Completeness of revascularisation by percutaneous coronary intervention

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Objective. To evaluate the relationship between the completeness of revascularisation by percutaneous coronary intervention and the one-year occurrence of adverse cardiac events in patients with multivessel disease.
Patients. Patients with stable or unstable angina pectoris, or with exercise-induced ischaemia, were enrolled in the Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI).
Methods. In CABRI, patients were randomised to coronary bypass grafting (CABG; n=513) or angioplasty (PTCA; n=541). Revascularisation in patients randomised to PTCA was defined as complete if no lesions with a diameter stenosis <50% remained post-procedure. Patients with complete revascularisation were distinguished from those with one, two, and three or more remaining lesions, respectively. Differences in baseline characteristics and in the one-year occurrence of death, myocardial infarction, (re)CABG, and (re)PTCA between these subgroups were evaluated. Comparisons were made with patients randomised to CABG.
Results. Complete revascularisation was obtained in 148 patients randomised to PTCA (27%). In 147 (27%) cases one lesion remained, while there were 122 (23%) and 119 (22%) patients with two and three or more remaining lesions, respectively. Five (1%) patients could not be classified. The one-year rates of either death or MI were 9.5%, 5.4%, 8.2%, and 12.6% in the respective PTCA subgroups (p=0.225), and 6.2% in patients randomised to CABG (comparison with three or more remaining lesions after PTCA: p=0.017). The percentages of repeat interventions during one-year follow-up were 29.7%, 29.3%, 39.3%, and 51.3% (p<0.001), much higher than after CABG (3.5%; p<0.001).
Conclusion. Complete revascularisation by PTCA in multivessel coronary disease did not result in a lower death or MI rate compared with incomplete revascularisation. Overall the patient's prognosis after PTCA is similar to CABG, but patients with three or more remaining lesions after PTCA had a worse prognosis than CABG patients. (Neth Heart J 2001;9:3-9.)

Key words: stable angina pectoris, unstable angina pectoris, multivessel coronary disease, revascularisation, follow-up

To date, percutaneous coronary interventions have a wide indication. Whereas some years ago coronary bypass surgery was the dominant therapeutic option in patients with multivessel coronary disease, due to gained experience and the availability of sophisticated devices as intracoronary stents, nowadays most of these patients are also eligible for percutaneous treatment. Randomised clinical trials indicate that, at least in the medium term, both revascularisation strategies are equally effective in terms of mortality and the occurrence of myocardial infarction.[1,2] The re-intervention rate, however, appears to be much higher after angioplasty, especially during the first year. This can partly be explained by the restenosis process. Another aspect is that complete revascularisation can be difficult to realise by percutaneous intervention, especially in patients with complex lesions. Therefore, interventional cardiologists regularly opt for the strategy of incomplete revascularisation to relieve cardiac symptoms. Recent reports indicated that this latter strategy is as safe and effective as the strategy of complete

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Table 1. Baseline characteristics.

Allocated strategy	CABG	PTCA				Comparison of PTCA subgroups (p value)
		Number of remaining lesions				
		0	1	2	≥3	
Number of patients	513	148	147	122	119	
Demographics and clinical presentation						
Median age (25th, 75th percentile) (years)	61 (54, 67)	60 (53, 66)	59 (52, 65)	61 (57, 66)	62 (55, 67)	0.145
Male gender (%)	78	76	84	68	81	0.018
Median LVEF (25th, 75th percentile) (%)	65 (55, 73)	70 (60,75)	65 (56, 73)	65 (52, 73)	63 (53, 73)	0.100
Angina (CCS classification) no angina or class I/ class II or III/ class IV or unstable angina (%)	11/60/29	13/62/25	13/65/22	8/62/30	13/63/24	0.716
Function (NYHA classification) class O or I/ class II/ class III or IV (%)	75/20/5	90/9/1	78/19/3	73/25/4	71/21/8	0.006
History						
Infarction (%)	42	40	42	33	53	0.020
Peripheral vessel disease (%)	6	6	4	8	11	0.188
CVA (%)	5	6	4	4	11	0.061
Smoking (%)	55	57	67	52	54	0.061
Diabetes mellitus (%)	12	9	9	14	17	0.142
Hypertension (%)	37	32	31	38	40	0.479
Medication						
Beta-blockers (%)	65	67	64	61	50	0.091
Calcium antagonists (%)	65	65	66	69	71	0.784
Nitrates (%)	70	62	64	68	66	0.875
Lesion characteristics						
Number - 2/3/4/≥5 (%)	-	49/35/ 11/5	33/40/ 18/9	4/43/ 34/19	0/12/ 29/59	<0.001
Median (average) number	-	3 (2.7)	3 (3.1)	4 (3.8)	5 (5.0)	<0.001
Bifurcation (%)	-	10	9	7	7	0.875
Eccentric (%)	-	54	44	42	42	0.208
Long (%)	-	73	83	80	96	<0.001
Tandem (%)	-	12	7	4	8	0.207
Total occlusion (%)	-	7	20	18	27	<0.001
Thrombus (%)	-	3	1	2	4	0.391
Calcification (%)	-	3	5	6	5	0.647

