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Does the completeness of revascularization affect early survival after coronary artery bypass grafting in elderly patients?☆

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Abstract

Objective: Usefulness and risks of incomplete versus complete revascularization are still matters of ongoing discussions. Because an increasing number of elderly patients are undergoing coronary artery bypass grafting (CABG), the question arises whether a less extensive surgical approach is more prudent than complete revascularization. **Methods**: Of 6531 patients undergoing isolated CABG, 859 were 75 and older at the time of operation. Mean age of the 859 patients was 77 ± 2.7 years (median: 76 years); 65% were men. Follow-up enquiry by questionnaire was performed at the 180th postoperative day with a completeness of 95.6%. Assessment of the impact of incomplete revascularization utilized both multivariable analysis and propensity score matching to account for selection factors. **Results**: Incomplete revascularization was performed in 133 patients (16%). The most common reasons for incomplete revascularization were small vessels (55%) and massive calcification (32%). Mortality until 180 days after CABG was higher ($n = 32$; 24%) after incomplete than after complete revascularization ($n = 105$; 15%; $P = 0.005$). By logistic multivariable regression, incomplete revascularization was identified as an independent risk factor for death (Odds ratio, 1.8; $P = 0.015$). By time-related analysis, incomplete revascularization predominantly affected the early period after CABG ($P = 0.001$). Aortic cross clamping time was only slightly shorter for the group with incomplete (59 ± 27 min (median: 55 min) vs. 63 ± 26 min (median: 58 min); $P = 0.1$). **Conclusions**: Incomplete revascularization increases the early risk of death after CABG in patients aged 75 years and older. The potential compensating benefit of the shorter aortic cross clamping time does not overweigh the advantages of complete revascularization. Thus, in the era of high-volume interventional approaches and minimally invasive techniques, the advantages of complete revascularization need to be considered.

Keywords: Coronary artery bypass grafting; Incomplete revascularization: Elderly patients

1. Introduction

An increasing number of elderly patients are being evaluated for coronary artery bypass grafting (CABG). The mortality after CABG in elderly patients has been decreasing [1–3]; therefore, CABG is a procedure with an acceptable risk. Nevertheless, it is important to minimize even more CABG-related mortality. Because the adverse effects of the extracorporeal circulation and surgical trauma per se are correlated with increased risk of early death after CABG, incomplete revascularization with shorter myocardial ischemic and cardiopulmonary bypass time might be superior to complete revascularization. Therefore, this study focuses on beneficial or jeopardising effects of complete versus incomplete revascularization in elderly patients.

2. Patients and methods

2.1. Patients

A total of 6531 unselected, consecutive patients underwent isolated CABG from June 1988 through December 1999. Of these, 859 of were aged at least 75 years at the time of operation. Mean age of the 859 patients was 77 ± 2.7 years (median: 76 years), 65% were men, with a male to female ratio of 1.8:1. In 133 (15.5%) of the 859 patients, incomplete revascularization was performed.

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2.2. Data acquisition and data management

For documentation of about 1500 items per case, tools of the Heidelberger Verein zur multizentrischen Datenanalyse e.V. (HVMD) were used [4,5]. Because all data are collected at the point of care and serve to create both medical reports and a scientific data base, the quality of the primary data is reliable. A regular follow-up procedure by questionnaires is performed at the 180th postoperative day. For the investigated group, follow-up completeness was 95.6%.

2.3. Definition of incomplete revascularization

Incomplete revascularization, according to the definition of the HVMD is the omission of revascularization of at least one vessel which was preoperatively evaluated for bypass grafting out of the preoperative diagnostics (coronary angiography, in some cases stress echocardiography and/or Technetium (Tc)-99 pyrophosphate scanning), judged by the responsible surgeon.

2.4. Statistical analysis

For statistical analysis, SAS® (SAS Institute, Cary, USA) Version 6.12 was used. Data are presented as mean ± standard deviation. The analysis was performed using descriptive methods, contingency tables and Wilcoxon χ^2 test, Student's unpaired *t*-test, logistic regression, Kaplan–Meier non-parametric estimation methodology [6], a rank statistics used to test homogeneity between the strata [7] and the parametric, time-adjusted Hazard Function by Blackstone et al. [8]. Investigated variables and the specification of the parametric, time-adjusted hazard function are summarized in Appendix B.

