

AUDIT

Immediate and long-term clinical outcome of coronary angioplasty in patients aged 35 years or less

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Abstract

Objective—To study the immediate and long-term clinical success of percutaneous transluminal coronary angioplasty in patients aged 35 years or less.

Design—Patients undergoing percutaneous transluminal angioplasty were prospectively entered into a dedicated database. Clinical and angiographic data on all patients aged 35 years or less were reviewed. Follow up data were collected by interview during outpatient visits, by questionnaire, or from referring physicians.

Setting—A tertiary referral cardiac centre.

Patients—57 patients aged 35 years or less (median 33, range 22–35) underwent coronary angioplasty because of unstable angina (32 patients), stable angina (23 patients), acute myocardial infarction (1 patient), and documented ischaemia in a cardiac transplant patient.

Results—The primary clinical success rate (reduction in diameter stenosis to <50% without in-hospital events) was 88%. A major procedure related complication occurred in 5 patients (9%): one patient died, two patients sustained an acute myocardial infarction, two patients underwent emergency bypass surgery, and in three patients repeat angioplasty was performed before hospital discharge. In 2 patients (4%) coronary angioplasty did not significantly reduce the diameter stenosis but there were no associated complications. A total of 60 lesions were attempted (balloon angioplasty in 57, directional atherectomy in 2). The initial angiographic success rate was 92%. The median (SD) follow up was 4.7 (3.0) years. During follow up 7 patients (12%) died, 10 sustained a myocardial infarction (18%), and 28 patients (49%) underwent repeat revascularisation (coronary artery bypass grafting in 7 (12%) and repeat angioplasty in 21 (37%)). The estimated 5 year survival and event-free survival (Kaplan-Meier method) was 87 (9)% and 50 (13)%, respectively. Multivariate logistic regression analysis showed that hypertension and the extent of vessel disease were the only independent predictive factors for event free survival.

Conclusions—In young patients coronary angioplasty had a high immediate success rate but many needed repeat

revascularisation procedures during the follow up period and survival was not improved. Coronary angioplasty in young patients should be regarded as a palliative procedure.

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Keywords: coronary angioplasty, young patients.

Obstructive coronary artery disease has been found in young healthy individuals.^{1,2} Clinical expression of early-onset disease is rare, however, and is generally regarded as indicating a rapidly progressive disorder with poor outcome. The annual mortality ranges from 4% to 7%.^{3,4} Coronary artery bypass grafting (CABG) relieves angina and may improve outcome in selected patients.⁵ But the long-term clinical outcome of CABG is less satisfactory in young patients.⁶⁻⁸ Some studies have indicated that coronary angioplasty may offer a better alternative.⁹⁻¹¹ To further elucidate the role of coronary angioplasty in young patients, we studied the immediate and long-term clinical outcome of this procedure in 57 patients aged 35 or less.

Table 1 Clinical and angiographic characteristics in 57 patients aged 35 or less

Characteristic	Patients (n) (%)
Age (yr):	
Median	33
Range	22-35
Male	48 (84)
Previous MI	19 (33)
Previous CABG	1 (2)
Risk factors:	
Smoking	45 (79)
Family history	39 (68)
Hypercholesterolaemia	28 (49)
Hypertension	24 (42)
Diabetes	5 (9)
Functional class:	
I	1 (2)
II	7 (12)
III	15 (26)
IV	34 (60)
Vessel disease:	
1	43 (75)
2	12 (21)
3	2 (4)
Ejection fraction (%):	
50	46 (81)
35-50	10 (18)
<35	1 (2)

CABG, coronary artery bypass grafting; MI, myocardial infarctions.

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Patients and methods

PATIENTS

Between January 1981 and July 1992 coronary angioplasty was performed in 57 patients aged 35 or less. In this period a total of 5790 patients had coronary angioplasty. Table 1 shows the clinical and angiographic characteristics of these young patients. The indication for coronary angioplasty was stable angina in 23 patients (40%), unstable angina in 32 patients (56%) (Braunwald II or IIIB in 15 patients (26%) and Braunwald II or IIIC in 17 patients (30%)), acute myocardial infarction in another patient, and documented ischaemia in a cardiac transplant patient.¹² Medical charts were reviewed for data on risk factors including hypercholesterolaemia (positive history associated with therapy or serum cholesterol ≥ 6.5 mmol/l), hypertension (systolic and/or diastolic blood pressure ≥ 145 and/or 95 mm Hg, respectively), cigarette smoking (smoking within the last year before the intervention), and family history of coronary artery disease and diabetes.

