Age cutoff for the loss of survival benefit from use of radial artery in coronary artery bypass grafting

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Background: Controversy still exists about the superiority of the radial artery (RA) over the saphenous vein graft (SVG) as a second conduit for surgical myocardial revascularization. We aimed to investigate the presence of any survival benefit from use of the RA and relate it to patients' age.

Methods: Propensity score matching was conducted on 9005 patients who underwent first-time isolated coronary artery bypass grafting (CABG) using the left internal thoracic artery at a single institution from 1996 to 2012. The use of RA was recorded in 936 patients, whereas the use of SVGs only was recorded in 8069 patients. The primary study end point was all-cause death. The interaction between patients' age and any survival benefit from the RA was assessed by spline analysis.

Results: After propensity matching, the sample size consisted of 809 matched pairs. In the matched group, mean follow-up was 6.4 ± 3.6 years (range, 0-13.6 years). Survival was $96.8\% \pm 0.6\%$ versus $96.0\% \pm 0.6\%$ at 1 year, $91.4\% \pm 1.1\%$ versus $90.1\% \pm 1.0\%$ at 5 years, and $83.2\% \pm 1.7\%$ versus $79.4\% \pm 1.9\%$ at 10 years for patients receiving RA or SVG, respectively. RA use was associated with a lower risk for late death (hazard ratio [HR], 0.75; 95% confidence interval [CI], 0.57-0.98; $P = .03$). However, the protective effect from RA on late survival was not equally present across all age groups, as shown by spline analysis. The survival advantage from RA was maximum in patients 60 years and younger (upper limit of 95% CI, <1) and gradually declined with increasing age, until it was no longer present in patients older than 70 years (adjusted HR, 0.90; 95% CI, 0.63-1.28; $P = .57$).

Conclusions: The use of the radial artery graft as a second conduit improves all-cause mortality in patients undergoing primary isolated CABG up to the age of 70 years. (J Thorac Cardiovasc Surg 2013;146:1078-85)

Patients undergoing coronary artery bypass grafting (CABG) achieve better survival rates when the left internal thoracic artery (LITA), rather than a saphenous vein graft (SVG), is grafted to the left anterior descending artery.^{1,2} As a result, several groups have been encouraged to investigate the use of additional arterial conduits, such as the radial artery (RA).³ After early disappointing experiences,⁴ improved harvesting techniques, together with potential benefits of calcium channel blockers,⁵ have led to the RA becoming an increasingly popular conduit, as evidenced by improved patency and survival rates in observational cohort studies, when compared with SVG.

However, controversy still exists about the superiority of the RA over the SVG as a second conduit in CABG.⁶ Conflicting results have been reported from randomized controlled trials, showing that the RA offers an advantage in terms of angiographic patency at longer-term follow-up.^{7,8} Therefore, it seems reasonable to expect the use of RA to improve clinical outcomes and, in particular, survival, in the younger segment of the surgical population, with longer life expectancy. In fact, observational studies reporting a survival advantage from the radial artery over SVG have included relatively young patients.⁹ However, whether the RA graft confers a survival benefit over the SVG in elderly patients remains unknown. Furthermore, the point at which "young" becomes "old" is in continuous transition and may continue to advance as improved public health and lifestyle changes allow people to live longer. There is no clear guidance on arterial grafts choice, aside from the LITA. In particular, the recommendation for a liberal use of arterial grafts in younger patients, including the RA, is not conclusive, and further evidence is needed to provide guidance on the optimal graft choice for CABG in various age groups.¹⁰

In the present study, we sought to investigate the presence of any age-related benefit conferred by the use of the RA, compared with the more conventional approach using the

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CI	= confidence interval
HR	= hazard ratio
LAD	= left anterior descending artery
LITA	= left internal thoracic artery
PS	= propensity score
RA	= radial artery
SVG	= saphenous vein graft

LITA, and additional SVG by observing the long-term mortality in many patients undergoing primary isolated CABG.

METHODS

The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the institutional review committee on human research.