For reducing the potential selection bias between patients with or without incomplete revascularization, we matched, subclassified and adjusted the data using propensity score methodology. First, the event incomplete versus complete revascularization was analyzed as the dependent variable by multivariable logistic regression independent from outcome using the variables listed in Appendix B. After this and investigation of potential interactions, the era of operation and risk factors not represented in the parsimonious model were added to form the propensity model. The area under the receiver operating curve for the model was 0.81. The propensity model was then used to calculate a propensity score for each patient. The predicted likelihoods of incomplete revascularization ranged from 0.0003 to 88.7%. All patients were sorted by propensity score and compared within quintiles [9]. The groups were well-matched. The propensity score as a logit unit and its transformation into a probability estimate were incorporated as continuous variables to adjust for possible confounding [10].

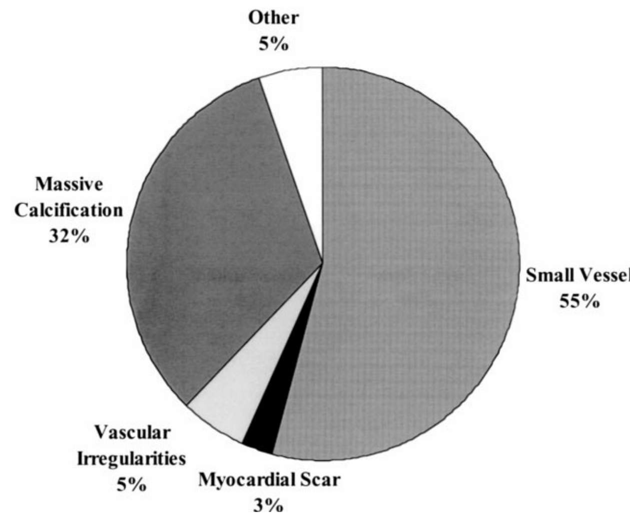


Fig. 1. Distribution of reasons for incomplete revascularization. The most common reasons for incomplete revascularization are small vessel diameter and massive coronary calcification.

3. Results

3.1. Incomplete revascularization

Incomplete revascularization was performed in 133 (16.0%) of the 859 patients. The reasons for incomplete revascularization were small vessels (55%), massive coronary calcification (32%), vascular irregularities (deep intramyocardial course etc.) (5%), other reasons like insufficient graft material etc. (5%) and scared alteration of the myocardium (3%) (Fig. 1).

3.2. Incomplete revascularization and survival

According to the different reasons for incomplete revascularization, the proportion of death within the groups is shown in Fig. 2. Aortic cross clamping time was not signif-

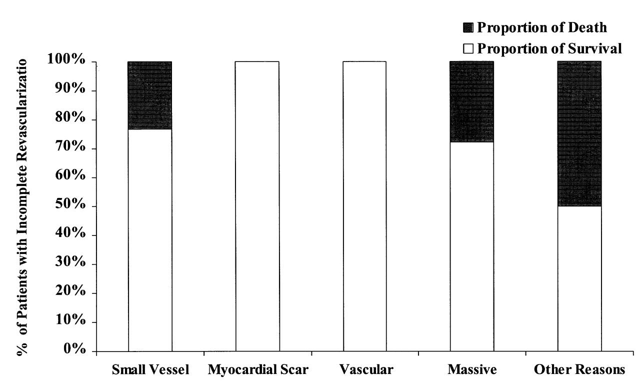


Fig. 2. Proportion of death according to the reason for incomplete revascularization. The relative similar proportion of death in case of small vessels and massive coronary calcification indicates, that not only the potentially worse coronary status of patients with incomplete revascularization plays a role in the increased risk of early mortality in the group of elderly patients with incomplete revascularization.

