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Incomplete Revascularization During OPCAB Surgery is Associated With Reduced Mid-Term Event-Free Survival

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Background. **The aim of this study was to compare early and mid-term outcome in patients undergoing off-pump coronary artery bypass surgery who have had complete revascularizations and incomplete revascularizations (IRs).**

Methods. **Patient and operative data were collected prospectively for all patients who had off-pump coronary artery bypass surgery. Patients with multivessel disease were classified as having IR if the number of diseased coronary systems (left anterior descending coronary artery, circumflex and right coronary artery) exceeded the number of distal anastomoses. In-hospital outcomes, survival, and event-free survival were compared between patients with complete revascularization and IR using propensity scores to take account of differences in prognostic factors.**

Results. **There were 1,479 off-pump coronary artery bypass surgery patients between April 1996 and December 2002 (30% of all coronary artery bypass graft patients), and 16.0% (237 patients) had IRs. Patients with IRs tended to be older and were female, had more extensive disease, worse dyspnea, a higher Parsonnet score, poorer ejection fraction, congestive cardiac failure, asthma or chronic obstructive airways disease, and previous cardiac surgery. The adjusted hazard ratio for patient survival with IRs versus complete revascularizations was 1.56 (95% confidence interval, 1.19 to 2.06; p = 0.001). Analyses for multiple time periods confirmed that IRs had a significantly increased risk of death, but also that the risk disappeared after the first 4 to 6 months of follow-up ($p < 0.0001$).**

Conclusions. **Compared with off-pump coronary artery bypass surgery patients with complete revascularizations, those with IRs have reduced survival, but only in the first 4 to 6 months after surgery. Patients' preoperative condition, rather than IR itself, may explain these findings because IRs should have mid-term as well as early effects.**

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Incomplete revascularization (IR) is known to have a negative influence on the outcome after coronary artery bypass grafting (CABG) [1–3]. Therefore complete revascularization (CR) has been considered the goal of coronary surgery. Prior studies have used different definitions for complete or adequate revascularization, which accounts for some controversies regarding mid and long-term event-free survival. The Arterial Revascularization Therapies Study (ARTS) and the Bypass Angioplasty Revascularization Investigation (BARI) trials [4, 5], for example, have tried to answer the question of what constitutes optimal surgical revascularization, showing only marginally lower event-free survival in patients after IR versus CR.

This issue is particularly important in the era of off-pump coronary artery bypass (OPCAB) surgery in which the possibility of IR and early failure resulting from technical difficulties in constructing bypass grafts to the lateral and inferior wall must be considered. Recent evidence showed that IR in OPCAB surgery did not affect early outcomes [6, 7]. However, with longer follow-up, IR may cause angina to recur more often requiring further revascularization.

Therefore the aim of this study is to compare early and mid-term outcomes of patients undergoing OPCAB surgery who have undergone CRs or IRs by using data from our cardiac surgery database.

Patients and Methods

Data for the study came from four sources: (1) an institutional database of preoperative characteristics, surgical information, and in-hospital outcomes collected prospectively (Patient Analysis & Tracking Systems [Dendrite Clinical Systems, London, UK]); (2) death registrations from the United Kingdom National Strategic Tracing Service; (3) responses to a postal questionnaire to patients and their family physicians about cardiac-related events [8]; and (4) operation notes.

Patient Selection, Data Collection, and Data Definitions

Data were analyzed for all patients who underwent OPCAB surgery between April 1996 and December 2002. Incom-

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Table 1. Prevalence of Prognostic Factors Among Patients Who Had Complete and Incomplete Revascularization