CORONARY ARTERIOGRAPHY AND ANGIOPLASTY

Coronary arteriography and angioplasty were performed by standard techniques as described elsewhere.¹³ Angioplasty was regarded as *angiographically successful* when the stenosis was reduced to less than 50% of the luminal diameter narrowing. A dissection was defined as the presence of intimal damage producing an intraluminal defect on the coronary angiogram and/or extraluminal extravasation of contrast material and/or the presence of linear luminal density or luminal staining. A *clinically successful angioplasty* was defined as an angiographically successful dilatation free of procedure related complications leading to death, acute myocardial infarction, emergency bypass surgery, or repeat angioplasty. A periprocedural infarction was determined by the development of new Q waves or an increase in the serum cardiac enzymes of more than twice the upper limit of normal.

FOLLOW UP

Procedural details, including immediate complications, were prospectively entered at the time of the intervention into a dedicated computer database. The median (SD) follow up time was 4.7 (3.0) years (range 1-11). Patients were screened for the occurrence of death, acute myocardial infarction, and recurrent angina pectoris necessitating repeat angioplasty or bypass surgery. Clinical follow up information was obtained retrospectively by interview during outpatient visits, questionnaire, or from the referring physician. Information was complete for all patients. Patient survival curves and event free plots were constructed by the Kaplan-Meier method. We used multivariate logistic stepwise regression analysis to determine independent predictors of event free survival. The following variables were selected: age, gender, current smoking, hypercholesterolaemia, hypertension, diabetes, family history, stable

Table 2 Lesion site and type of 57 patients aged 35 or less (60 lesions attempted)

Lesion	No (%)
Lesion site:	
LAD	38 (63)
RCA	18 (30)
LCX	4 (7)
Lesion type*:	
A	5 (8)
B	44 (73)
C	11 (18)

*Classification according to the guidelines of the American College of Cardiology/American Heart Association Task Force on assessment of diagnostic and therapeutic cardiovascular procedures.²⁹ LAD, left anterior descending; RCA, right coronary artery; LCX, left circumflex.

or unstable angina, history of myocardial infarction, ejection fraction less than 50%, single or multiple vessel disease, type C or type A/B lesion, angioplasty before or after 1985, and presence of dissection after angioplasty.

Results

ANGIOGRAPHIC RESULTS

Coronary angioplasty was performed in 57 patients aged 35 or less (balloon angioplasty in 55 and directional atherectomy in two). A total of 60 lesions were attempted (one lesion in 54 and two lesions in three patients). Table 2 shows the lesion site and type. Fifty five lesions were successfully dilated, resulting in an overall primary angiographic success rate of 92%. The lesion could not be crossed in two patients (4%). Abrupt vessel closure immediately after attempted angioplasty occurred in three other patients (5%): one was referred for urgent bypass surgery, one underwent bail-out stent implantation, and the remaining patient was treated with prolonged balloon dilatation. The postoperative course was uneventful in all, except in the last patient who sustained a non-Q wave myocardial infarction (creactive kinase 322 U/l).

CLINICAL RESULTS

The primary clinical success rate for the total study population was 88% (table 3). In two patients (4%) the angioplasty did not reduce the diameter stenosis, but there were no complications. Five patients (9%) sustained a major procedure related complication. One female patient, admitted because of an acute myocardial infarction complicated by cardiogenic shock, died 24 hours after successful

Table 3 Clinical success of coronary angioplasty and procedure related complications in 57 patients aged 35 or less

	No (%)
Clinical success	50 (88)
Unsuccessful angioplasty without complications	2 (4)
Unsuccessful angioplasty with complications:	5 (9)
Death	1 (2)
AMI	2 (4)
CABG	2 (4)
Bail-out stent/repeat PTCA (acute closure)	3 (5)

AMI, acute myocardial infarction, CABG, coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty.