Table 1
Contingency table for complete/incomplete revascularization and 180-day survival

Revascularization	*n*	180-day Deaths	
		No.	%
Complete	726	105	15
Incomplete	133	32	24
Total	859	137	16
P (χ^2)			0.005

icantly shorter in patients with incomplete versus complete revascularization (59 ± 27 min; median: 55 min versus 63 ± 26 min; median: 58 min; $P = 0.1$). By univariate contingency table analysis, mortality was higher after incomplete revascularization until the 180th day after CABG ($n = 32$; 24%) compared to complete revascularization ($n = 105$; 15%, $P = 0.005$) (Table 1). By logistic regression, incomplete revascularization was found to be an independent risk factor for death after CABG (Odds ratio, 1.8; $P = 0.015$); renal disease, as well as exercise-related dyspnea and urgency were identified as further independent risk factors (Table 2) out of the evaluated variables (Appendix A). In Fig. 3, the stratified Kaplan–Meier survival curve indicates, that incomplete revascularization predominantly affects the early period after operation until about the 30th postoperative day ($P = 0.001$). Using the time-adjusted, parametric hazard function, a two-phase model identified incomplete revascularization as one of four independent risk factor of the early phase (incomplete revascularization, diabetes, chronic pulmonary edema, emergent operation). Variables influencing the second, later phase were renal disease, acute heart failure history and preoperative use of aspirin (Appendix B). Fig. 4 illustrates the well-fitting time-adjusted, parametric model, stratified for incomplete revascularization.

3.3. Adjustment for selection factors

These differences in survival could relate to selection factors for incomplete revascularization. Therefore, the patients were subcategorized into five subclasses (quintiles) according to the propensity score. We observed no extensive or consistent differences within propensity quintiles, indicating that the propensity score had achieved balance in the covariates. Differences in survival between patients with incomplete versus complete revascularization still remained detectable within all quintiles by stratified Kaplan–Meier survival analysis. The estimated propensity score was also included as a model covariate in all multivariable models to assess outcomes of the two treatments that explicitly accounted for selection factors. Neither logistic regression model nor parametric, time-adjusted models demonstrated substantial residual bias in our reported comparisons.

Table 2
Results of the Logistic regression analysis

	Estimate	Wald χ^2	$P > \chi^2$	Odds ratio
Intercept	−3.08	52.26	0.0001	
Renal Disease	0.74	13.09	0.0003	2.1
Inc. Revasc.	0.57	5.94	0.015	1.8
Dyspnea	0.48	4.69	0.030	1.6
Urgency	0.41	4.41	0.036	1.5

4. Discussion

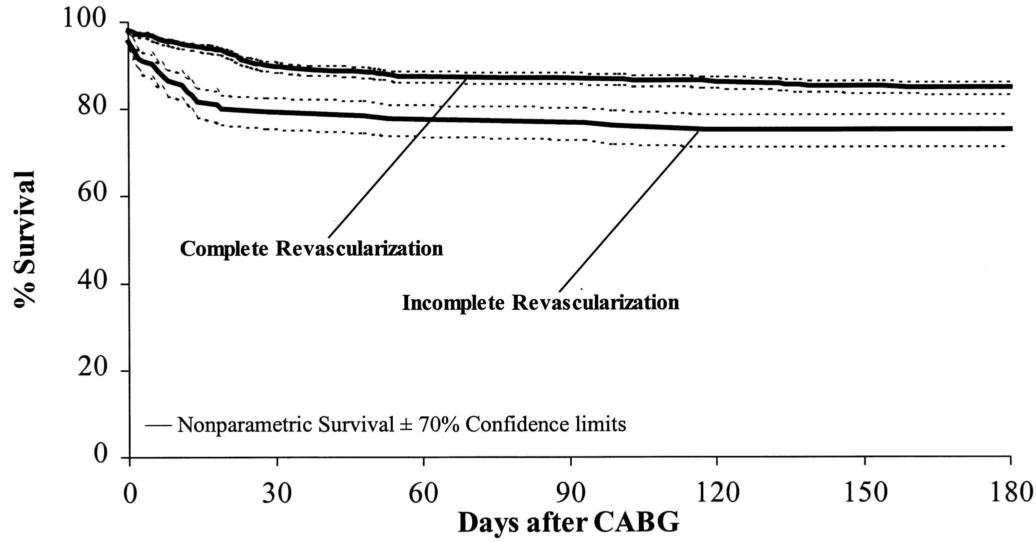
4.1. Principal findings

Complete revascularization is a primary goal of conventional coronary artery bypass grafting. This goal derives from the nature of the disease, because once a stenosis is present, progression of the coronary artery disease is likely. Incomplete revascularization has been demonstrated to decrease late survival. However, it may be argued that the natural history of the patients is such that these individuals are unlikely to live long enough to reap this benefit. Our study indicates that, in addition, complete revascularization increases survival early after CABG.

