Arterial grafts balance survival between incomplete and complete revascularization: A series of 1000 consecutive patients with coronary artery bypass graft with 98% arterial grafts

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Objective: Coronary artery bypass grafting (CABG) with incomplete revascularization (ICR) is thought to decrease survival. We studied the survival of patients with ICR undergoing total arterial grafting.

Methods: In a consecutive series of all-comer 1000 patients with isolated CABG, operative and midterm survival were assessed for patients undergoing complete versus ICR, with odds ratios and hazard ratios, adjusted for European System for Cardiac Operative Risk Evaluation category, CABG urgency, age, and comorbidities.

Results: In this series of 1000 patients with 98% arterial grafts (2922 arterial, 59 vein grafts), 73% of patients with multivessel disease received bilateral internal mammary artery grafts. ICR occurred in 140 patients (14%). Operative mortality was 3.8% overall, 8.6% for patients with ICR, and 3.2% for patients with complete revascularization ($P = .008$). For operative mortality using multivariable logistic regression, after controlling for European System for Cardiac Operative Risk Evaluation category ($P < .001$) and CABG urgency ($P = .03$), there was no evidence of a statistically significant increased risk of death due to ICR (odds ratio, 1.73; 95% confidence interval, 0.80-3.77). For midterm follow-up (median, 54 months [interquartile range, 27-85 months]), after controlling for European System for Cardiac Operative Risk Evaluation category ($P < .001$) and comorbidities ($P = .017$) there was a significant interaction between age $\geq$ 80 years and ICR ($P = .017$) in predicting mortality. The adjusted hazard ratio associated with ICR for patients older than age 80 years was 5.7 (95% confidence interval, 1.8-18.0) versus 1.2 (95% confidence interval, 0.7-2.1) for younger patients.

Conclusions: This is the first study to suggest that ICR in patients with mostly arterial grafts is not associated with decreased survival perioperatively and at midterm in patients younger than age 80 years. Arterial grafting, because of longevity, may balance survival between complete revascularization and ICR. (J Thorac Cardiovasc Surg 2013;■:1-10)

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The concept of complete revascularization (CR) in coronary artery bypass graft (CABG) surgery portending to improved patient outcomes was first espoused by McNeer and colleagues in 1974.[1] This gold standard may not be applicable today because data suggesting the benefits of CR included young, stable patients, first-time procedures, and predominantly vein grafting.[1] Newer studies are needed to evaluate contemporary CABG surgery, including use of total arterial grafting; off-pump CABG; and revascularization procedures in older, sicker patients. The goal of our study was to determine if there was a survival advantage of completely revascularized patients compared with ICR in a patient cohort with predominantly (98%) arterial grafting. We hypothesized that the long-term advantage of arterial grafts would potentially counteract the reduced survival of ICR in an all-comer group of CABG patients.

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METHODS

From July 2003, to October 2012, total arterial grafting was performed where possible in all patients by 1 surgeon at a high volume academic tertiary care center. Patients were divided into 2 groups: Those in whom revascularization was complete and those in whom it was not.

All patients were entered into the Alberta Provincial Program for Outcome Assessment in Coronary Heart Disease study,[2] a prospective data collection initiative in the province of Alberta, Canada, since 1995. Patients are enrolled at initial cardiac catheterization and are followed to assess long-term survival and repeat revascularization with percutaneous coronary intervention (PCI) or CABG. Mortality is verified by linkage to Alberta Vital Statistics. All study patients were also entered into a prospective surgical database, recording patient demographics and relevant surgical data. This study was approved by our institution's research ethics board.

Angiogram and operative reports, and office charts of each patient were independently reviewed by both an interventional cardiologist and a cardiac surgeon to determine completeness of the revascularization. Revascularization was considered complete when all diseased arterial territories in left anterior descending (LAD) artery, circumflex artery (CIRC), and right

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Abbreviations and Acronyms

CABG	= coronary artery bypass graft
CIRC	= circumflex artery
CR	= complete revascularization
EuroSCORE	= European System for Cardiac Operative Risk Evaluation
FFR	= fractional-flow reserve
ICR	= incomplete revascularization
IMA	= internal mammary artery
LAD	= left anterior descending
PCI	= percutaneous coronary intervention
RCA	= right coronary artery

coronary artery (RCA) regions, with ≥70% stenosis—or ≥50% in the left main artery—received at least 1 bypass graft for coronary arteries measuring >1 mm in diameter. Left main revascularization was considered complete if grafts were placed to the LAD and CIRC.

Five categories of reasons for incomplete revascularization (ICR) were obtained from operative reports: small vessel (<1 mm diameter), diffuse disease precluding healthy anastomosis, coronary artery inaccessible for grafting (location in the atrioventricular groove), infarcted territory (akinetic wall, thinned segment, or nonviable myocardium), technical problems (adhesions in reoperative surgery, high-risk or porcelain aorta needing off-pump procedure).

Surgery Details

All operations were performed off- or on-pump. For on-pump procedures, we used intermittent antegrade blood cardioplegia and systemic hypothermia to 32°C. Off-pump CABG was performed with the Octopus stabilizing device (Medtronic, Inc, Minneapolis, Minn). Internal mammary artery (IMA) conduits were harvested in a skeletonized manner, with the left IMA anastomosed to the LAD and the right IMA to either the CIRC or RCA. IMAs were used mostly as in-situ grafts and were wrapped in papaverine-soaked gauze after harvesting. High spinal anesthesia (local anesthetic and opioid) supplemented by light general anesthesia was used. Intraoperative transesophageal echocardiography was used except where contraindicated. Long-acting nitrates were used postoperatively for 6 weeks in only patients with radial artery grafts.

