate of BITA use increased over consecutive years but remained low during the entire study period: 3.6% in 2002 to 4.5% in 2005 [7].

The reason for the disappointing adoption of BITA use is multifactorial. The choice to use both ITA conduits depends strongly on the motivation of the surgeon. Surgeons in favour of BITA grafting cite evidence of observational studies that reported improved long-term survival, while those surgeons not particularly in favour of BITA grafting refer to the fact that there is currently no randomized clinical trial with long enough follow-up to confirm that BITA is indeed better than SITA. Moreover, surgeons may be reticent to using both ITA grafts because of the higher complexity of the procedure and the increased risk of sternal wound complications found particularly in diabetic, obese women. Besides patient characteristics like diabetes, body mass index and gender, age is a decisive factor [7], as the benefit of BITA over SITA only occurs after prolonged follow-up. A life expectancy of at least 10 years appears to be needed to show significant benefit of BITA use. In this regard, the current issue of the *European Journal of Cardio-Thoracic Surgery* includes a retrospective study from Pettinari *et al.* in which they performed a propensity-matched analysis comparing BITA with SITA in elderly patients >70 years of age, to assess whether the benefit of BITA grafting can be extended to elderly patients [8].

The authors showed that patients who underwent BITA grafting, when compared with patients who received only a SITA, were younger, and less often had peripheral vascular disease, diabetes, chronic obstructive pulmonary disease or a recent myocardial infarction, all factors known to be associated with impaired survival during follow-up. The authors therefore were correct in performing a propensity-matched analysis after which no differences in the BITA and SITA groups existed. In terms of outcomes, BITA grafting showed to have superior survival after 3 months, 1 year and 10 years in the unmatched groups. After matching and as

anticipated due to the differences in baseline characteristics, the difference between BITA and SITA was smaller, with BITA grafting only being superior after 10 years of follow-up (multivariate hazard ratio of 0.78, 95% CI 0.64–0.96;  $P = 0.04$ ) [8].

The authors have to be congratulated for achieving such good results with BITA grafting. However, several significant limitations of the current study should be acknowledged, putting these results in the correct perspective. Of the 1328 and 2168 patients who underwent BITA and SITA grafting, respectively, only 892 propensity-matched pairs could be achieved. The fact that two-thirds of patients could not be matched indicates that these groups were significantly different. Although there were no longer any significant differences between the groups after matching, the authors were unable to match patients on the refinement of the surgical technique; the inclusion was during 1972–2006, with BITA being performed in the later decades, during which the CABG procedure changed considerably with improved outcomes. Furthermore, clinical variables as well as clinical judgement, which were not collected, will play an important but unquantifiable role that can obliterate the significance of BITA grafting.

It is unlikely that the results from Pettinari *et al.* will have a significant impact on current practice, as already six previous studies have compared BITA with SITA grafting in specific age groups and reported conflicting results [9–14] (Table 1). Four of these studies showed that BITA was superior to SITA grafting in groups of patients >65 or >70 years of age [9–12]. Two studies included patients of all ages to determine the impact of age on the comparison between BITA and SITA grafting: Mohammadi *et al.* found that BITA grafting was only superior to SITA grafting below the age of 60 [13], while Kieser *et al.* provided evidence to extend the use of BITA grafting in patients up to 70 years of age [14]. Such a design is preferred to provide a hazard ratio of BITA grafting in elderly patients that can be compared with the hazard ratio in younger patients, and therefore allows one to conclude whether age is an important factor in the debate of BITA versus SITA grafting. Unfortunately, Pettinari *et al.* did not perform such an analysis.

Although the evidence from observational studies provides some incentive to perform BITA grafting, it clearly is not convincing enough for the majority of surgeons to routinely use both

IMAs. One cannot deny that the only randomized trial, the ART trial, which is currently ongoing to complete a 10-year follow-up [15], will be crucial to determine the role of BITA grafting in contemporary CABG. Not only will it allow strong evidence in the debate on BITA versus SITA, but it will also help determine whether an age cut-off is apparent as hypothesized in observational studies. Until then, further observational studies will not significantly strengthen the prospect of improved outcomes with BITA grafting and its routine use in clinical practice.

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