We retrospectively analyzed data collected in real time in the surgical database of Papworth Hospital, Cambridge, England, from March 1996 to May 2012. This database is maintained by a team of full-time clinical information analysts, who are responsible for continuous data collection as part of a robust audit process, linked to a national database. Data collection is validated regularly. Information about death from any cause is regularly obtained from the General Register Office approximately 1 week after the event.

Patients included in the present analysis met the following criteria: (1) isolated first-time CABG, (2) multivessel coronary artery disease requiring 2 or more grafts to different target vessels, (3) in situ LITA grafted to the left anterior descending artery (LAD), and (4) RA and/or SVG used to complete revascularization. Patients receiving other arterial conduits, such as the right internal thoracic artery or the gastroepiploic artery, were excluded. The decision to use RA instead of SVG only to complete revascularization was at the discretion of the consultant surgeon.

Patients who received LITA-LAD, RA as the second conduit, and SVGs when needed formed the RA group. Patients undergoing conventional surgical strategy, with LITA-LAD and SVGs only formed the SVG group.

The primary study end point was all-cause late death; this represents the most robust and unbiased index event because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments. The impact of RA grafting on perioperative (within 30 days) mortality was also investigated.

Surgical Procedures

Indications for myocardial revascularization were based on standard clinical and angiographic criteria. All patients were operated on through a median sternotomy. LITAs were dissected with either electrocautery as a pedicled graft or scissors and clips without cauterization as skeletonized conduits. RAs were harvested with the use of scissors and clips. ITAs and RAs were stored in a diluted solution of papaverine. Most of the operations were performed with standard cardiopulmonary bypass, with few performed on the beating heart. Myocardial preservation during cardiopulmonary bypass involved intermittent, antegrade crystalloid or blood cardioplegia.

Statistical Analysis

Variables were summarized as mean $\pm$ SD for continuous variables and as proportion for categorical variables in the 2 groups. Covariates included in the analysis were as follows: age, sex, left ventricular function, presence

of unstable angina, critical preoperative state, preoperative renal failure, cerebrovascular accident, diabetes while taking insulin, extracardiac arteriopathy, chronic obstructive pulmonary disease, surgical priority, off-pump bypass grafting, number of grafts, grafted obtuse marginal branches, grafted right coronary artery, sequential grafts, and year of operation. Because of the significant imbalances in baseline covariates between groups, we used propensity score (PS) matching. A PS representing the probability of having RA as opposed to SVG only was calculated for each patient by using a logistic regression model that identified variables associated independently with the conduit used. Variables used in the model are shown in Table 1. Pairs of patients with RA and SV were derived using greedy 1:1 matching with a calipers of width 0.2 SDs of the logit of the PS. Covariate balance was measured using the standardized differences, by which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance. A multiphase model including early (log-linear) and late (Weibull) phases was used to derive mortality hazard function in the matched sample. An additional adjustment for covariates, which were still unbalanced in the matched sample, was also used. The effect of age on survival from RA versus SVG was then investigated. For this purpose, the hazard ratio, with its 95% confidence interval (CI), was calculated for each quartile of the continuous variable "age" using the matched sample. Then, spline analysis (cubic method) was used to derive the hazard function across all patient ages. $P < .05$ was used to indicate statistical significance. All statistical analyses were performed using R, version 2.15.2 (R Foundation for Statistical Computing, Vienna, Austria; available at: <http://www.R-project.org>). The "nonrandom" package (available at: <http://cran.r-project.org/packages/nonrandom>) was used.

RESULTS**Study Population**

A total of 16,057 patients underwent first-time isolated CABG at Papworth Hospital during the study period. Reasons for exclusion are listed in Figure 1.