Statistical Analysis Methods

Descriptive analysis. Descriptive statistics (Table 1) for categorical variables and the means ± standard deviation for normally distributed continuous variables and the median and interquartile range (IQR) for non-normally distributed variables were provided for all patients. Comparisons of baseline variables were made between patients who experienced ICR and those who did not, only in patients with multivessel disease (single-vessel disease patients by virtue of their inability to be incompletely revascularized were excluded) (Table 2). Comparisons were made using the Fisher exact test for categorical variables and the *t* test (for normally distributed) or Wilcoxon signed rank tests (for non-normally distributed) continuous variables.

Regression modeling strategy for both logistic and proportional hazards regression. Initially we used individual regression models for each variable in Table 1 to examine if they were significant predictors of outcome. The functional form for continuous variables was examined using residuals analysis and if nonlinearity was detected, suitable transformations were used or the variable was categorized using appropriate cut-points to aid interpretation of the model. Next we entered each variable in Table 1 into a regression model, including the ICR variable to assess for confounding. In the event of evidence of confounding we examined the possibility of an interaction between ICR and that variable. All variables significant at $P < .2$ in the individual regression, interactions significant at $P < .20$ and variables that appeared to be confounding were entered into a multivariable logistic regression model. The possibility of collinearity was examined between predictor variables; the inclusion of highly correlated predictor variables that might cause instability of the model was avoided. To avoid overfitting, we reduced the model by excluding nonsignificant variables (starting with the largest *P* value), provided that this did not change the estimate of the primary predictor variable, ICR (ie, the excluded variable did not contribute to confounding). This process continued until the appropriate number of degrees of freedom in the model was retained (n/10) where n is the number deaths in each model.

Logistic regression was used to assess operative mortality, with the effect of univariate predictors presented as odds ratios (ORs) with 95% confidence intervals (CIs) and estimates of 30-day mortality for each level of the variable. The multivariable model was presented as ORs and adjusted 30-day morality rates were estimated using predictive margins.

Midterm survival was estimated in the operative-survivor patient population, using proportional hazards regression. Out-of-province patients not available for follow-up were excluded. The assumption for proportional hazards was examined using Schoenfeld residuals.[3]

RESULTS

Study Population

From July 18, 2003, to February 2, 2013, 1000 consecutive patients underwent CABG surgery with 98% (2922 out of 2981) arterial grafts. Excluding 59 patients (6%) with single vessel coronary artery disease, 73% (686 out of 941) of patients had bilateral IMA grafts. The majority of patients had triple vessel disease (60%; 600 out of 1000) and 34% had double vessel disease (341 out of 1000). Graft conduits consisted of 70% IMAs, 28% radial arteries, 2% venous grafts, and 4 grafts were inferior-epigastric arteries. Eighty-six percent of the ICR group (120 out of 140 patients) had triple vessel disease. Demographics of the patient groups are shown in Table 1. Patients with ICR were older, had higher European System for Cardiac Operative Risk Evaluation (EuroSCORE) category, experienced more reoperative CABG, underwent off-pump procedures, and were less likely to have normal ejection fraction.

ICR Versus CR

CR was achieved in 801 out of 941 patients (85%) with multivessel disease and ICR occurred in 140 patients (15%). Significant predictors of ICR are presented in Table 2. The ICR group had less bilateral IMA grafting, more off-pump procedures, higher logistic EuroSCORE category, was more likely to have collaterals, was older, more patients with ejection fraction <30%, fewer outpatients, and more likely to undergo reoperative surgery. The numbers for very low ejection fraction and reoperation were small in both groups. No other cardiac risk factors or comorbidities were associated with ICR.

TABLE 1. Baseline characteristics of the study population of 1000 patients; 801 with complete revascularization 140 with incomplete revascularization and 59 with single vessel disease

	All patients (N = 1000)*	CR (n = 801)	ICR (n = 140)	*P* value†
Bilateral internal mammary artery grafts	686 (68.6)	626 (78.2)	60 (42.9)	<.001
Off-pump coronary artery bypass graft	387 (38.7)	283 (35.3)	64 (45.7)	.023
EuroSCORE (median [IQR])	2.9 (1.5-6.2)	2.7 (1.5-5.9)	5.0 (2.7-10.2)	<.001
Collaterals	628 (62.9)	489 (61.2)	116 (82.9)	<.001
Demographics				
Age, mean ± standard deviation‡	64.9 ± 10.4	64.4 ± 10.3	68.9 ± 9.4	<.001
Male	779 (77.9)	624 (77.9)	112 (80.0)	.657
Outpatient	435 (43.5)	370 (46.2)	44 (31.4)	.004
Inpatient	454 (45.4)	345 (43.1)	76 (54.3)	.138
Emergent	111 (11.1)	86 (10.7)	20 (14.3)	.279
Comorbidities				
Hypertension	690 (69.0)	549 (68.5)	102 (72.9)	.323
Hypercholesterolemia	697 (69.7)	555 (69.3)	102 (72.9)	.426
Diabetes	344 (34.4)	279 (34.8)	53 (37.9)	.503
Ever smoked	587 (58.7)	470 (58.7)	87 (62.1)	.457
Active smoker	208 (20.8)	171 (21.3)	31 (22.1)	.824
Ejection fraction >50%	66 (6.6)	45 (5.6)	21 (15.0)	<.001
Ejection fraction 30%-50%	228 (22.8)	182 (22.7)	37 (26.4)	.455
Ejection fraction <30%	706 (70.6)	574 (71.7)	82 (58.6)	.177
Body mass index ≥30	338 (33.8)	275 (34.3)	45 (32.1)	.630
Chronic obstructive pulmonary disorder	131 (13.1)	103 (12.9)	24 (17.1)	.180
Cerebrovascular disease	101 (10.1)	79 (9.9)	18 (12.9)	.292
Peripheral vascular disease	105 (10.5)	87 (10.9)	17 (12.1)	.661
Renal disease§	35 (3.5)	27 (3.4)	7 (5.0)	.328
Reoperative coronary artery bypass graft	37 (3.7)	23 (2.9)	10 (7.1)	.021