Table 4 Major cardiac events during hospital stay and after discharge in 57 patients aged 35 or less

Event	In hospital (n = 57) No (%)	After discharge (n = 56*) No (%)	Total (n = 57) No (%)
Death	1 (2)	6 (11)	7 (12)
AMI	2 (4)	8 (14)	10 (18)
CABG	2 (4)	5 (9)	7 (12)
Re-PTCA	3 (5)	18 (32)	21 (37)
Total of events	8 (14)	37 (66)	45 (79)

*One hospital death. See footnote to table 3 for abbreviations.

reperfusion and dilatation of an occluded left anterior descending artery. In two other patients, balloon angioplasty was complicated by a non-fatal acute myocardial infarction (serum creatine kinase 1200 and 322 U/l). Acute vessel closure occurred in three other patients: 1 was referred for emergency bypass surgery, one was managed with a bail-out stent, and the remaining patient was treated conservatively. The postoperative course was uneventful in all. Thus a total of eight events occurred in five patients. If the patient in whom angioplasty was performed because of acute myocardial infarction and cardiogenic shock is excluded there were seven events in four patients.

FOLLOW UP RESULTS

Table 4 lists the occurrence of major events after hospital discharge. There were six deaths (11%) of which five were cardiac and one non-cardiac (cerebrovascular accident). Eight patients (14%) sustained a non-fatal myocardial infarction. Eighteen patients (32%) underwent repeat angioplasty during the follow up period (the same lesion in 14 patients, a newly acquired lesion in four and one of these was referred for emergency bypass surgery). A further five patients (9%) underwent elective bypass surgery with an uncomplicated postoperative course. The mean (SD) estimated survival 5 years after the index angioplasty for the entire study population was 87 (9%) (95% confidence interval 78% to 96%, figure). Event free survival at 5 years

(free of myocardial infarction, bypass surgery, and repeat angioplasty) was 50 (13%) (95% confidence interval 37% to 63%, figure). The only independent predictors of event free survival were hypertension and the extent of vessel disease. The probability of sustaining a cardiac event was increased 11-fold (95% confidence interval 1.4 to 83.0) in patients with hypertension and 3.5-fold (95% confidence interval 1.0 to 13.0) in patients with multivessel disease. At the end of follow up, 40 (80%) of the 50 patients were still alive and symptom free, six patients were in New York Heart Association class II, and four patients were in class III.

Discussion

Atherosclerosis of the coronary arteries starts very early in life and progresses over decades. It generally becomes manifest clinically in the middle and the older age groups.¹⁴ None the less, 0.3–4.0% of the patients with angiographically documented obstructive coronary artery disease and 0.7–8.9% of the patients undergoing coronary artery bypass grafting or coronary angioplasty are aged 40 years or less.^{4,10,15} The reported annual mortality in medically treated young patients ranges from 4.0% to 6.8% and contrasts with the reported annual mortality of 0.3% to 0.5% in age matched controls.^{3,4,10} There is still uncertainty about whether age itself is an independent predictor of long-term survival. Both clinical and angiographic variables have been identified as independent predictors of mortality and event free survival.^{11,16} Whereas some found that multivessel disease and impaired left ventricular function predicted late mortality, Webb *et al* identified diabetes and hypertension as independent predictors of subsequent death.^{3,11,16} The presence of coronary risk factors such as diabetes and raised concentrations of serum cholesterol, however, seem to have more influence on event free survival.^{3,16} In the present study, hypertension and multivessel disease were the

Survival and event free survival (Kaplan-Meier) of patients aged 35 or less who underwent coronary angioplasty.