The final study population consisted of 9005 patients. The use of RA was recorded in 936 patients. In the treatment (RA) group, 504 patients had total arterial revascularization with RA grafts only used to complete revascularization. The use of SVGs only aside from the LITA was recorded in 8069 patients. The baseline characteristics among the unmatched RA group and the unmatched SVG group are summarized in Table 1. Prematching standardized differences exceeded 10% for 10 of the 17 covariates in the RA group, when compared with the SVG group. Patients receiving RA tended to be younger, were more likely to be female, and were more likely to have a reduced left ventricular function. The use of RA was associated with more off-pump bypass grafting procedures and sequential grafts. Finally, patients receiving RA had surgery in the earlier years of the study period. Patients in the SVG group were more likely to have a critical preoperative state, previous cerebrovascular accidents, more total grafts, and the right coronary artery grafted.

Propensity Score Matching Analysis

PS matching created a total of 809 matching sets. After matching, all covariates were well balanced among the 2

TABLE 1. Baseline characteristics between the RA and SVG groups before and after matching

	RA (unmatched) (n = 936)	SVG (unmatched) (n = 8069)	StDf (before matching)	RA (matched) (n = 809)	SVG (matched) (n = 809)	StDf (after matching)
Age, mean $\pm$ SD, y	65 $\pm$ 10	68 $\pm$ 9	28.2	64 $\pm$ 10	65 $\pm$ 10	3.14
Female sex, %	20.4	18.0	33.5	22.0	19.4	9.7
LV function, %			15.3			11.6
Moderate	41.9	36.3		41.2	38.2	
Poor	12.6	10.2		12.7	10.3	
Unstable angina, %	8.5	6.9	5.9	7.5	8.6	4.0
Critical preoperative state, %	1.8	3.4	10.3	1.9	1.8	0.9
Renal failure, %	0.7	0.6	0.9	0.7	0.7	0
Cerebrovascular accident, %	0.2	1.6	14.6	0.2	0.4	4.0
Diabetes, %	10.2	11.5	3.1	10.1	12.1	4.1
Extracardiac arteriopathy, %	13.8	11.7	6.2	13.1	12.0	3.3
COPD, %	11.8	10.9	0.7	11.4	10.3	3.6
Surgical priority			6.8			1.0
Urgent, %	22.9	19.8		22.9	22.6	
Emergent, %	3.1	3.5		3.2	2.8	
OPCAB, %	37.6	2.7	96.4	27.8	25.5	5.3
No. of grafts, mean $\pm$ SD	3.0 $\pm$ 0.7	3.3 $\pm$ 0.7	35.6	3.0 $\pm$ 0.7	3.1 $\pm$ 0.7	6.1
OM branches grafted, %	85.9	87.0	3.3	86.2	85.3	2.4
RCA grafted, %	72.9	80.8	18.8	73.4	74.8	3.1
Sequential grafts performed, %	27.0	13.7	99.5	24.5	20.4	9.7
Year of operation (median)	2004	2005	39.5	2004	2005	17.8

SVG, Saphenous vein graft; StDf, standardized difference; SD, standard deviation; RA, radial artery; LV, left ventricle; COPD, chronic obstructive pulmonary disease; OPCAB, off-pump coronary artery bypass grafting; OM, obtuse marginal; RCA, right coronary artery.

groups, aside from the year of operation and a slight residual difference in left ventricular function (Table 1). Therefore, these covariates were selected for additional adjustment in the final model for late mortality.

In the matched sample of 809, there were 17 (2.1%) and 18 (2.2%) perioperative deaths (within 30 days) in the RA and SVG groups, respectively ($P = .7$). Use of the RA did not influence operative mortality (unadjusted odds ratio [OR], 0.75; 95% CI, 0.28-1.96) and mortality after adjustment (adjusted OR, 1.56; 95% CI, 0.44-5.56).

Mean follow-up was 6.4 ± 3.6 years (range, 0-13.6 years). During follow-up, 98 patients in the RA group and

115 patients in the SVG group died. When all matched cases were included, survival was $96.8\% \pm 0.6\%$ versus $96.0\% \pm 0.6\%$ at 1 year, $91.4\% \pm 1.1\%$ versus $90.1\% \pm 1.0\%$ at 5 years, and $83.2\% \pm 1.7\%$ versus $79.4\% \pm 1.9\%$ at 10 years for patients receiving RA or SVG, respectively. RA was associated with a lower risk for late death (hazard ratio [HR], 0.75; 95% CI, 0.57-0.98; $P = .03$).