Data are presented as n (%) unless otherwise indicated. *CR*, Complete revascularization; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *IQR*, interquartile range; *ICR*, incomplete revascularization. *Includes 59 single vessel disease patients. †Comparing ICR patients (n = 140) to CR patients (n = 801). ‡Range (29-96 years). §Creatinine >200 mg/dL.

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Operative Mortality

Overall operative mortality was 3.8%. In ICR patients, 30-day mortality was 8.6% compared with 3.2% in patients with complete revascularization ($P = .008$).

Examination of the continuous variables age and logistic EuroSCORE categories revealed substantial nonlinearity in the prediction of mortality. Although log transformation of the logistic EuroSCORE category and a quadratic form for age described this nonlinearity well, we decided to categorize the variables to ease interpretation. Age categories were <65 years, 65 to 80 years, and ≥80 years. For EuroSCORE, there was substantial heterogeneity in the highest risk category (EuroSCORE >6); therefore we subdivided this category into 6 to 9.99, 10 to 19.99, and ≥20.

Baseline factors associated with 30-day mortality are shown in Table 3. Most were also confounders of the relationship between ICR and operative mortality and were considered eligible for entry into the multivariate logistic regression model. Off-pump procedure history and sex were potential confounding variables and were therefore entered into the multivariable model.

In this full model, the effect of ICR was not significant (OR, 1.82; 95% CI, 0.78-4.22; $P = .168$). In the reduced model (Table 3), containing only ICR, EuroSCORE category, and urgency, the estimated OR was 1.73 (95% CI, 0.80-3.77; $P = .166$). Adjusted operative mortality was 5.6% (95% CI, 2.7-8.5) for ICR patients and 3.6% (95% CI, 2.3-4.6; $P = .166$) for CR patients, indicating that after controlling for EuroSCORE category and urgency the effect of ICR on 30-day mortality, although higher than that for CR patients, was not significantly different. For the 65 octogenarians (1 patient aged 96 years), there was no difference in operative mortality due to ICR (for ICR: 9.5%; 95% CI, 1.2-30.3 and for CR: 6.8%; 95% CI, 1.4-18.6; $P = .655$), even though the 37 octogenarians with off-pump CABG history had a significantly higher rate of ICR compared with the non-octogenarians. (48.7% for age ≥80 years; 95% CI, 31.9-65.6 compared with 10.7% for age <80 years; 95% CI, 2.3-28.2; $P < .001$).

Midterm Follow-up

Thirty-eight patients who died during the 30-day postoperative period and 62 patients who were out-of-province were excluded from the midterm follow-up, leaving a total of 841 patients for follow-up (723 with CR and 118 with ICR). The median follow-up time was 56 months. ICR was a significant predictor of midterm mortality (hazard

TABLE 2. Significant predictors (*P* < .15) of incomplete revascularization

Variable	% ICR (95% CI)	*P* value
Overall	14.9 (12.7-17.3)	
Off-pump		.023
Yes	18.4 (14.5-22.9)	
No	12.8 (10.2-15.8)	
Bilateral internal mammary artery grafts		<.001
Yes	8.8 (6.7-11.1)	
No	31.4 (25.7-37.5)	
EuroSCORE		<.001
0-2.99	8.7 (6.3-11.6)	
3-5.99	18.6 (13.6-24.5)	
≥6	23.4 (18.3-29.1)	
Age		<.001
<65	10.6 (7.8-14.0)	
65-79	16.5 (13.1-20.3)	
≥80	32.3 (21.1-45.1)	
Urgency		.004
Elective	10.6 (7.8-14.0)	
Urgent in	18.1 (14.5-22.1)	
Emergency	18.9 (11.9-27.6)	
Ejection fraction		<.001
<30	31.8 (20.9-44.4)	
30-50	16.9 (12.2-22.5)	
>50	12.5 (10.1-15.3)	
Collaterals		<.001
Yes	19.2 (16.1-22.5)	
No	7.2 (4.7-10.6)	
Reoperative CABG		.021
Yes	30.3 (15.6-48.7)	
No	14.3 (12.2-16.8)	

CI, Confidence interval; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *CABG*, coronary artery bypass graft; *ICR*, incomplete revascularization.