revascularisation by percutaneous treatment.[3-7] So far, however, no comparison has been made with coronary artery bypass surgery. Furthermore, little is known about the relationship between the degree of (in)completeness and the occurrence of adverse events. The current paper concentrates on these two aspects, and presents data from the Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI) with respect to the completeness of revascularisation after coronary intervention and the occurrence of cardiac complications at one-year follow-up.

Methods

Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI)

CABRI is a multicentre, randomised trial comparing the strategies of revascularisation by percutaneous transluminal coronary balloon angioplasty (PTCA) and coronary artery bypass grafting (CABG) in patients with multivessel coronary disease.[8] Included were patients <75 years of age with a diameter stenosis (DS) <50% in at least two main epicardial or large side

Table 2. Major adverse cardiac events in relation to the completeness of revascularisation.

Allocated strategy	CABG	PTCA				Comparison (p values)		
		Remaining lesions				*CABG vs. PTCA with 0 remaining lesions (complete)*	*CABG vs. PTCA with ≥3 remaining lesions*	*Trend in PTCA with increasing number of remaining lesions*
		0	1	2	≥3			
Separate event rates from randomisation to intervention + 30 days								
Death (%)	0.8	2.1	0.7	0.8	2.5	0.203*	0.147*	0.826
MI (%)	2.9	4.9	2.8	3.3	5.0	0.291*	0.258*	0.944
(re)CABG (%)	0.6	2.8	1.4	7.4	20.2	0.053*	<0.001	<0.001
(re)PTCA (%)	0.2	4.2	3.5	5.7	5.9	<0.001*	<0.001*	0.386
Combined event rates from randomisation to intervention + 30 days								
Death or MI (%)	3.6	6.3	3.5	4.1	7.6	0.155	0.057	0.666
Death, MI or (re)CABG (%)	4.2	7.0	4.9	10.7	24.4	0.173	<0.001	<0.001
Death, MI, (re)CABG or (re)PTCA (%)	4.2	11.2	7.7	16.4	29.4	0.002	<0.001	<0.001
Separate event rates during one year after randomisation								
Death (%)	2.7	5.4	2.0	3.3	5.0	0.110	0.194	0.942
MI (%)	4.5	5.4	3.4	4.9	6.7	0.640	0.308	0.665
(re)CABG (%)	0.8	7.4	9.5	18.0	37.0	<0.001	<0.001	<0.001
(re)PTCA (%)	2.7	25.0	22.5	23.8	19.3	<0.001	<0.001	0.729
Combined event rates during one year after randomisation								
Death or MI (%)	6.2	9.5	5.4	8.2	12.6	0.175	0.017	0.225
Death, MI or (re)CABG (%)	7.2	14.9	14.3	22.1	42.9	0.004	<0.001	<0.001
Death, MI, (re)CABG or (re)PTCA (%)	9.2	36.5	34.0	43.4	55.5	<0.001	<0.001	0.002

* Fisher's exact test

branches as viewed online in two projections on the baseline angiogram. At least one of the lesions had to be amenable to PTCA. Patients with either stable or unstable angina pectoris were eligible, as well as asymptomatic patients who exhibited unequivocal ischaemia during exercise testing. Excluded were patients with left main disease, overt cardiac failure, those with a recent myocardial infarction (MI) or a recent cerebrovascular accident, and patients with a previous PTCA or CABG.