However, the protective effect from RA on late survival was not equally present across all age groups, as shown by spline analysis (Figure 2, Table 2); in fact, it was maximum in patients aged 60 years or younger (upper limit of 95% CI, <1). The survival advantage conferred by RA use gradually declined with increasing patients' age, and it was no longer present beyond 70 years of age.

An age of 70 years was then considered as the cutoff point, and it provided good discrimination for the age-related loss of survival benefit from the RA. RA was associated with improved survival in patients aged 70 years and younger, with 34 of 536 deaths (expected $n = 46.1$) in the RA group versus 55 of 353 deaths (expected $n = 49.2$) in the SVG group (adjusted HR, 0.57; 95% CI, 0.37-0.88; $P = .01$). Survival was $98.7\% \pm 0.4\%$ versus $97.5\% \pm 0.6\%$ at 1 year, $95.8\% \pm 0.9\%$ versus $94.1\% \pm 1.0\%$ at 5 years, and $91.6\% \pm 1.4\%$ versus $85.4\% \pm 2.0\%$ at 10 years for patients receiving RA or SVG only, respectively.

However, RA was no longer protective for late mortality in patients older than 70 years, with 64 of 273 deaths (expected $n = 65$) in the RA group versus 60 of 274 deaths (expected $n = 59$) in the SVG group

FIGURE 1. Study flow chart. CABG, Coronary artery bypass grafting; NA, no information available; GEA, gastroepiploic artery; RITA, right internal thoracic artery; LITA, left internal thoracic artery; LAD, left anterior descending artery; RA, radial artery; SVG, saphenous vein graft.

FIGURE 2. Hazard ratios (*HR*) and 95% confidence intervals for radial artery (*RA*) versus saphenous vein graft as second conduit, according to age of patients at surgery. *LL*, Lower limit; *UL*, Upper limit.

(adjusted *HR*, 0.90; 95% *CI*, 0.63-1.28; *P* = .57). Survival was 93.0% ± 1.5% versus 93.0% ± 1.5% at 1 year, 82.5% ± 2.5% versus 81.8% ± 2.6% at 5 years, and 65.3% ± 4.6% versus 65.5% ± 4.3% at 10 years for patients receiving *RA* or *SVG*, respectively (Figure 3).

Unadjusted Analysis

In the unmatched sample, early mortality (within 30 days) was 20 (2%) of 936 in the *RA* group and 154 (1.9%) of 8069 in the *SVG* group, and the use of *RA* did not affect this outcome (crude *OR*, 1.22; 95%

CI, 0.71-1.79). Mean follow-up was 6.4 ± 4.0 years (range, 0-15.4 years). The use of the *RA* was associated with a marginally significant risk reduction for late mortality when patients of all ages were included in the analysis (crude *HR*, 0.83; 95% *CI*, 0.69-0.99; *P* = .05). By using 70 years of age as the cutoff, the *RA* was associated with better late survival in patients 70 years or younger (crude *HR*, 0.62; 95% *CI*, 0.47-0.82; *P* = .005), but not in patients older than 70 years (crude *HR*, 1.21; 95% *CI*, 0.94-1.55; *P* = .1).

DISCUSSION

The data emerging from this analysis indicate that, in patients with multivessel coronary disease undergoing first-time CABG, the use of *RA* as a second conduit (in addition to *LITA-LAD*) is associated with improved long-term survival, when compared with patients receiving only *LITA-LAD* and only *SVGs*. However, this benefit is not constant across all age groups: the survival benefit conferred by the use of *RA* gradually becomes less evident with increasing age, and it is no longer present for patients older than 70 years.