4.2. Interpretation of findings

In different studies, the beneficial effect of complete revascularization on long-term survival supports theoretical considerations [11–14]. It is to be stressed, that obviously the diagnostic methods did not succeed in reflecting adequately the intraoperative status of the coronary arteries. So, an underestimation of the severity of coronary disease in patients with incomplete revascularization is likely. Therefore, the higher risk of death early after incomplete revascularization may be the simple consequence of an advanced disease state that cannot be detected prior to any surgical or interventional effort. Although we did not observe a decisive bias between the patients with incomplete or complete revascularization concerning the preoperative cardiac and non-cardiac comorbidity out of the preoperatively performed examinations, underestimation of the disease is likely. However, this underestimation occurs independent on the therapeutic approach. The direct tactile and visual impressions of the status of the coronary arteries during open heart surgery is still a major advantage of the conventional approach, because neither the minimally invasive nor primary interventional methods so far succeed in giving the information necessary for judgement of the coronary vessel status.

The definition of incomplete revascularization in our study has been chosen by the surgeon’s intention to treat. This is in contrast to other studies that compared the number of vessels with a stenosis of greater than or equal to 50% from coronary angiography with the number of grafted vessels [15]. However, in clinical practice, 50% stenoses and sometimes even high-degree stenoses are not necessarily considered for bypass grafting; this is especially true for



Patients	**Compl. Rev.**	**726**	**612**	**584**	**579**	**572**	**562**	**559**
at Risk	**Incompl. Rev.**	**133**	**98**	**97**	**97**	**92**	**92**	**92**

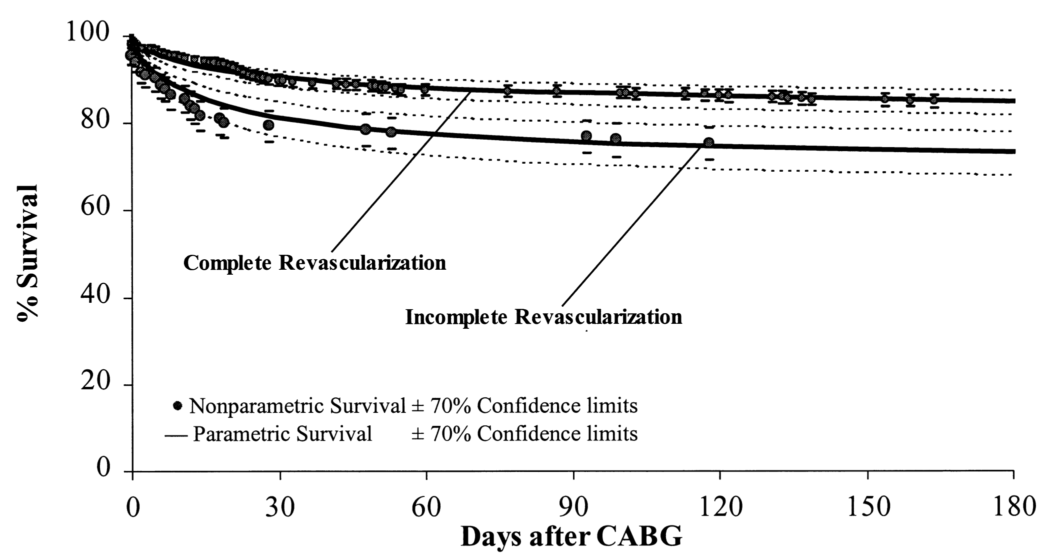
Fig. 3. Stratified Kaplan–Meier survival curve for patients with complete versus incomplete revascularization. The shaping of the curve indicates the main difference in survival during the first 30 days after CABG.

septal, small diagonal and small marginal branches or peripheral parts of the right coronary system. Another definition by Sergeant et al. [14] compared the number of vessels with a diameter of at least 1.5 mm and a stenosis ≥70% with the number of grafted vessels. In the CASS study, the beneficial effect of complete revascularization on long-term results after CABG was shown; the study included only patients with three-vessel disease and indicated a non-revascularization of the at least one of the three systems to be incomplete [11].