ratio [HR], 2.0; 95% CI, 1.3-3.3). Unadjusted overall survival curves are presented in Figure 1, *A*. Examination of the linearity continuous variables revealed that different cut-points were more appropriate when predicting midterm mortality. Thus age had 2 categories (<80 and ≥80 years) and EuroSCORE had 3 categories (0-2.99, 3-5.99, and ≥6). (see Table 4.) There was evidence against the proportional hazards assumption for urgency; therefore, this variable was not included in the model, but used for stratification. Only 2 variables were confounding factors: age >80 years and EuroSCORE. Interactions between these 2 variables and ICR were examined and the interaction with EuroSCORE was not significant (*P* = .240), whereas the interaction with age was significant (*P* = .072). The unadjusted HR was 4.7 (95% CI, 1.5-14.4) for patients older than age 80 years and 1.5 (95% CI, 0.9-2.7) for patients younger than age 80 years in a model that contained only the interaction between age and ICR. Therefore the age × ICR interaction along with the predictors significant at *P* < .2 were entered into the multivariable proportional hazards model, stratified by urgency due to the nonproportional hazards for this variable. Chronic obstructive pulmonary disease, renal disease, cerebrovascular disease, peripheral vascular disease, and diabetes were all combined into a single variable of a comorbid condition. The final model (Table 5) included the age × ICR interaction (*P* = .017), comorbid conditions (*P* = .017), the 3 category EuroSCORE (*P* <.001), and sex (*P* = .25) because this was a confounding factor. The adjusted HR associated with ICR for patients aged ≥80 years was 5.7 (95% CI, 1.8-17.7) indicating a higher risk of mortality due to ICR in older patients. The estimated adjusted HR for patients younger than age 80 years was 1.2 (95% CI, 0.7-2.1). The unadjusted 5-year survival rate for patients younger than age 80 years was 90.9% for CR patients and 86.0% and for ICR patients. For patients aged ≥80 years the 5-year survival rate was 77.7% for CR patients and 56.4% for ICR patients. (Figure 1, *B*). Three factors significantly predicted decreased long-term survival in the octogenarians and older patients: ICR (*P* = .006), higher logistic EuroSCORE category (*P* = .006), and male sex (*P* = .029). When included in the same regression model all 3 variables were simultaneously significant (*P* = .029 for EuroSCORE, *P* = .032 for ICR, and *P* = .021 for men.) This indicates that even controlling for fragility using EuroSCORE category, the HR for ICR was 2.9 (95% CI, 1.1-7.7) and HR for male sex was 4.4 (95% CI, 1.2-15.4).

Examination of these unadjusted survivor functions indicates that midterm survival in ICR patients younger than age 80 years was not statistically significantly different from CR patients, either before (*P* = .141) or after adjusting for other predictive factors (*P* = .544).

Other Outcomes

There was no difference between ICR and CR patients for recurrence of angina (6.4%; *P* = .99), myocardial infarction (1.8%; *P* = 1.0), and postoperative angiography either for any reason (15.5%; *P* = .787) or symptom-directed (13.3%; *P* = 1.00). Repeat revascularization procedures with either PCI or CABG were also similar (0.7%; *P* = .267).

Reasons for ICR

Reasons for ICR in 140 patients included small vessel <1 mm in 64% (n = 92), diffuse disease in 17% (n = 24), inaccessible location in 14% (n = 20), infarct territory in 22% (n = 31), technical reasons in 9% (n = 13), and multiple reasons in 25% (n = 36). The RCA was the most common artery not bypassed (52%), with 48% for the CIRC. A diseased LAD territory was bypassed in all patients at this or at a previous surgery. The most common reasons for not bypassing the CIRC was small vessel and location, whereas reasons for not grafting the RCA were small vessel and diffuse disease. For 138 of 140 patients (99%) 1 territory of 3 was not bypassed; in 2 patients

TABLE 3. Predictors of operative mortality

	Single predictor variable analysis			Multivariable model	
Variable	% Operative mortality (95% CI)	OR (95% CI)	*P* value	OR (95% CI)	*P* value*
Constant				0.002 (0.00-0.01)	<.001
Incomplete revascularization			.008	1.73 (0.80-3.77)	.166
Yes	3.2 (2.0-4.5)	2.8 (1.4-5.7)			
No	8.6 (3.9-13.2)	1			
EuroSCORE†			<.001	1	<.001
<3	0.4 (0.05-1.5)	1			
3-5.99	3.3 (0.9-5.6)	7.9 (1.6-38.6)		5.4 (1.1-27.1)	
6-9.99	6.8 (2.3-11.4)	17.3 (3.6-82.7)		10.2 (2.0-50.6)	
10-19.99	7.8 (3.1-15.4)	19.9 (4.1-97.5)		8.9 (1.7-47.8)	
≥20	31.1 (17.6- 44.6)	106 (23.2-490)		42.2 (8.0-223.5)	
Urgency†			<.001	1	.03
Elective	0.7 (0.0-1.5)	1			
Urgent in	4.0 (2.2-5.9)	5.8 (1.7-19.8)		3.2 (0.88-11.4)	
Emergency	17.0 (9.8-24.1)	28.0 (8.1-97.2)		5.6 (1.4-21.9)	
Bilateral internal mammary artery grafts†			.017		
Yes	6.7 (3.6-9.7)	0.44 (0.23-0.85)			
No	3.1 (1.8-4.4)	1			
Age†, y			.061		
<65	2.5 (1.1-4.0)	1			
65-80	5.0 (2.9-7.0)	2.0 (1.0-4.2)			
>80	7.7 (1.2-14.2	3.2 (1.1-9.5)			
Hypertension			.03		
Yes	4.9 (3.3-6.6)	2.4 (1.0-5.9)			
No	2.1 (0.1-3.7)				
Ejection fraction†			.021		
<30	10.6 (3.2-18.0)	1			
<30-50	4.6 (1.8-7.3)	0.4 (0.2-1.1)			
>50	3.2 (1.9-4.5)	0.3 (0.1-0.7)			
Cerebrovascular disease			.013		
Yes	8.2 (2.7-13.7)	2.4 (1.1-5.5)			
No	3.6 (2.3-4.8)				
Peripheral vascular disease			.145		
Yes	6.7 (1.9-11.5)	1.9 (0.8-4.4)			
No	3.7 (2.4-5.0)				
Renal disease					
Yes	14.6 (2.8-26.6)	4.6 (1.7-12.6)	.003		
No	3.6 (2.4-4.9)				
Reoperative CABG†					
Yes	15.2 (2.9-27.4)	4.7 (1.7-13.0)	.003		
No	3.6 (2.4-4.9)				