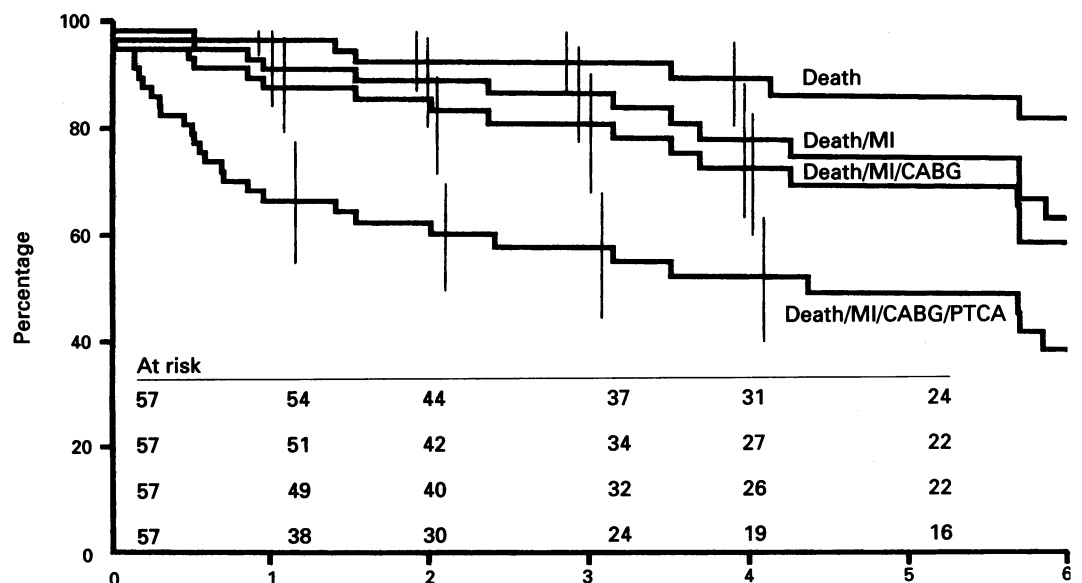


Table 5 Clinical events during hospital stay and after discharge in young patients who underwent coronary artery bypass grafting

Author	Study period	Cases	Baseline characteristics (%)			Events in hospital (%)				Follow up data (Events (%))			
			Presence of MVD	LV EF	History of AMI	Death	AMI	No (%)	Time to FU (yr) (Mean (SD) or (range))	Death	AMI	CABG	Symptom free at end of FU (%)
Lytle, <i>et al</i> ⁶ Cohen, <i>et al</i> ⁸	71-75	107	63	Normal in 70%	Patients 35 or less				9.6 (1.4)	14.1	21.6	12.5	65
	70-80	41	73	62 (2.4)	—	0.9	4.6	106 (100)	5.0 (1-13)	19.5	NR	12.1	—
Almeida de Olivera, <i>et al</i> ²⁶ Laks, <i>et al</i> ²⁰ Kelly, <i>et al</i> ¹⁷ Jones, <i>et al</i> ¹⁹ Gelfand <i>et al</i> ²⁷ Fitzgibbon, <i>et al</i> ⁸ Kelly, <i>et al</i> ⁷	69-74	100	84	Normal in 30%	Patients 40 or less				2.7 (1-5)	2.0	3	NR	78
	76-77	70	61	Normal in 35%	64	0	2	84 (84)	2.7 (0.5-4)	3.8	8	2.9	67
	71-77	68	74	NR	49	0	4	69 (99)	1.0-6.2	5.9	≥2.9	—	47
	71-78	116	NR	Normal in 52%	53	0	1.5	68 (100)	1.0-9.0	6.9	—	—	—
	70-80	92	68	46	—	0	1.7	(98)	3.5 (0.5-9)	3.2	NR	4.8	79
	72-85	138	85	Normal in 58%	58	3.3	3.3	62 (67)	≥10	13.8	≥7.9	16.6	NR
	68-84	242	NR	NR	54	0	4.3	85 (0)	7.9	10.5	NR	16.2	62.5
					47	2.9	NR	172 (74)					

See footnote to table 3 for abbreviations. FU, follow up; MVD, multiple vessel disease; NR, not reported.

only independent predictors of event free survival. These observations suggest that coronary atherosclerosis may be a more progressive disease in the subset of young patients with a high coronary risk factor profile. In general, young patients with coronary artery disease are known to have a higher incidence of coronary risk factors, especially hypercholesterolaemia, cigarette smoking, and family history of coronary artery disease.^{4,7,17} Although, several studies indicate that reducing serum cholesterol may favorably influence progression of coronary atherosclerosis, it still remains uncertain whether risk factor modification improves longevity and event free survival.¹⁷⁻¹⁹