Despite these different definitions, a clear message is, that better outcome occurs with complete revascularization.

4.3. Clinical inferences

The proportion of patients with incomplete revasculariza-



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at Risk	**Incompl. Rev.**	**133**	**98**	**97**	**97**	**92**	**92**	**92**

Fig. 4. Comparison of nonparametric survival (Kaplan–Meier) and the parametric, time-adjusted hazard function, stratified by complete versus incomplete revascularization.

tion remains at about 15%. In the era of minimally invasive surgery, an increasing number of patients are called eligible for the minimal invasive approach by inclusion of patients with multi-vessel disease [16,17]. Because incomplete revascularization predominantly has been described as a risk factor in the long term, elderly patients may be an ideal group for incomplete intervention, since demography itself prevents most patients from experiencing adverse events. However, at least in this group of elderly patients, the beneficial impact of complete revascularization on early survival justifies to perform complete revascularization as the method of choice as well in elderly patients. Furthermore, recently Blackstone and Lytle succeeded in showing, that even elderly patients profit by surgical procedures with proven beneficial long-term effects [18].

The majority of patients in our study has been incompletely revascularized because of small vessels. The question arises ‘How small is too small?’ In a study of Corbineau et al. [19], age over 70 was found to represent an independent risk factor for an impaired run-off of grafted vessels which indicates, that coronary arteries in elderly patients are more diffusely diseased.

The potential advantage of shorter aortic cross-clamping time, especially in the older patient group, could not be confirmed by our analysis. However, the intention to treat includes a careful consideration of the surgeon according to each individual coronary status, so that a primary incomplete approach might have been accompanied by shorter aortic cross-clamping and operation time. However, it remains questionable, whether even a more prolonged extracorporeal circulation for plus/minus one or two distal anastomoses in the range of 10–30 min would have substantial effect on early mortality.

4.4. Limitations of the study

Observational studies such as this one bear the risk of a systematic bias of the investigated groups, such as patients with complete or incomplete revascularization. Thus, the observed differences in survival could relate to the underlying reason that the intended revascularization was not performed. This may be different from deliberate election not to revascularize an area. Because the decision to completely or incompletely revascularize a given patient was not made at a random, direct comparison of outcome may be biased. Therefore, we first attempted to adjust for selection factors by multivariable analysis, investigating outcome by both multivariable logistic regression and time-related analysis. In addition, we used propensity score matching of patients, including various variables concerning the coronary status and further variables of cardiac and non-cardiac comorbidity. Both strategies for reducing potential bias from selection identified that patients with incomplete revascularization were at higher risk of mortality than those completely revascularized.

5. Conclusion

Incomplete revascularization reduces early survival after CABG in elderly patients. Therefore, the beneficial effects of complete revascularization should be kept in mind if any approach for incomplete revascularization is considered. Perhaps, in these cases, a more conservative approach may help to avoid adverse early and late effects of ‘intended’ incomplete revascularization.

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Appendix A.

Variables included in the logistic regression model:

Age, male, weight, year of surgery, unstable angina, smoking, obesity, hypertension, preoperative on diuretics, dyspnea at exercise, ejection fraction, end-diastolic left ventricular pressure, LV aneurysm, LV dilatation, LV akinesia, left main disease, LAD occlusion, peripheral vascular disease, diabetes, pulmonary obstructive disease, renal disease, dialysis-dependency, preoperatively on β-blocker, preoperative sinus-rhythm, permanent pacemaker, number of previous cardio-thoracic surgery, use of IMA, urgency, incomplete revascularization.

Appendix B.

B.1. 1. Specifications of the time-adjusted, parametric hazard function

Parameters of the time-adjusted hazard function for the total 859 elderly patients after CABG.