CI, Confidence interval; *OR*, odds ratio; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *CABG*, coronary artery bypass graft. *Likelihood ratio statistic. †Significant predictors of incomplete revascularization.

both RCA and CIRC territory were not grafted because coronary arteries were too small in 1 patient and both diffusely diseased and small in the second.

DISCUSSION

In this large contemporary series of 1000 CABG patients with 98% arterial grafts, we have shown that after adjusting for factors affecting operative mortality and midterm survival, there is no evidence that ICR decreases survival perioperatively in all patients and at midterm in patients younger than age 80 years. Ours is the first study to evaluate outcomes from ICR in a cohort of patients with extensive (98%) arterial grafting. Midterm follow-up analysis yielded a dichotomous result: for patients younger than age 80 years ICR did not affect survival before or after adjusting for 11 significant predictors, even though 1 of these (EuroSCORE) was a confounding variable. There was, however, a significant effect of ICR on reduced midterm survival in patients aged ≥80 years (7% of the overall cohort). Other studies have shown age conundrums: Girerd and colleagues[4] found that patients aged <60 years had increased mortality with ICR but not in patients aged >60 years. Three articles

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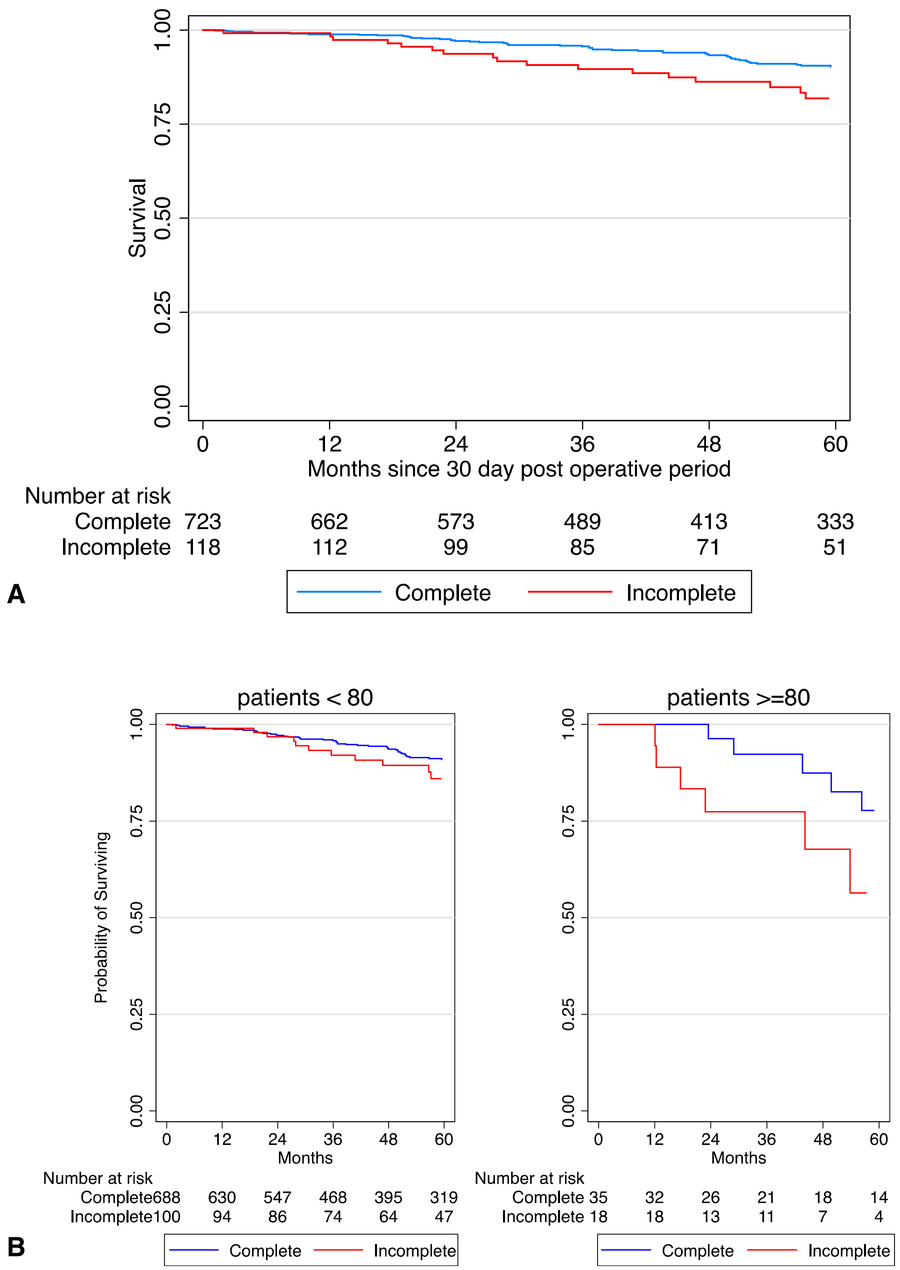