	Complete (N = 1242)[a]		Incomplete (N = 237)[a]		
Prognostic Factor	n	(%)	n	(%)	*p* Value
Age at operation: (y)					
≥ 16 and < 55	188	(15.1)	42	(17.7)	0.10[b]
≥ 55 and < 65	409	(32.9)	69	(29.1)	
≥ 65 and < 75	506	(40.7)	88	(37.1)	
≥ 75	139	(11.2)	38	(16.0)	
Male gender	1023	(82.4)	178	(75.1)	0.009
CCS class > 2	740	(60.0)	153	(65.4)	0.12
NYHA functional class > 3	46	(3.7)	18	(7.7)	0.006
Preoperative risk factors					
Ejection fraction < 30%	61	(4.9)	23	(9.8)	0.003
MI in the last month	59	(4.8)	13	(5.6)	0.61
Congestive cardiac failure	29	(2.4)	19	(8.1)	< 0.001
Previous stroke	35	(2.8)	7	(3.0)	0.90
Creatinine > 150	70	(5.7)	23	(9.8)	0.02
Asthma/COAD	124	(10.0)	37	(15.8)	0.01
Peripheral vascular disease	106	(8.6)	30	(12.8)	0.04
Previous cardiac surgery	19	(1.5)	14	(6.0)	< 0.001
Hypercholesteraemia	1032	(83.8)	191	(82.0)	0.50
Hypertension	734	(59.4)	141	(60.3)	0.80
Diabetes	231	(18.7)	47	(20.1)	0.62
Triple vessel disease	741	(59.7)	198	(83.5)	< 0.001
Urgent, emergency, or salvage operation	555	(44.9)	108	(46.2)	0.73
Parsonnet score > 10	272	(22.0)	75	(32.0)	< 0.001

[a] Denominators were not always 1242 and 237 respectively because some data were missing for a small number of patients. [b] $p = 0.04$ for patients aged < 75 *versus* ≥ 75 years.

CCS = Canadian Cardiovascular Society; COAD = chronic obstructive airways disease; NYHA = New York Heart Association; MI = myocardial infarction.

plete revascularization was identified by comparing the number of distal anastomoses with the number of diseased coronary systems observed on the preoperative angiogram. Patients who had more diseased coronary segments (ie, > 50% stenosis in the left anterior descending coronary artery, circumflex and right coronary artery systems) than distal anastomoses were classified as having IRs. This is one of the definitions (ie, definition 3) that was used in the BARI trial [5] and it is similar to that used by Sabik and colleagues [9].

A number of risk factors were derived from the information in the database, as previously described [10, 11]. These factors are widely accepted as predictive of early postoperative mortality or morbidity: age greater than 75 years, ejection fraction less than 30%, myocardial infarction in the previous month, current congestive cardiac failure, previous stroke, creatinine greater than 150 μmol/L, respiratory impairment (current chronic obstructive airways disease or asthma), peripheral vascular disease, and previous cardiac surgery requiring a sternotomy. In-hospital mortality was defined as deaths registered by the National Strategic Tracing Service (NSTS) for patients who did not have a date of discharge. Early hospital morbidity was defined as previously reported [11].

Anesthetic and Surgical Technique and Postoperative Management

Anesthetic technique and the method of exposure and stabilization for performing anastomoses in patients undergoing OPCAB surgery have been previously described [12]. After surgery, patients were transferred to the intensive therapy unit and managed according to the unit protocol [10, 11].

Patient Follow-Up

Information about vital status was available for all patients from the NSTS. Non-fatal cardiac-related events included: (1) the need for a further coronary revascularization procedure (whether reoperation or percutaneous transluminal coronary angioplasty); (2) patient reported hospital attendance for myocardial infarction, coronary angiography, congestive heart failure, or recurrent angina; (3) Canadian Cardiovascular Society (CCS) class greater than 1; (4) New York Heart Association functional class greater than 2; and (5) report of cardiac-related hospital admission by the family physician. These criteria for cardiac-related events are similar to those used previously to validate

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Table 2. Incidence of In-Hospital Outcomes Among Patients Who Had Complete and Incomplete Revascularizations[a]

	Complete (N = 1242)[b]		Incomplete (N = 237)[b]	
In-Hospital Outcome	N	(%)	N	(%)
Death in-hospital	13	(1.1)	8	(3.4)
Perioperative MI	32	(2.6)	11	(4.7)
Postoperative atrial fibrillation	183	(14.9)	33	(14.2)
Neurologic complication	11	(0.9)	1	(0.4)
Renal complication	12	(1.0)	3	(1.3)
Infective complication	10	(0.8)	2	(0.9)
Pulmonary complication	26	(2.1)	5	(2.2)
Postoperative inotropes	532	(43.3)	104	(44.1)
Blood loss > 1,000 mL	482	(39.1)	79	(33.1)
Duration of ventilation > 12 hours	302	(24.9)	55	(24.2)
Duration of ITU stay > 1 night	275	(22.4)	54	(23.2)
Postoperative stay > 7 days	322	(26.2)	57	(24.5)

[a] Unadjusted and adjusted *p* values for comparisons between groups are shown in Table 3. [b] Denominators were not always 1,242 and 237, respectively, because some data were missing for a small number of patients.