The improvements in graft-harvesting techniques, avoidance of mechanical dilation, new preservation methods, and the use of postoperative calcium channel blocker therapy to prevent early vasospasm led to a resurgence in the use of the *RA* as a bypass graft. This has led the *RA* to emerge as an attractive and remarkably simple alternative to the right internal thoracic artery to achieve coronary revascularization with multiple arterial grafts.^{5,9}

The question of whether *RAs* should be used routinely for CABG has been addressed by several randomized

TABLE 2. Radial artery– versus saphenous vein graft–related hazard ratio for late death according to patient age

Age, y	Hazard ratio	Lower limit	Upper limit
59.00	0.07	0.008	0.58
60.86	0.18	0.039	0.81
62.73	0.29	0.07	1.04
64.60	0.42	0.13	1.28
66.46	0.57	0.21	1.50
68.33	0.74	0.31	1.72
70.20	0.92	0.44	1.92
72.06	1.09	0.56	2.09
73.93	1.21	0.66	2.21
75.80	1.29	0.72	2.27
77.66	1.33	0.76	2.29
79.53	1.34	0.77	2.27
81.40	1.32	0.77	2.21
83.26	1.27	0.75	2.14
85.13	1.22	0.72	2.04
87.00	1.15	0.68	1.94

Spline analysis (cubic method) results are given.

FIGURE 3. Survival curves for patients receiving radial artery (RA) versus saphenous vein graft (SVG) in the matched sample in patients aged 70 years and younger and older than 70 years. *adj*, Adjusted.

controlled trials, reporting conflicting results about its superiority in terms of angiographic patency.^{7,8} In particular, a trend toward better patency rates of RA when compared with SVG has been shown only in studies with long-term follow-up.⁸ This finding suggests that the survival advantage conferred by the use of RA may be expected only in patients with a longer life expectancy. Several studies have reported a favorable impact of an LITA + RA grafting strategy on intermediate to late survival after CABG, when compared with the conventional LITA + SVG approach for multivessel coronary revascularization.^{9,11} However, most of those studies included relatively younger patients receiving RA as a second conduit. In fact, surgeons have been often hesitant to adopt radial arterial grafting in elderly patients, because of the perceived unfavorable risk/benefit ratio in this age group.

Zacharias and colleagues⁹ reported RA use associated with an improved survival in a cohort of patients with a mean age of 61 years. Tranbaugh and colleagues¹² recently concluded that RA significantly improved long-term survival compared with using the LITA and SVG only in a study population with a mean age of 58 years. RA grafts were recently reported to improve survival when compared with SVG in patients with type 2 diabetes, but not in patients treated with insulin.¹³ Mean age of the diabetic population receiving RA grafts was 61 years. These data from small retrospective cohort studies make it difficult to derive definitive conclusions on the impact of RA use for CABG in elderly patients.

On the other hand, in a prospective randomized trial, Hayward and Buxton¹⁴ found no difference in terms of patency rate and late survival in patients older than 70 years

receiving RA or SVG as a second conduit for CABG. In a previous study, Tranbaugh and colleagues¹¹ concluded that RA failed to improve survival in patients older than 65 years, but this age cutoff was arbitrarily chosen. Furthermore, the point at which “young” becomes “old” continues to advance, and it may continue to do so, as improved public health and lifestyle changes cause people to live longer. As a consequence of the lack of conclusive data regarding the effect of patients’ age on survival associated with the use of RAs for CABG, current guidelines do not provide any advice on this matter.¹⁰

The present analysis investigated the interaction between RA-related survival advantage over all patient age groups. We found that at younger than 60 years, RA was strongly protective for late death. This benefit gradually declined, and it was no longer present after 70 years of age. In patients 70 years and younger, the RA was associated with an absolute risk reduction for late death of 43% at long-term follow-up. In patients older than 70 years, the RA did not confer any survival benefit, when compared with patients receiving SVGs, suggesting that other risk factors play a prominent role in affecting survival in elderly persons.