FIGURE 1. A, Unadjusted overall survival rates by complete and incomplete revasculariztion. B, Unadjusted Kaplan-Meier survival curves stratified by age <80 years (n = 788) and age ≥80 years (n = 53).

studying octogenarians have opposing views: Mohammadi and colleagues[5] found no difference in survival in octogenarians with ICR whereas Aziz and colleagues[6] found 18% decline and Kozower and colleagues[7] found 10% reduced 8-year survival in octogenarians with ICR. For the 53 patients aged ≥80 years in this series who survived the operation, ICR carries an almost 6-fold risk of dying but this may be sample-specific. This finding of reduced survival in octogenarians with ICR is not explainable within the data/scope of our study but deserves careful consideration regarding its validity and/or meaningfulness. Given that operative survival was not affected by ICR in this age group, surgeons may wisely opt for early survival rather than subject frail elderly patients to a CR operation of greater risk; for example a difficult-to-graft lateral wall target performed off-pump. Although well-selected elderly patients undergoing CABG have good outcomes, an objective assessment of frailty has been found to be associated with increased risk for morbidity and mortality after cardiac surgery.[8,9]

TABLE 4. Individual predictors of midterm mortality, single predictor variable analysis

Variable	Hazard ratio	*P* value	95% CI
Incomplete revascularization	2.0	.003	1.3-3.3
Off-pump	1.4	.151	0.9-2.4
Male	0.5	.004	0.4-0.8
Chronic obstructive pulmonary disease	2.0	.006	1.2-3.2
Renal disease	3.8	<.001	1.9-7.6
Peripheral vascular disease	2.5	<.001	1.6-4.2
Re-do coronary artery bypass graft	2.0	.090	0.9-4.2
Cardiovascular disease	2.2	.002	1.3-3.7
Diabetes mellitus	1.5	.049	1.0-2.3
Bilateral internal mammary artery grafts	0.8	.176	0.5-1.1
Age >80 y*	2.8	.001	1.6-5.0
EuroSCORE*			
3-5.99	1.9	<.001	1.1-3.3
≥6	4.0		2.5-6.4

CI, Confidence interval; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation. *Variable was also a confounding factor. Estimates for urgency were not included because there was evidence against the proportional hazards assumption for urgency.

Previous studies suggesting superiority of CR over ICR have included patients in which the majority of grafts were venous. Poorer outcomes with ICR in such populations may not be due to the ICR in and of itself but rather due to relatively early occlusion of venous conduits. Early postoperative vein graft occlusion has not changed in 4 decades: at <3 weeks postoperatively in the study by FitzGibbon and colleagues[10] of 5065 venous grafts performed from 1969 to 1994, vein graft occlusion was 12%, similar to the more contemporary study from Kim and colleagues[11] wherein 7-day vein graft occlusion was 11.8%. One-year graft occlusion rates have also stayed the same since the study by FitzGibbons and colleagues[10]: 24% compared with the 1-year vein graft occlusion in the Prevent IV trial[12] of 25.7%. This rapid attrition of vein grafts would convert a patient with single vessel disease (1 territory not bypassed) at the time of CABG to double vessel disease in 12% of patients at early postoperation and in 24% to 26% of patients at 1 year and could well explain the poorer survival of patients with ICR. The use of more arterial conduit known to last longer could therefore mitigate the effect of ICR.

TABLE 5. Multivariable proportional hazards regression model predicting midterm survival in patients who survived the postoperative period, stratified by urgency

Variable	Hazard ratio	*P* value	95% CI
Incomplete revascularization			
Age >80 y	5.7	.003	1.8-17.7
Age <80 y	1.2	.544	0.7-2.1
Comorbid condition	1.74	.017	1.10-2.73
EuroSCORE		<.001	
3-5.99	1.71		0.96-3.04
≥6	3.25		1.84-5.73
Male	0.71	.125	0.46-1.10

CI, Confidence interval; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation.