ITU = intensive therapy unit; MI = myocardial infarction.

the accuracy of the reporting of events by patients and their family physicians [8].

Sample Size

Sample size calculations were carried out prior to any analysis to check if there were sufficient data to answer the research question with adequate power. Separate calculations were done for outcomes of death or cardiac-related event. From previous literature we estimated that the rate of IR would be approximately 10% to 15%, or 1 in every 6 patients. We anticipated an overall mortality rate at 2 years of less than 5% and a cardiac-related event rate of about 10% [9]. This allocation ratio, the expected event rate and the total available sample size of 1,479 patients meant the study had 80% power to detect an absolute increase in risk of cardiac-related events at 2 years of approximately 7% (ie, 9% vs 16 %) in the IR group. For mortality the study had 80% power to detect an absolute increase in risk of cardiac-related events at 2 years of approximately 4% (ie, 2% vs 6%) in the IR group. Changes of these magnitudes in the probability of an outcome were considered clinically important and plausible on the basis of previous literature for

Table 3. Unadjusted and Adjusted Effects (Odds Ratios) of Incomplete Revascularization on Short-Term Outcomes

	Unadjusted (n = 1479)[a]			Adjusted (n = 1469)[b]		
	Odds Ratio	95% Confidence Interval	*p* Values	Odds Ratio	95% Confidence Interval	*p* Values
Death in-hospital	3.33	2.35–4.71	< 0.001	2.54	1.72–3.75	< 0.001
Perioperative MI	1.85	1.36–2.51	< 0.001	1.89[c]	1.10–3.26	0.02
Postoperative atrial fibrillation	0.95	0.76–1.18	0.62	0.91[d]	0.70–1.19	0.50
Neurologic complication	0.48	0.15–1.49	0.20	0.35[c]	0.13–0.97	0.04
Renal complication	1.32	0.19–9.14	0.78	0.72	0.13–3.83	0.70
Infective complication	1.06	0.15–7.29	0.96	0.99	0.14–7.00	1.00
Pulmonary complication[e]	1.01	0.41–2.50	0.98	0.67	0.29–1.56	0.38
Postoperative inotropes	1.02	0.88–1.17	0.83	0.85[d]	0.73–0.98	0.03
Blood loss > 1,000 mL	0.77	0.56–1.06	0.11	0.83	0.56–1.23	0.36
Duration of ventilation > 12 hrs	0.96	0.66–1.40	0.84	0.89	0.57–1.39	0.61
Duration of ITU stay > 1 night	1.05	0.85–1.28	0.66	0.94	0.78–1.13	0.50
Postoperative stay > 7 days	0.92	0.51–1.67	0.79	0.76	0.40–1.45	0.40

[a] Unadjusted analyses took into account clustering of patients within consultant teams carrying out the operation but did not adjust for any preoperative risk factor. [b] Adjusted analyses also took into account clustering of patients within consultant teams and deciles of propensity score. Propensity scores were derived from the demographic and preoperative risk factors (see Methods). Ten patients (3 with incomplete and 7 with complete revascularization) with several missing risk factors were dropped from these analyses. [c] Interactions of incomplete revascularization and age > 75 years (and for neurologic complication, the interaction of incomplete revascularization and period of operation) could not be estimated because there were too few events in the older age group. [d] Interactions of incomplete revascularization and period of operation were statistically significant (postoperative atrial fibrillation, $p = 0.003$; use postoperative inotropes, $p = 0.003$). [e] Quintiles, cf. deciles, of propensity score were modelled because of the paucity of events.

ITU = intensive therapy unit; MI = myocardial infarction.

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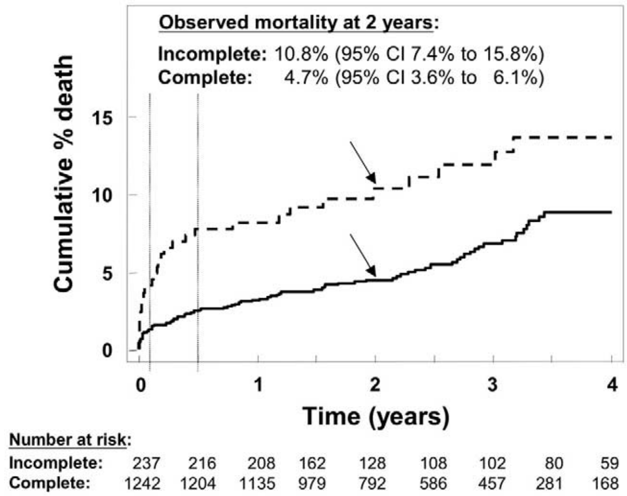