Early phase: Mue = 0.09 Thalf = 10.9 nu = 0 m = −1.7, Delta = 0, Rho = 30.3.

Constant phase: Muc = 3.6E-05.

B.2. 2. Variables at the beginning of the multivariable analysis of death

Demographic

Gender, age (years) at operation, weight, height, body mass index, obesity (men: height in cm: 90, women: height in cm: 100).

Cardiac comorbidity

NYHA (1, mild; 2, mild symptoms; 3, symptoms with normal activities; 4a, severe with symptoms at rest; 4b, unstable angina), Holper (1, mild; 2, mild symptoms at higher degree of physical stress; 3, symptoms at mid degree of physical stress; 4, symptoms at low degree of physical stress; 5, stable out of unstable angina; 6, beginning unstable angina; 7, unstable angina; 8, cardiogenic shock), severe heart failure in history, subjective impression of heart failure, clinical sign of heart failure, dyspnea at excercise, dyspnea at rest, excercise-related angina, angina at rest, treatment for unstable angina (0, neither oral nor i.v.-medication. 1, oral medication; 2, intravenous medication), pathologic valvular findings without neccessity for surgical treatment, urgency of operation (elective, urgent, emergent, emergent + CPR).

Left ventricular function

Normal left ventricular size, left ventricular hypertrophy, left ventricular dilatation, left ventricular hypokinesia, left ventricular akinesia, left ventricular aneurysm, systolic aortic pressure, diastolic aortic pressure, mean aortic pressure, left ventricular systolic pressure, left ventricular enddiastolic pressure, left ventricular function qualifier (0, good; 1, fair; 2, bad). Ejection fraction was available for only 63% of all patients, acute myocardial infarction, chronic pulmonary edema, acute pulmonary edema, cardiogenic shock.

Preoperative drugs

Diuretics, ACE inhibitors, antibiotics, aspirin, digitalis, β-blocker, calcium antagonists, anticoagulation, antiarrhythmic agents, any preoperative drug.

Non-cardiac comorbidity

Smoking, diabetes, hyperlipoproteinemia, hypertension, hyperuricemia, positive family history, any of the known, risk factors, syncope, embolism, gastrointestinal disease, extracardiac vascular disease, calcified aortic wall, pulmonary obstructive disease, pulmonary restrictive disease, any pulmonary disease, renal disease, dialysis dependency, neurologic disease.

Coronary status

Number of affected vessels, diffuse arteriosclerotic affection of coronary arteries, left main disease, dominant vessel, number of coronary vessels disease ≥50%, ≥70%, ≥90%, 100% stenosis, number of coronary systems disease ≥50%, ≥70%, ≥90%, 100% stenosis, stenosis of LAD ≥50%, ≥70%, ≥90%, 100%, stenosis of RCA ≥50%, ≥70%, ≥90%, 100%, stenosis of Circumflex artery ≥50%, ≥70%, ≥90%, 100%, diagonals.

Preoperative rhythm

Sinus rhythm, atrial fibrillation, ventricular tachycardia, pacemaker, ventricular ectopic beats.

Previous procedures

PTCA, coronary stent implantation, laser ablation, complication of PTCA, unsuccessful PTCA, bypass occlusion, bypass stent implantation, thrombolytic therapy (within the last 14 days), reoperation for CABG, number of previously performed CABG procedures.

Surgical strategy

Use of IMA, incomplete revascularization, surgeon.

B.3. 3. Selected variables (coefficients, standard error, P values)

Early phase: Intercept: − 2.409.

Diabetes, 0.4 ± 0.2, $P = 0.04$, chronic pulmonary edema, 0.8 ± 0.3, $P = 0.03$, incomplete revascularization, 0.8 ± 0.2, $P = 0.001$, emergent operation, 0.8 ± 0.3, $P = 0.007$.

Constant phase: Intercept: −10.2197.

Acute heart failure in history: <0.0001 ± 2.0, $P = <0.0001$, preoperative on aspirin, 1.1 ± 0.5, $P = 0.04$, renal disease, 2.1 ± 0.5, $P = 0.0001$.