Other Studies of CR and Arterial Grafting

The literature on ICR is difficult to interpret due to lack of a universal definition; varying lengths of follow-up; differing amounts of arterial and venous grafting; studies including just PCI, just patients undergoing CABG, or a combination of both; and studies including only specific subgroups such as patients with diabetes and octogenarians. Hence there is no consistent negative correlation between ICR and survival; studies showing reduced survival with ICR include the 10-year follow-up of the Medicine, Angioplasty, or Surgery Study for Patients Undergoing PCI (MASS II),[13] the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial in persons with diabetes,[14] the 4-year SYNTAX trial results (including both randomized and registry patients),[15] patients younger than age 60 years by Girerd and colleagues,[4] studies in octogenarians,[6,7] a study by Synnergren and colleagues[16] in patients with 2 of 3 territories missed, and a 5-year follow-up study by Kleisli and colleagues.[17] Studies showing the opposing view—no difference in survival between ICR and CR groups—include as many studies and some even in similar patient subgroups: the 10-year follow-up of the MASS II trial for patients undergoing CABG[11]; a study of octogenarians by Mohammadi and colleagues[5]; a study with left internal thoracic artery to LAD in only 75% to 77% of patients by Kim and colleagues[11]; McNeer and colleagues' 1974 study[1] of patients with all vein grafts; a study of patients older than age 60 years by Girerd and colleagues[4]; a study by Sarno and colleagues,[18] including patients undergoing PCI with less complex disease; a study by Rastan and colleagues[19] with no difference at 1 and 5 years follow-up; the SYNTAX trial (randomized patients) at 1 year[20]; a study by Synnergren and colleagues[16] for no difference if 1 of 3 territories missed; and the Bypass Angioplasty Revascularization Investigation trial, which also noticed that multiple grafting resulted in worse survival.[21]

Other investigators have assessed the effects of ICR in patients with multiple arterial grafts, and similar to our own findings, found no difference in survival between CR and ICR: MASS II with 1 IMA in 92%, 1 IMA with radial artery grafts in 36% and epigastric artery grafts in 10%.[13] Rastan and colleagues' study[19] with 21.9% total arterial grafting in the CR group and 32.2% in the ICR group found that arterial revascularization was protective for decreased mortality, and Kleisli and colleagues' study[17] showed that use of the right IMA (22.6%) and radial artery (58.7%) correlated with improved survival at a mean of 5 years (HR, 0.51 for right IMA use and 0.49 for radial artery use). Hayward and colleagues[22] showed that use of arterial grafts for lesions (largely severe) in the right

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circulation were protective against progression of native vessel disease whereas bypassed moderate lesions with saphenous vein caused greater native lesion progression to severe 40% versus 14% of the time if not bypassed. Arterial grafting especially with IMAs prevents native disease progression.[23] Because a randomized controlled trial comparing patients with CR versus ICR is not possible, evidence for rationale of the CR dogma is dependent on retrospective observational studies. Our study of almost pure arterial grafting eliminates 1 important variable: The venous graft.

Early theories of what were appropriate revascularizations and hence the definition of ICR must by necessity, change. Before the advent of angioplasty,[24] coronary arteries with 50% stenosis were routinely bypassed to avoid reoperation for disease progression. Venous conduits offer almost no resistance to flow whereas competitive flow is a significant factor when using arterial conduits.[25] Also, use of fractional-flow reserve (FFR) has demonstrated that many lesions[26] are not hemodynamically significant. In the ongoing Evaluation of Xience Prime Everolimus Eluting Stent System (EECSS) or Xience V EECSS Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial[27] randomizing low SYNTAX score patients with left main stenosis to PCI or CABG, CR for the PCI arm favors addressing 70% narrowed coronary arteries, whereas for the CABG arm it is 50% stenosis. Opinion as to the level of significant stenosis appears to be changing, but should change similarly for both PCI and CABG. Gössl and colleagues[28] proposed a new definition for both PCI and CABG: CR complete anatomic (>50% stenosis; >1.5 mm coronary arteries), ICR anatomic but functionally adequate (FFR >70%), and ICR anatomical and functionally inadequate (FFR ≤70). This third category is probably significant for survival; the authors state: "…CR based on anatomic criteria alone may soon become obsolete, emphasizing physiology driven coronary interventions."[28] There is even evidence to show that "overgrafting" may be detrimental.[21] However unless FFR testing becomes routine for pre-revascularization assessment at coronary angiography, perhaps what is simplest is best: the definition of CR used in our study is the same as the very first used by McNeer and colleagues[1] in 1974: a revascularization by "territory"; that is, 1 bypass for each territory that has a 70% stenosis in a major branch.

Limitations

Limitations of our study include the relatively small number of the ICR group, the small number of octogenarians (and older) and the number of factors found to significantly influence survival. This real-world, single-center study evaluating total arterial grafting performed by a single operator may be advantageous because it provides consistent techniques, skills, and decision making but at the same time may not be applicable to other centers. Ongoing use of evidence-based medications for secondary prevention, which is known to affect outcome, was not evaluated in this study. Finally, we evaluated outcomes out to 4.5 years but longer follow-up may be required to better evaluate the consequences of ICR, especially because the advantage of arterial grafts may last decades.

CONCLUSIONS

Contrary to current beliefs regarding completeness of revascularization, we have demonstrated that ICR in this unique series of all-comer CABG with 98% arterial grafts is not associated with decreased survival perioperatively and at midterm in patients younger than age 80 years. However many factors affect survival and may act synergistically or independently. Use of arterial grafts minimizes the adverse effects of not grafting the third region.