Our results provide robust evidence strengthening the current recommendations to use the RA in the younger segment of the surgical population.¹⁰ Furthermore, our data provide scientific evidence for an age cutoff for the loss of benefit from arterial grafts, as previously suggested by investigations on bilateral internal thoracic arteries and age-related survival benefit.^{15,16}

Although a benefit extending into older age cannot be formally excluded, the perceived increased technical complexity related to the use of arterial grafts suggests the need to use clinical judgment on the selection of grafts

for individual patients, until data from well-powered and suitably designed randomized controlled trials will be available.

Muneretto and colleagues¹⁷ conducted a prospective trial with 160 patients older than 70 years randomized to the use of RA or SV grafts. The RA group had superior results in terms of angiographic patency and recurrence of angina after a mean follow-up of 16 months. The authors were not able to assess the impact of RA on late death because of the short follow-up and the small sample size. However, RA grafts were used to achieve total arterial revascularization in all cases; this aspect might partially account for the additional clinical benefit associated with the use of RA grafts in elderly patients.

Habib and colleagues¹⁸ recently reported that the benefit related with the use of RA over SVG for elderly persons may exceed that for younger patients at short-term follow-up. This controversial conclusion might be mostly related to the inherent bias in patients' selection and risk adjustment. The main difference in survival curves between subjects who received RA or SVGs only was observed in the early phase. This suggests a prominent role of patients' risk profile, rather than the late effect of the RA, on survival differences between the 2 groups.

There are limitations to this study. This is a retrospective, single-center study analyzing clinical outcomes during a 16-year period; thus, its conclusions may not be generalizable to other experiences, populations, and current practices. Also, despite the use of propensity score matching as one of the most robust tools (except for a randomized controlled trial) to compare treatment effects, this remains a retrospective analysis with its known inherent limitations of patient selection and treatment bias. There were many staff surgeons operating at Papworth Hospital during the time frame of the present study, and surgeon performance may be an unexplained factor that accounts for the observed results. However, a sensitivity analysis showed that individual surgeon performance did not affect late survival (data not reported). It could be argued that, for older patients, the RA was used because of limited conduit options, as in the case of varicose saphenous veins, but this potential bias is unlikely to affect the study end point. As reported in the study flow chart, a significant number of patients were excluded because of missing data. However, basic baseline demographic characteristics (age and sex) and the probability of late death were compared between patients with complete data included in the final analysis and subjects who were excluded from the study sample because of missing data on baseline covariates (data not reported). No statistically significant differences were found between the 2 groups, thus supporting the notion that the final results were not significantly affected by this limitation.

We are unable to unambiguously attribute the improved survival to RA effects, specifically its presumed enhanced patency rates, as neither the cause of death nor graft patency

data are available. Nevertheless, all-cause death is recommended to be considered in studies investigating results of coronary intervention as a more reliable end point than cause-specific mortality.¹⁹ However, this is only one of the outcomes relevant to the elderly population, and our study has not analyzed other important effects, such as improvement in quality of life, recurrent ischemia or angina, or need for repeat revascularization. Furthermore, we have no data on the severity of stenoses in the target vessel of RA grafts, which is well known to affect its patency because of competitive flow.⁶

In conclusion, the present findings show that the use of RAs is strongly associated with improved long-term survival in patients younger than 60 years, and this survival benefit extends until 70 years of age. On the basis of these data, although the choice of surgical strategy should be individualized for each patient, the use of RA grafts for first-time isolated CABG should be considered as the best option in patients, at least until the age of 70 years.

The results presented in this study may help in guiding surgical treatment of patients undergoing CABG and have the potential to improve recent guidelines, which recommend the use of RA regardless of patients' age.¹⁰

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Discussion

Dr Stephen Fremes (Toronto, Canada). I wish to thank the authors for providing me with a copy of the manuscript and the presentation in advance.