Appendix C. Conference discussion

Dr M. Perko (*Copenhagen, Denmark*): You claim that you compare incomplete versus complete revascularization, but I think that your study is not randomized and in fact you compared more sick versus less sick patients. You said that the main reason for incomplete revascularization was calcifications and poor vessel status or small vessels. So it means that you have more sick patients in one group and less sick patients in another group.

Dr Osswald: That's maybe true.

Dr Perko: So I think that the design of this study is wrong and the conclusions are misleading.

Dr Osswald: It depends on what you want to discuss, because if you look at patients with a preoperative status only, you have only coronary angiography, you have the diagnostic steps which you can go, but during operation you have perhaps a completely different status. However, if any different therapy is chosen, you do not know out of the preoperative available information the direct coronary status. This has been one of the points I wanted to stress, because whether you perform minimally invasive CABG, PTCA or conventional CABG, you do not know whether the coronary status is correctly reflected by the preoperative diagnosis.

Dr P. Sergeant (*Leuven, Belgium*): My comments are very similar but maybe differently formatted than the previous commentator. Basically what you have shown is information about involuntary incomplete revascularization.

Dr Osswald: This is true.

Dr Sergeant: And I think that this needs to be differentiated from voluntary incomplete revascularization. You are pointing very well and very clear that there is a major risk at the voluntary incomplete revascularization, but in these 75-year-old patients we are very often confronted with an involuntary situation.

Dr E. Covino (*Catanzaro, Italy*): After all, I agree with the conclusions of this study; however, I would have liked to know which coronaries are not revascularized. In fact, it may make a difference to neglect an important or a less important coronary artery.

Dr Osswald: Well, if we are looking at these incomplete versus complete, we just have decided out of the preoperative diagnostic to operate on that vessel. Most of these vessels are major vessels like the circumflex, the LAD or the RCA, however, it is very likely that you might have even prominent vessels which are the smaller ones, the marginals, the diagonals, whatever. The coronary status is highly individual, so that we are including all of the vessels selected for revascularization.

Dr J. Melo (*Carnaxide, Portugal*): I think you are raising an important issue. My first reaction was like the previous speakers. It is difficult to understand that you have performed incomplete revascularization but the cross-clamp time for both groups is the same. So what was the number of grafts per patient in each group? What was the number of LADs that were not grafted on the incomplete revascularization? The differences between groups happened in the first 30 days after surgery. What were the major reasons for this?

Dr Osswald: Well, to address the first part, we have had no patient where we just decided primarily to do an incomplete revascularization. We intended to do the complete revascularization in all of these patients. It was not too surprising that we did have no big differences in the aortic cross-clamping time, because we intended to perform total revascularization. It is probably completely different for the minimally invasive groups where you will have a shorter aortic cross-clamping time, because you primarily do not intend to do complete revascularization.

The reasons for the deaths after CABG, we have not yet divided between different groups, however, most of them have had an LV function dysfunction.

Dr D. Saksena (*Bombay, India*): I would like to take issue with one of the statements that you made. The implications of this study are on minimally invasive or OPCAB surgery, because I believe OPCAB is more like an angioplasty and when you don't clamp the aorta, you don't go on a heart-lung machine, the mortality in the early period will not be any different if you leave one or two vessels which are not critically blocked alone, as the cardiologists do when performing angioplasty. Now, in a 75-year-old patient I agree that if you don't do a complete revascularization, the long-term results might not be that good, but the immediate results are satisfactory with low mortality unlike you have shown when you have done the patients bypass.

Dr Osswald: This was an issue of our investigation to show that early mortality represents an important aspect of incomplete revascularization. Retrospectively, any less invasive procedure could have been beneficial for those patients who received incomplete revascularization. However, all of the patients have been carefully selected for the conventional CABG out of their preoperative cardiac and non-cardiac status. To do incomplete revascularization is in all of the cases decided when the patient is already on cardiopulmonary bypass. Therefore, a less invasive or OPCAB procedure does not represent an alternative. Whether the early deaths are primarily related to the adverse effects of extracorporeal circulation cannot be answered. However, from the ethical and medical point of view, it is and hopefully will be not justified to withhold the beneficial effects of complete revascularization generally from elderly patients and to perform either of the available incomplete interventions as the intervention of choice only because of age.