The primary endpoint in CABRI was mortality and anginal status at one-year follow-up. Secondary endpoints were MI and the need for repeat revascularisation. CABRI was conducted in the first half of the 1990s, an era in which neither stents nor glycoprotein IIb/IIIa inhibitors were available in clinical practice.

Completeness of revascularisation

The location of lesions in the coronary tree is described according to the American Heart Association 15-segment system (figure 1). In patients allocated to PTCA, an initial strategy of partial revascularisation was allowed, i.e. not all significant lesions had to be attempted. Consequently, for each lesion three possible situations could appear: no attempt was made to dilate the lesion, a successful attempt was made, or an unsuccessful attempt was made. A lesion was defined to be successfully dilated if the post-procedural DS was less than 50%, as viewed online in two angiographic projections. Revascularisation by percutaneous treatment was defined as complete if all lesions were successfully dilated – i.e. if there were no remaining lesions with DS <50% – and incomplete otherwise. A degree of (in)completeness was distinguished on the basis of the number of remaining lesions. Surgery was viewed as the gold standard for restoration of the coronary perfusion. Therefore, patients randomised to PTCA who crossed to CABG (i.e. who underwent cardiac surgery before or instead of a percutaneous intervention) were classified as completely revascularised.

Data analysis

Patients randomised to PTCA were divided into separate groups according to the completeness of the

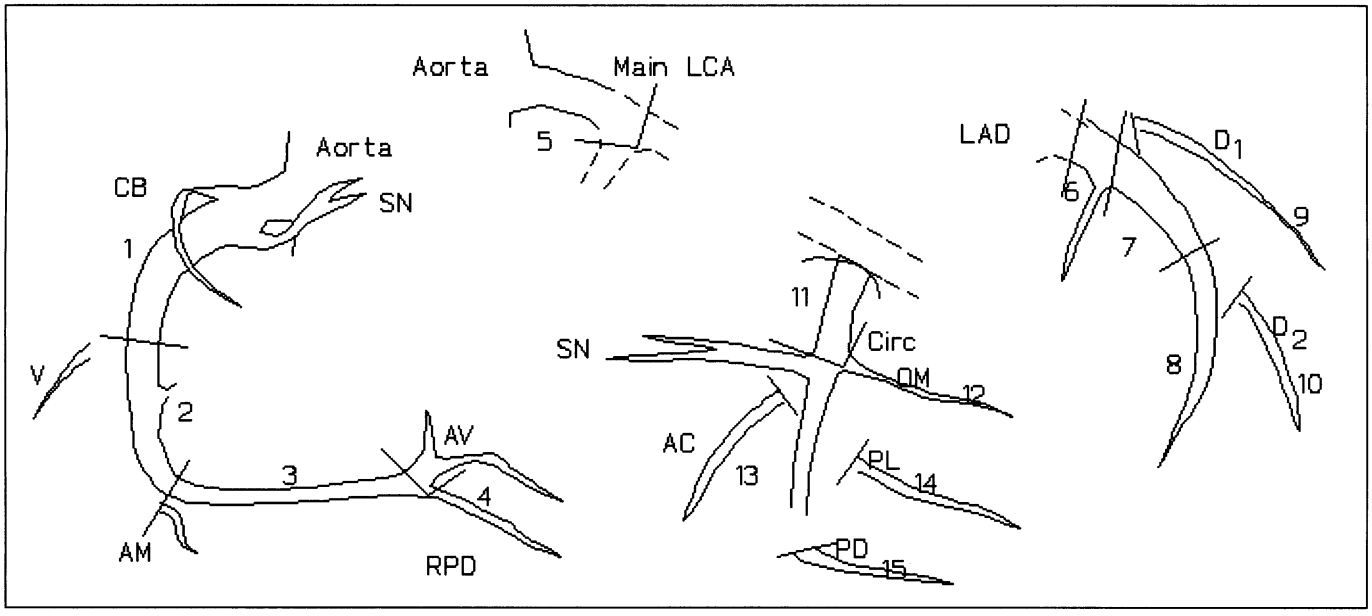

Figure 1. Schematic view of the coronary tree according to the American Heart Association 15-segments system.
1=proximal RCA; 2=mid RCA; 3=distal RCA; 4=posterior descending from dominant RCA; 5=left main stem; 6=proximal LAD (proximal to first septal); 7=mid LAD (distal to the first diagonal); 8=distal LAD (distal to the first diagonal); 9=first diagonal of LAD; 10=second diagonal of LAD; 11=main circumflex; 12=obtuse marginal (lateral) circumflex; 13=mid circumflex; 14=posterolateral circumflex; 15=posterior descending from dominant LCA.