The authors have performed a single-center observational study to evaluate whether the benefits observed with the use of radial grafting are evident across the spectrum of patient age. Conduit selection was according to the decision of the consultant. Late survival from the national registry was the primary study end point. The authors used complex, appropriate, and sophisticated statistical analysis to minimize bias inherent in the data. The average follow-up was 5.7 years in the propensity-matched populations. The investigators demonstrated that there was an overall survival advantage with radial grafting; however, this benefit in survival was only evident in patients younger than 70 years.

There are conflicting data in the literature regarding the appropriateness or added value of increased arterial revascularization in older patients, and this applies to both the use of radial arteries as well as bilateral mammary arteries. I have several questions which I will ask one at a time.

First of all, there were over 16,000 patients initially undergoing isolated coronary surgery at Papworth over 16 years; however, the study population consisted of 9000 patients, and there were more than 4000 excluded because of information lacking on the choice of arterial conduit. So, do you think that this would differentially affect the results of your study one way or the other?

Dr Benedetto. Thank you for your question. The number of missing data was equally distributed over across all study periods. We did assess the impact of missing data on outcomes by conducting a simple analysis on the rate of late mortality in patients with missing data, and we found no differences between patients with missing data and patients included in the final analysis. This was the only tool that we had to confirm that our conclusions are reliable, even if it is a high number of patients with missing data. However, the final sample study is large and allowed us to reach reliable conclusions.

Dr Fremes. Thank you. One of the potential explanations for the observed results is bias in the selection of the second arterial conduit by the consultant surgeon. In other words, the radial artery may have been preferentially used in younger patients, who are excellent revascularization candidates, but restricted in older patients, unless there were no other options. Do the authors believe this or other sources of bias may have explained the lack of benefit in older patients?

Dr Benedetto. Excellent question, thank you. The nonparsimonious, saturated, propensity matching used in this study tried to minimize the effects of selection and treatment bias, a limitation inherent in any retrospective analysis. Furthermore, it is unlikely that surgeon's choice of conduits may have been forced by lack of venous conduits, as most patients received saphenous vein grafts in addition to the radial artery graft.

We also investigated the effect of the surgeon's experience, the surgeon effect on the final estimates of effect of radial artery use, but we did not find a significant effect of surgeon on late survival. In view of the high number of surgeons involved in this analysis, we decided to adjust it not for a single surgeon but for the year of operation, because we found a significant relationship with between operative mortality and year of operation. Over time, we found a decreasing operative mortality rate. This was also adjusted for surgeon's experience.

Dr Fremes. A potential explanation is the notion of competing risk, and I assume this is what you assume explains the lack of benefit. In other words, as patients age, the risk of death from noncardiac causes increases. So one way to illustrate this would be to examine the cause of death in these patients and to see if, in fact, they are dying from noncardiac causes. Do the authors plan to examine cause-specific mortality in these patients?

Dr Benedetto. When we investigated our data set, we observed that we did not have reliable information about specific cause of death, and we decided to conduct this analysis on all-cause mortality. We are going to complete our data set, going through the notes, and try to obtain a more complete data set, which will include specific cause of death. However, we decided to use all-cause mortality as the primary outcome measure for this analysis because it is well known that all-cause death is the most robust and unbiased index to investigate the effect of a treatment in a retrospective study. So, we are confident that all-cause mortality in this retrospective analysis is a more reliable index than cardiac-specific mortality to investigate the effect of an arterial conduit.

However, we agree with your point and we intend to complete our data set, going through the notes to try and obtain reliable information on specific causes of death.

Dr Fremes. Two more questions. One potential explanation that the radial artery may be a worse conduit in older patients compared to younger patients is perhaps due to thickening of the radial artery or plaque. In our institution, we actually screen older patients with a duplex scan to look for irregularities of the radial artery as well as assessing the adequacy of ulnar collateral circulation. What is the screening process at Papworth?

Dr Benedetto. It was mostly the Allen test before surgery, and intraoperatively before harvesting the radial artery, we assessed the finger saturation during temporary occlusion of the radial artery, to confirm the finding of the Allen test. We did not conduct any ultrasound duplex scans of the radial artery before surgery. It is possible and reasonable that atherosclerosis of the radial artery in patients beyond 70 years of age may be one of the causes that affects the survival benefit from this conduit in elderly.