Fig 1. Inverted Kaplan Meier curves showing the observed cumulative percentage of patients with incomplete (dashed line) *and complete* (solid line) *revascularizations who died with increasing duration from the time of operation.* Vertical lines *show the epochs considered (ie, < 30 days, 31 days to 6 months, > 3 months). The* arrows *indicate the time (2 years) of the observations.*

patients having conventional CABG or OPCAB surgery with IR [1–3, 9].

Statistical Analysis

Frequencies and percentages of early outcomes are tabulated for patients with CRs and IRs. Some outcomes were dichotomized for analysis (eg, intensive therapy unit and postoperative length of stay and blood loss). The relative risks for IR versus CR for early outcomes are presented as odds ratios (ORs) and 95% confidence intervals. The effects of IR versus CR on survival and event-free survival were calculated using Cox regression and are presented as hazard ratios (HRs) and 95% confidence intervals. Follow-up was censored either at the time of the last available follow-up or when a "failure" (death or a cardiac-related event) occurred.

First, analyses were carried out without adjustment for potential confounding. Second, analyses were adjusted for confounding by including indicator variables for deciles of propensity score. Propensity scores for IR were derived from demographic and preoperative prognostic factors (details available from the authors). Analyses calculated robust confidence intervals (STATA, version 8.2; StataCorp LP, College Station, TX) to take account of the clustering of patients within consultant surgeons. All analyses were carried out using STATA version 8.2. (Additional analyses compared IR and CR patients matched by propensity score; the results were similar and are not reported here but are available from the authors.)

No subgroup comparisons were identified at the outset. However, interactions between IRs versus CRs and age greater than 75 years were investigated because of increasing evidence of the benefits of OPCAB surgery in elderly patients. Interactions between IRs versus CRs and period of operation (before and after January 1, 2000) were also investigated to explore the effects of the learning curve for OPCAB surgery or changes in the characteristics of OPCAB patients.

Plots of ln (survival probability) vs ln (analysis time) converged for patients with IRs and CRs. Therefore, additional survival models were fitted for different epochs of time, even though proportional hazards assumptions were not consistently violated. (Epochs were chosen to ensure similar numbers of events in each epoch (ie, 1 to 30 days, 31 days to 6 months, > 6 months). We also described the characteristics and in-hospital outcomes of patients who did and did not send back the follow-up questionnaire to investigate the likely magnitude and direction of informative censoring in analyses of event-free survival. No correction was made for multiple comparisons, but confidence intervals and exact *p* values are presented throughout. Our interpretation of the findings takes into account the consistency of the findings and their magnitude, as well as their statistical significance.

Results

Study Population

A total of 4,965 patients with double-vessel or triple-vessel disease underwent CABG alone at our institution between April 1, 1996 and December 31, 2002. The overall hospital mortality was 1.2%. Of these, 1,479 patients (30%) underwent OPCAB surgery; operations were acutely converted for 20 patients. The proportion of CABG operations carried out using OPCAB has steadily increased during this period, from 1% in 1996 and 1997 to 63% in April 2002 to December 2002 [13, 14]. A second arterial conduit (either the radial or the right internal thoracic artery) was used in 28% of all OPCAB patients, 30.0% of those with CRs and 19.0% of those with IRs.

Two hundred thirty seven (16.0%) of the 1,479 patients who had OPCAB surgery had IR, compared with 249 (7.1%) of the 3,486 patients who had conventional CABG surgery. The distribution of prognostic factors in OPCAB patients with CRs and IRs are described in Table 1. On average, patients with IRs had much worse prognostic factors. The rate of IRs in OPCAB patients declined with time from 26.0% before January 1, 2000 (n = 331) to 13.2% subsequently (n = 1,148; $p < 0.0001$). Reasons for IRs were the presence of small or calcified coronary arteries (49%), infarcted or scarred myocardium (14%), hemodynamic instability (6%), lack of conduits (5%); or no reason given (26%).