initial procedure. Patients who ultimately had a complete revascularisation were distinguished from those with one, two, and three or more remaining lesions, respectively. Differences in baseline characteristics between these subgroups were evaluated by uncorrected χ^2-square tests (dichotomous variables) or one-way analyses of variance (continuous variables), with statistical significance at the conventional p=0.05 level.

The occurrence of major adverse cardiac events [death, MI, (re)CABG, and (re)PTCA] during one-year follow-up is presented as a percentage. Differences in event rates between patients randomised to CABG on the one hand, and those randomised to PTCA with no or three or more remaining lesions on the other hand, were evaluated by a series of two uncorrected χ^2-square tests.

To prevent increasing type I error, significance of these tests was stated at p=0.025. Furthermore, within the group of patients randomised to PTCA, the relation between the completeness of revascularisation and the occurrence of adverse events was studied by means of Mantel-Haenszel χ^2-square tests (significance at p=0.05).

Results

Angiographical success rates

In CABRI, 513 patients were randomised to CABG and 541 to PTCA. Fifteen patients randomised to PTCA crossed to CABG, and the baseline coronary angiogram was lacking in five additional patients. Thus there were 521 PTCA patients who were treated as randomised with complete pre- and post-procedural angiographic information. Among these patients, 1856 significant lesions were reported on the baseline angiogram, implying an average of 3.6 lesions per patient. There were 314 total occlusions (17% of all lesions). A stenosis in the proximal part of the LAD was observed in 233 (13%) cases. An attempt to dilate a lesion was made in 66% of the non-total occlusions (figure 2) and in only 39% of the total occlusions (p<0.001; figure 3). The proximal LAD was more often attempted than the other lesions (79% vs. 64%, p<0.001 in non-total occlusions and 57% vs. 38%, p=0.121 in total occlusions). In the non-occluding lesions, 93% of the attempts were successful. Although this percentage was significantly lower in the total occlusions (p<0.001), 72% of the attempts in the latter lesions were still successful.

Completeness of revascularisation in patients randomised to PTCA

The initial intervention resulted in a complete revascularisation in 148 of the patients randomised to PTCA (27%; 133 patients who were treated as randomised plus 15 who crossed to CABG). In another 147 (27%) cases there was only one remaining lesion, while there were 122 (23%) and 119 (22%) patients with two and three or more remaining lesions, respectively. The five (1%) patients with a missing baseline angiogram could