Dr Fremes. Lastly, based on the findings of our study, what do the surgeons at Papworth recommend in terms of conduit selection for their older patients?

I wish to thank the AATS for the privilege to discuss this excellent and provocative paper.

Dr Benedetto. It is difficult to change an individual's belief about the choice of graft, because at the moment we have no definitive evidence or recommendations to guide choice of grafts other than the LITA to complete surgical revascularization. I hope that, on the basis of these data, surgeons would consider arterial grafts more often to complete surgical revascularization than they do at present.

Dr Philip Hayward (*Melbourne, Australia*). Thank you for a very nice talk. As you know, our randomized trial that you quoted in your meta-analysis has not shown any survival advantage yet, only at midterm follow-up. But I just wanted to agree with a couple of things that Steve Fremes said.

Analysis of the Melbourne-based database of Brian Buxton and colleagues, with about 10,000 patients, has focused on total arterial revascularization versus mixed grafts. We have found differently from you, with a survival advantage in the total arterial group which was not age dependent. However, as you suggest and in our data set, this probably does not apply in peripheral vascular disease. It does relate to radial quality, as Steve Fremes said, with patients in peripheral vascular disease having probably poor quality radials, and I suspect the older patients with peripheral vascular disease are dying of other causes, which is why there is no benefit.

But a nice talk, and we will discuss it again when we finalize our data.

Dr Benedetto. Thank you for your question. A recent paper reporting outcomes of radial artery use in the elderly concluded that it may be advantageous to use it even in such patients. However, looking at the survival curves, we found that the main difference in survival between the 2 groups is to be found in

younger patients. In turn, this raises a concern about the surgical profile of patients receiving radial artery versus saphenous vein, because the main difference in mortality is related to the younger age at the time of surgery. So, I think that we need to conduct robust and reliable adjusting in a retrospective analysis to be sure that we are looking at the same main population. In a retrospective analysis, it is generally difficult to adjust for all factors that may affect the outcome measures under consideration, because patients receiving radial artery may be different from patients receiving only saphenous vein grafts. Therefore, it is possible that some of the discordant conclusions you are referring to may be related to selection bias.

Dr Codispoti. As the senior author on Dr Benedetto's paper, I rise to complete the answer to Dr Fremes' insightful question, related to what are the current recommendations and practice in Papworth, in light of these data. The search for an answer to the question of which patient is more likely to benefit from use of the radial artery is exactly the reason why we wanted to conduct this analysis, and we obviously stand by the solidity of its results. Based on this, we will adopt a more coherent strategy towards choice of the radial artery and more in general of arterial grafts in patients younger than 70 years. We look forward to seeing Phil Hayward's and the Melbourne group's results next year.

Dr Pieter Kappetein (*Rotterdam, The Netherlands*). You propose a randomized trial as one of your last points in your conclusion slide. If we look at the trial from David Taggart, who is randomizing patients with 2 mammary arteries versus 1 mammary artery, 16% of those patients that were randomized with 2 mammary arteries only got 1 mammary artery graft. So, there were a lot of crossovers, which underpowers his study tremendously. The only thing to overcome that is to analyze it as an as-treated population. What would be your recommendation? How would you design a randomized trial to show that a radial artery is better than a saphenous vein graft?

Dr Benedetto. This is a pertinent question, to which there is no easy answer. I think that before producing a new randomized control trial comparing the saphenous vein graft with an arterial graft, we need to understand better and investigate the causes for differences observed in previous randomized controlled trials using similar outcome measures. I believe that many of the different conclusions in respect to similar outcome measures reached in previous trials are due to differences in their study design. It is also possible that the different conclusions reached by studies on similar patient populations using the same outcome measures may be related to surgeons' experience, or perioperative management with calcium antagonists. Therefore, before we start another randomized controlled trial, I think we need to better understand why we have different conclusions from previous randomized studies.