Effects of Incomplete Revascularization

The frequencies of in-hospital outcomes for patients with CRs and IRs are described in Table 2. The effects (ORs) on these outcomes of having IR versus CR (both unadjusted and adjusted) are shown in Table 3. Patients with IRs were significantly more likely to die in the hospital (adjusted OR = 2.54; $p < 0.001$) or experience a perioperative myocardial infarction (adjusted OR = 1.89; $p = 0.02$); however they also appeared to be less likely to experience a stroke (adjusted OR = 0.35; $p = 0.04$) or to require postoperative inotropic support (adjusted OR = 0.85; $p = 0.03$).

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Table 4. Unadjusted and Adjusted Effects (Hazard Ratios) of Incomplete Revascularization on Event-Free Survival

	Unadjusted (n = 1469)[a]			Adjusted (n = 1469)[b]		
	Hazard Ratios	95% Confidence Interval	*p* Value	Hazard Ratios	95% Confidence Interval	*p* Value
All cause death	1.93	1.44–2.58	< 0.001	1.56	1.19–2.06	0.001
Epoch analysis			< 0.0001[c]			< 0.0001[c]
0 to 30 days	3.36	1.97–5.72	< 0.001	2.75	1.49–5.08	0.001
31 days to 6 months	3.11	1.81–5.34	< 0.001	2.56	1.57–4.19	< 0.001
> 6 months	1.24	0.87–1.77	0.23	1.00	0.74–1.36	0.99
Serious cardiac-related event	1.67	1.25–2.23	< 0.001	1.56	1.08–2.25	0.02
Epoch analysis			< 0.0001[c]			< 0.0001[c]
0 to 30 days	2.79	1.45–5.34	0.002	2.59	1.21–5.53	0.01
31 days to 6 months	1.95	1.30–2.91	0.001	1.82	1.30–2.53	< 0.001
> 6 months	1.27	0.94–1.70	0.12	1.18	0.83–1.69	0.36

[a] Unadjusted analyses took into account clustering of patients within consultant teams carrying out the operation, but did not adjust for any preoperative risk factor. [b] Adjusted analyses took into account clustering of patients within consultant teams and deciles of propensity score. Propensity scores were derived from the demographic and preoperative risk factors (see Methods). Ten patients (3 with incomplete and 7 with complete revascularization) with several missing risk factors were dropped from these analyses. [c] Overall test of the significance of epoch.

There were no significant interactions between completeness of revascularization and age greater than 75 years, but there were two significant interactions with period, namely for postoperative atrial fibrillation ($p = 0.003$) and inotropic support ($p = 0.003$). Both interactions showed the same pattern. Patients with IRs had a higher risk of adverse outcome in the earlier period. The relative risk of the adverse outcome increased in the more recent period for patients with CRs, but decreased for those with IRs. These joint effects made the absolute risk for patients with IRs in the recent period slightly lower than for those with CRs.

Follow-up for vital status was 100%. After 2 years of follow-up, the observed cumulative percentages of patients who died during this time in the CR and IR groups were 4.7% and 10.8%, respectively (Fig 1). The median durations of follow-up were 2.40 and 2.22 years, respectively. Hazard ratios for unadjusted and adjusted survival analyses showed that IR was associated with a significant risk of death (see Table 4). Secondary analyses found no significant interactions between completeness of revascularization and age greater than 75 years ($p = 0.79$) or period ($p = 0.18$). Additional adjusted survival analyses found significant differences between the HRs for different epochs (overall effect of epoch; $p < 0.0001$) (see Table 4). There was a significant hazard from IRs in the first 30 days (HR = 2.75) and between 31 days to 6 months (HR = 2.56), but not subsequently (HR = 1.00).

The postal questionnaire was completed by 1,108 patients, with informative data available for 1,102. Six of the 1,102 patients subsequently died without them or their family physician having reported a nonfatal cardiac-related event. Cardiac-related events were ascertained from clinical records for 3 patients who did not respond but were known to be alive from the NSTS registry. A further 115 patients were identified as having died from the NSTS registry, giving a total follow-up rate of 82.5% (1,220 of 1,479). The rate of nonresponse did not differ for early and late period.

Among patients known to be alive from the NSTS registry, nonresponders were younger ($p < 0.0001$), had lower Parsonnet scores ($p = 0.01$), were less likely to have an elevated preoperative creatinine level ($p = 0.02$), or had greater than 50% stenosis of the left main stem ($p = 0.03$). However, these patients were more likely to have hypertension ($p = 0.05$) and to be current smokers ($p < 0.0001$). Nonresponders had very similar in-hospital outcomes. Nonresponders with CRs and IRs did not differ with respect to their prognostic factors or in-hospital outcomes.