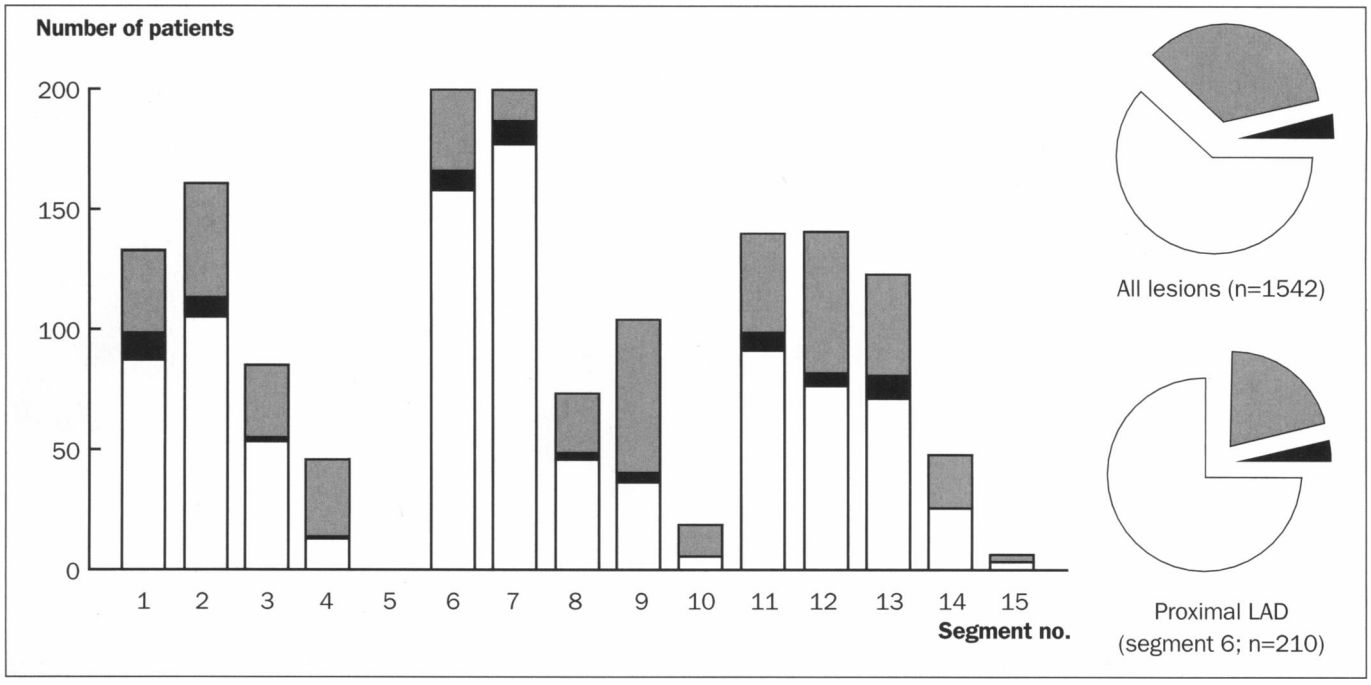

Figure 2. Number of lesions in patients randomised to PTCA with a pre-procedural diameter stenosis >50% and <100%. The location of the lesions is indicated by the segment number according to the American Heart Association 15-segments system (see figure 1). The white, black and grey part of the bars indicate lesions that were attempted with success, attempted without success, and not attempted at all, respectively.

not be classified. Table 1 presents the baseline characteristics of these groups. There were some statistically significant differences in patient demographics (gender), clinical presentation (NYHA class), and history (previous infarction) between the four groups. Furthermore, a significant relationship was observed between the number of lesions at presentation and the number of remaining lesions: e.g. 49% of patients with complete revascularisation had two lesions at baseline, while this percentage was only 4% among those with two remaining lesions. Also the length and severity (total occlusion) of the lesion were significantly related to the degree of completeness of revascularisation in patients randomised to PTCA. On the other hand, the percentage occurrence of otherwise more complex lesions (e.g. eccentric lesions, lesions with thrombus formation, calcified lesions) was similar among the four groups.

Major adverse cardiac events

Table 2 presents the occurrence of cardiac complications in CABRI in relation to the completeness of revascularisation. Follow-up information was complete in all but four patients. Among the patients randomised to PTCA, both short-term (up to 30 days after the initial procedure) and long-term mortality was lowest in those with one remaining lesion after the initial procedure (0.7% and 2.0%, respectively). Mortality was relatively high in patients with complete revascularisation (2.1% at short-term and 5.4% at long-term follow-up) and in those with three or more remaining lesions (2.5% and 5.0%). There was no significant relationship between the degree of completeness of revascularisation and mortality, neither so if the group of patients with no remaining lesions was ignored. The percentage occurrence of MI (and the occurrence of either death or MI) showed a similar pattern: lowest event rates in patients with one remaining lesion, highest rates in those with no and three or more remaining lesions, and no significant relation between the degree of completeness and short-term and long-term event rates. The observed differences in mortality rates between CABG and the PTCA subgroups with no and three or more remaining lesions were not statistically significant. The combined rate of death or MI at one-year follow-up, however, was significantly higher in PTCA patients with three or more remaining lesions than in those randomised to CABG (12.6% vs. 6.2%; p=0.017).

The rate of subsequent coronary bypass operations among patients randomised to PTCA was related to the degree of (in)completeness of the initial procedure. During the first 30 days after this procedure, 2.8% of patients with no remaining lesions underwent a CABG versus 20.2% of those with three or more remaining lesions (p<0.001). At one-year follow-up these percentages were 7.4% and 37.0% (p<0.001), respectively. In contrast, the percentage occurrence of re-PTCA was similar among the PTCA subgroups.