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Discussion

Dr Philip A. Hayward *(Melbourne, Australia)*. I'd like to thank the American Association for Thoracic Surgery Committee for the invitation to discuss this work and also thank Dr Kieser for supplying me with a draft of the manuscript in a timely fashion.

Dr Kieser, you are to be congratulated on an important study. You've done a sophisticated analysis of your own coronary practice, and your commitment to arterial grafting and to completeness of revascularization is impressive.

You state as a limitation that this is a single-surgeon experience, but in this context this may be 1 of the merits of the study because it allows us to really tease out the effect of incomplete revascularization. Other series published can be pools of patients done by different surgeons, with varying thresholds for grafting small or poor targets, and it is difficult to tease out the effect of incomplete revascularization when there have been 2 different revascularization strategies and thresholds. You have a uniformity of your threshold for revascularization—the same eyes, the same hands, the same threshold—I think that's why your study is unique.

Fractional-flow reserve (FFR) is redefining what we think needs revascularization now. It's all about physiology, not anatomy, we know that from percutaneous intervention and the Fractional Flow Reserve versus Angiography for Multivessel Evaluation study. FFR depends on the volume of distal antegrade flow, not just the stenosis. Vessels that are small or running into scar or that are well collateralized do not have significant FFR. About 87% of the vessels you left fall into this category. I suggest that really your ''incomplete revascularization'' group was in fact functionally completely revascularized for the most part, and the vessels that you left alone really were functionally insignificant. And that's probably why you've not shown any effect on survival from your ''incomplete revascularization'' and that's reflected in the lack of a difference in angina, myocardial infarction, or percutaneous coronary intervention thereafter.

You say that your findings differ from other authors because you used arterial grafts rather than vein grafts and that you therefore avoided early vein graft failure. But, of course, you also avoid the progression of native vessel disease that's seen primarily after vein grafts, and it is this progression that can damage the collateralization that had been providing protection from the effects of incomplete revascularization. An all-arterial graft population has been shown to produce less native vessel disease progression, so perhaps the collaterals are better preserved and hence your different findings.

I would like to pose 2 questions: The surprise finding clearly is the difference in the long-term outcome in the octogenarians who had incomplete revascularization. Do you really think this is a different effect of incomplete coronary revascularization in older people, or is there another factor here—a frailty factor—where really this was a different pool of frail elderly people where you lowered your threshold for leaving targets alone, such that really their poorer survival comes from their frailty rather than the fact that you decided to leave 1 target?

The second question follows from that. You told us that incomplete revascularization didn't affect in-hospital mortality overall, but was that also true for the octogenarians whose long-term outcome you say is poorer with incomplete revascularization? Perhaps their long-term outcome is just a reflection of a turbulent perioperative period. I think that shorter-term outcome data might influence most surgeons' practice more than the long-term survival, because many of us faced with frail octogenarians are really focused on getting them out of the hospital intact and we tend to lower our horizons. If I'm faced with that frail octogenarian patient and I want to get him or her safely through, does complete or incomplete

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revascularization matter in the short term, irrespective of if it matters in the long term?

Dr Teresa Kieser *(Calgary, Alberta, Canada)*. Your point regarding FFR is very well taken. Rastan and Fred Mohr had an article in *Circulation* in 2009 that spoke to this. They didn't say the reason was FFR, but they spoke about vessels that were within scar, for example. So it didn't matter if you didn't completely revascularize them. I think your reason is correct, the FFR would be insignificant. However, being the bilateral internal mammary artery graft fanatic that I am, I would still like to invoke the untimely demise of the vein graft as a mechanism.

With respect to poorer survival coming from surgical frailty or not wanting to put an older patient through the stress of surgery, I think the reasons are 2-fold: Operating on frail people does cause a surgeon to possibly scale down the operative procedure. But experience has taught me that when you operate on an 80-year old, everything has to go correctly. They cannot tolerate the slightest complication the way a younger patient would. The wheels easily fall off the wagon.

Incomplete revascularization in an octogenarian patient perioperatively, you are right, we probably should have included this. There were only 70 patients older than age 80 years, 53 were incompletely revascularized, so that's 76%.

The operative mortality was not different. There were 2 out of 23 incompletely revascularized patients who died, and 3 out of 47 of the completely revascularized patients died—a *P* value that was insignificant. We looked at the cause of death of these 5 patients: 1 died from fulminant sepsis at another hospital, very quickly; another had a massive stroke; another died of necrotic bowel because he had embolized from a calcified aorta (we had had to perform the procedure on him off-pump and he was a redo). The deaths of 2 patients of the 5 were probably due to graftability issues or graft failure. Incomplete revascularization did not make a difference in these patients. So the answer is if you can get a patient—an 80-year-old—out of hospital alive and intact with incomplete revascularization this is better.

Dr Hayward. That's a great relief. Thank you.

000 Arterial grafts balance survival between incomplete and complete revascularization: A series of 1000 consecutive patients with coronary artery bypass graft with 98% arterial grafts

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In 1000 patients who had undergone coronary artery bypass grafting (98% arterial grafts), no evidence shows incomplete revascularization decreased survival perioperatively or at midterm in patients younger than age 80 years. Reduced midterm survival occurred in 53 of 70 patients with incomplete revascularization aged ≥80 years. Beneficiality of complete revascularization cannot be tested with a randomized controlled trial, but only with retrospective/observational studies. This study eliminates the venous-graft variable.

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