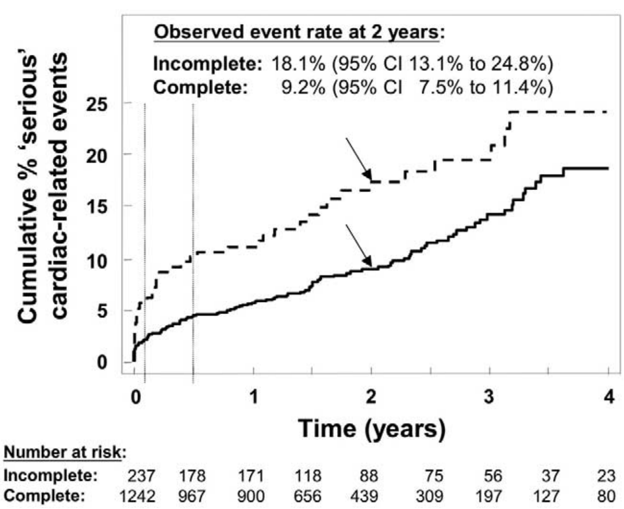

Fig 2. Inverted Kaplan Meier curves showing the observed cumulative percentage of patients with incomplete (dashed line) *and complete* (solid line) *revascularizations who died or had a serious cardiac-related event (nonfatal myocardial infarction or further revascularization (percutaneous transluminal coronary angiography or CABG) with increasing duration from the time of operation.* Vertical lines *show the epochs considered (ie, < 30 days, 31 days to 6 months, > 3 months). The* arrows *indicate the time (2 years) of the observations. Note that the numbers of patients in the incomplete and complete revascularization groups described as being at risk for this analysis decreased markedly during the first part of follow-up, which reflected censoring of patients who did not respond to the questionnaire.*

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We also carried out a survival analysis for survival free from death, nonfatal myocardial infarction, and further revascularization (percutaneous transluminal coronary angioplasty or CABG, or ie, "serious" events) to compare observed event rates with other published but less inclusive event rates [9, 15, 16]. After 2 years of follow-up, the observed cumulative percentages of patients dying or experiencing a serious cardiac-related event with time in the CR and IR groups were 9.2% and 18.1%, respectively (Fig 2). The median durations of follow-up were 1.55 and 1.49 years, respectively.

Hazard Ratios again indicated a significantly increased risk of death or a serious cardiac-related event in patients with IRs (see Table 4). Secondary analyses found no significant interactions between completeness of revascularization and age greater than 75 years ($p = 0.62$) or period ($p = 0.07$). Additional adjusted survival analyses found significant differences between HRs for different epochs (overall effect of epoch; $p < 0.0001$) (see Table 4). There was a significant hazard ratio from IRs in the first 30 days (HR = 2.59) and between 31 days to 6 months (HR = 1.82), but not subsequently (HR = 1.18).

Comment

There were three main findings from the study: (1) the rate of IRs in off-pump patients was 16%, approximately the same as previously reported for on-pump and off-pump patients [1–7, 9], but higher than for on-pump patients during the same period in our institution; (2) patients who had IRs clearly had worse prognostic factors; and (3) patients who had IRs were significantly more likely to die in the hospital or to have a perioperative myocardial infarction, and these patients were also more likely to die during follow-up, but the increase in risk seemed to be confined to the first 4 to 6 months after surgery.

The most common reason for IRs in this study was the poor quality of the target coronary arteries judged by the surgeon to be unsuitable for grafting. The observed rate of IRs was similar to previous studies of patients having conventional CABG or OPCAB surgery [1–7, 9], but this was approximately twice the rate for patients undergoing conventional CABG in our institution during the same period. Some of the reasons reported by surgeons for not completely revascularizing the patients in this study (eg, vessel too small to graft) may arise more often during OPCAB surgery than during conventional CABG surgery. However, because OPCAB surgery is often preferred for high-risk patients, the higher rate of IRs may have arisen because patients were less fit for surgery before the operation and the surgeon wanted to minimize the risks of mortality and morbidity by adopting what Kilo and colleagues [6] have described as "target vessel revascularization" in high-risk patients.