An interesting aspect is the difference in timing of

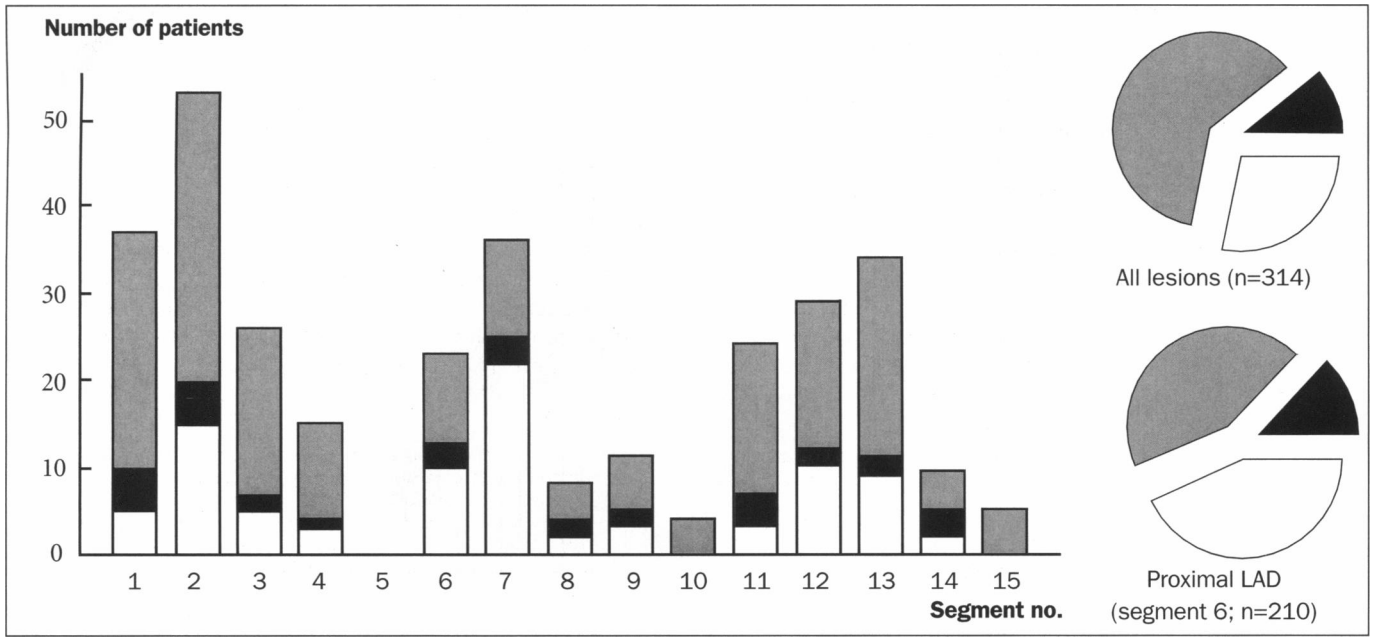

Figure 3. Number of lesions in patients randomised to PTCA with a pre-procedural diameter stenosis of 100% (total occlusion). For legends see figure 2.

repeat procedures between the distinct subgroups. In patients with three or more remaining lesions, 55% of the CABGs (and 51% of the repeat interventions) were performed within 30 days of the initial procedure. These percentages were apparently lower in those with two and one remaining lesion: 41% and 15% of the CABGs (and 33% and 14% of the repeat interventions) were done within one month. In patients with a complete revascularisation, 38% of the CABGs (and 24% of the repeat interventions) were performed during the first month.

Discussion

Patients with multivessel coronary disease usually benefit from invasive treatment strategies that aim at revascularisation of the coronary system: coronary surgery or percutaneous intervention. To relieve patients' complaints and restore myocardial perfusion it would seem logical to try to achieve a complete revascularisation. However, several investigations have demonstrated that a strategy of incomplete revascularisation is as safe (no excess death or MI rate) and effective (pain relief) as complete revascularisation.[3-7] The presented data confirm these conclusions to a large extent, although some remarks need to be made.

Completeness of revascularisation and life-threatening events

Among the PTCA patients who were treated as randomised, approximately seven out of each ten non-occluding lesions were attempted with a success rate of over 90%. Total occlusions were less frequently attempted, with a lower, but still high rate of success. These data affirm other observations in the pre-stent era.[4] A complete revascularisation was only realised in one quarter of the patients, similar to findings in a registry of consecutive patients with multivessel disease who underwent a PTCA in the same period (17%),[3] and with results from the Multivessel Angioplasty Prognosis Study (MAPS).[9]

The subdivision of patients randomised to PTCA according to the completeness of the initial revascularisation procedure was not prespecified by the protocol, and results of analyses on these subgroups should therefore be interpreted with caution. Differences in event rates between the PTCA subgroups might be biased by known or unknown differences in baseline clinical and angiographical characteristics. Indeed, differences were observed with respect to medical history and to the number and severity of lesions to be treated. From a formal statistical point of view the current data did not show a relation between the rate of death or myocardial infarction during one-year follow-up and the degree of completeness of revascularisation by PTCA. It is true that the percentage occurrence of life-threatening complications moved upwards in patients with one, two, and three or more remaining lesions, respectively, but event rates were also high among patients with no remaining lesions. On the other hand, PTCA patients with three or more remaining lesions had a doubled risk of death or MI within the first year after the procedure compared with bypass surgery. Furthermore, the possibility of type II errors should not be ignored, as the number of patients in each subgroup was relatively small. Finally, it cannot be excluded that the relatively high event rate in patients with complete revascularisation is caused by unjustifiable attempts to obtain an optimal angiographic result.

Repeat interventions

Patients with remaining significant lesions after percutaneous intervention most likely suffer from severe and diffuse coronary disease, and an early bypass operation is therefore warranted. Indeed, the need for repeat interventions to prevent life-threatening thrombotic events has been largely recognised, as the percentage of CABG increased steeply with increasing incompleteness of revascularisation by PTCA.

Patients with incomplete revascularisation not only underwent a repeat intervention more often, but also much earlier than those with a more complete revascularisation. Patients without remaining lesions formed an exception: 38% of CABGs during follow-up were performed in the first month. This observation might again be explained by a relatively high percentage of 'bail out' situations after the PTCA procedure in this group of patients, and leads as a matter of course to the most important limitation of our investigation: CABRI was conducted in the pre-stent era. As the immediate outcome of percutaneous treatment can be improved by coronary stenting,[10,11] the percentage of patients with a complete and more stable result after percutaneous coronary intervention in today's clinical practice will likely be higher than in our population. Indeed, in the Arterial Revascularisation Therapies Study (ARTS: a randomised comparison of bypass surgery and coronary stenting in multivessel coronary patients), 73% of the stent procedures resulted in a complete revascularisation,[12] which is considerably higher than the 27% obtained after balloon angioplasty in our dataset. The favourable angiographic result by coronary stenting, however, did not result in an improved outcome, as the one-month death and MI rates in the angioplasty arms of CABRI and ARTS were similar.[12] Hence, our data of the pre-stent era regarding the relation between the completeness of revascularisation by percutaneous treatment and patient's prognosis are still valuable.

Percutaneous intervention or bypass surgery?

The strategy of complete revascularisation by PTCA in patients with multivessel coronary artery disease did not result in a lower death or MI rate during one-year follow-up as compared with a strategy of incomplete revascularisation. Thus, complete revascularisation by percutaneous intervention does not seem sensible in all patients. This is supported by the observation that patients with one remaining lesion after PTCA had a lower rate of life-threatening events than patients who initially underwent cardiac surgery, be it at the cost of a higher re-intervention rate. Additional analyses among patients with the worst angiographical result after PTCA (three or more remaining lesions) demonstrated that 71% of the deaths or MIs occurred before an additional CABG was performed (if any), suggesting that a number of life-threatening events would have been prevented had the CABG been performed earlier. In view of the above, we are of the opinion that in patients with multivessel coronary artery disease, coronary bypass surgery and percutaneous intervention should not be played off against each other, but should be considered as complementary parts of an umbrella coronary revascularisation strategy. Treatment should be tailored to the individual patient's situation, taking into account the pros and cons of both strategies. These considerations should also include cost aspects. In contrast to the ARTS trial, however, CABRI was not designed to study cost-effectiveness relations between percutaneous intervention and surgery. Future analyses of the ARTS trial data may therefore be of great value in this respect. ■

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