The lower rate of IRs in patients who had conventional CABG warrants a comment about the criteria for selection of patients for OPCAB surgery. By far the most dominant factor is surgeon preference. This could only cause a selection bias if different kinds of patients are referred to different consultant teams and we have no evidence for this. Very occasionally, a consultant who prefers conventional CABG surgery may refer a patient to a consultant who prefers OPCAB surgery if there are specific indications (eg, calcification of the aorta); this practice could cause a selection bias if OPCAB surgeons practiced target vessel revascularization (ie, choose to trade-off a reduced risk of operative complications from a shorter operation time against the possibility of an increased risk of a poor long-term outcome from IRs).

The possibility that OPCAB surgeons were indeed practicing target vessel revascularization in patients who had IRs is supported by the distribution of prognostic factors in patients who had CRs and IRs; the latter patients were clearly less well before the operation. This finding implies that one should be cautious about interpreting the increased risk of morbidity and mortality from IRs as truly due to the failure to graft all diseased coronary systems. One may be comparing "apples with oranges" [17] and inadequately characterizing factors associated with IRs. Whatever method is used to control for difference in prognostic factors between groups, some residual confounding is inevitable. Another possibility is that IR, for whatever technical reason, is a surrogate marker for another, unmeasured prognostic factor (eg, more complex coronary pathology).

We believe that the epoch analyses help to interpret the findings; these show that the adverse effects of IRs are confined to the first 6 months with no differences between the two groups in mortality and cardiac-related events thereafter. These observations suggest that the early adverse effects are probably due to the preoperative condition of the patient, not IR, because one would expect IR to have mid-term as well as early effects.

Definitions of IR are controversial. The definition we used is likely to underestimate the proportion of patients who had IRs because some patients may have had more than one graft to one coronary system. However, the definition has the advantage of being simple and transparent, and the BARI investigators found that their results were not markedly affected by using different definitions (including the one used here) [5].

We did not observe any interaction between age and completeness of revascularization. The survival models estimated three quantities: (1) the effect of IRs versus CRs for one age group (ie, for patients $\leq$ 75 years); (2) the effect of being $<$ 75 vs $>$ 75 years old for one revascularization group (ie, for patients with CRs); (3) the difference in the effects of IRs versus CRs for the second age group (ie, $>$ 75 years) compared with the first age group (ie, $\leq$ 75 years). Therefore the lack of any interaction means elderly patients are not differentially affected by having IRs compared with younger patients.

In contrast, we did observe some interactions between period of operation and completeness of revascularization, which suggested that some adverse effects associated with IRs in the hospital were no longer present in the more recent period. A similar pattern was observed in the survival analyses although the interaction terms did not reach significance. These findings may have

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arisen because the preoperative risk profile of patients who had OPCAB surgery worsened over time; if this is true, it would support the strategy of target vessel revascularization in patients at highest risk of perioperative complications.

The trade-off between the potential benefits of less invasive surgery and the potential harms of IRs have been discussed in several other studies intended to evaluate whether a strategy of OPCAB surgery could be justified for high-risk patients. Kilo and colleagues [6] have shown that target vessel revascularization of the culprit lesion without CPB was associated with a significant reduction of in-hospital and mid-term mortality, and major postoperative complications compared with CR with CPB in older and high-risk patients. Demaria and colleagues [18] also showed a benefit of target revascularization compared with CR in octagerians undergoing either OPCAB or on-pump CABG surgery. The differences between their findings and ours may arise from the careful selection of patients for comparison in those two studies (ie, patients who were at a very high risk from having CPB). Nevertheless all studies seem to suggest that OPCAB surgery may be the technique of choice in elderly and high-risk patients despite IR.

We observed an unremarkable low mortality rate. With respect to survival free from serious cardiac-related events, there was no evidence of differential nonresponse between completely and incompletely revascularized groups, so loss to follow-up is unlikely to have biased the estimates of the hazard ratio from IRs. The analysis of death or serious cardiac-related events confirms that the increase in hazard from IRs disappears after 6 months and that the rate of death or serious events are comparable with previous studies [9, 15, 16].

We conclude that IR is associated with reduced early and mid-term survival, and survival free from serious cardiac-related events after OPCAB surgery. However, these differences disappear after 6 months of follow-up. The preoperative condition of patients, rather than IRs may be the cause of these findings, because one would expect IRs to have mid-term as well as early effects on mortality and cardiac-related events.

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