In addition to interventions aimed at prevention, palliation is of the utmost importance. Though coronary revascularisation techniques do not address the pathophysiology of the underlying disorder and thus cannot be expected to cure or halt the process of atherosclerosis, they can relieve symptoms. There is no doubt that coronary artery bypass grafting can be performed safely and effectively in young patients (table 5). However, it is a major intervention and vein graft failure has been reported to be higher in young patients than in the general population.^{16,17,20} As a result younger patients are more likely to need reoperation than middle aged and older patients.^{6,7} No relation could be established between the presence of coronary risk factors and the inferior patency rate in young individuals.^{8,19} Young age at the initial operation is the single most important predictor of the need for subsequent reoperation.²¹ Reoperation is not only associated with an increased risk of perioperative myocardial

infarction but also with less successful relief of symptoms.⁸ To overcome the problem of vein graft failure, Lytle *et al* advocated the use of internal mammary artery grafts.¹⁶ In their series of 107 patients aged 35 and less, they reported a patency rate of 93% at a mean postoperative interval of 47 months that was significantly higher than the patency rate of 56% for vein grafts.¹⁶ Because of the progressive nature of atherosclerosis in the young it remains to be seen whether this will be translated into enhanced palliation and superior long-term clinical outcome. Cosgrove *et al* found that the absence of an internal mammary artery graft was an adverse predictor of reoperation-free survival only in patients older than 40 but not in those younger than 40 years.²¹ In these patients, hypertension and smoking were the only risk factors predictive of reoperation-free survival.

It is not appropriate to use earlier surgical series as historical controls for comparing the results of surgery with those of coronary angioplasty, because both surgical and anaesthesiological techniques have improved considerably and surgical patients are more likely to have multiple vessel involvement. However, it seems that angioplasty can be performed with a similar or an even higher immediate success rate and safety than coronary artery bypass grafting (tables 5 and 6). Rates for perioperative death and acute myocardial infarction range from 0% to 2% and from 0% to 5% respectively after balloon angioplasty compared with 0% to 5% and 2% to 5% respectively after surgery. Furthermore, there is no difference in the procedural success rate of balloon angioplasty between young patients and all patients. Reported

Table 6 Clinical events during hospital stay and after discharge in young patients who underwent PTCA

Author	Study period	Cases	Baseline characteristics (%)			Events in hospital (%)				Follow up data (Events (%))						
			Presence of MVD	LV EF	History of MI	rate (%)	Death	AMI	CABG*	No (%)	Time to FU (yr) (Mean (SD))	Death	AMI	CABG	Re-PTCA	Symptom free at end of FU (%)
Stone, <i>et al</i> ⁰ Simpfendorfer ⁹ Buffet, <i>et al</i> ²⁸ This study	80-88	71	58	<40% in 14%	—	96	0	0	1.1	69 (97)	2.7	1.4	5.8	10.1	24.6	73
	81-87	33	52	Normal in 58%	39	94	0	0	0	33 (100)	2.5 (1.5)	6.7	3.3	3.3	27	74
	80-91	57	16	59 (12)	53	81	0	3.5	7.0	57 (100)	6.0 (3.0)	3.5	3.5	8.7	33	92
	81-92	57	25	<50 in 20%	33	92	1.8	3.5	3.5	56 (100)	4.7 (3.0)	10.7	14.2	8.9	32.1	80
Webb, <i>et al</i> ¹	78-89	148	49	<45% in 14%	44	91	0.7	0.7	0.7	142 (97)	3.7 (3.0)	5.4	3.8	8.5	22.3	79

Abbreviations: see table 3. *Emergency.

overall perioperative mortality and incidence of acute myocardial infarction range from 0% to 1.2% and from 0% to 4.9% respectively.²²⁻²⁴ Moreover, the use of the intracoronary stent may enhance the safety of the procedure by reversing acute or threatened vessel closure, thus reducing the risk of fatal or non-fatal periprocedural acute myocardial infarction and need for emergency bypass surgery.²⁵

Long-term clinical outcome is not as good as the immediate results, however. In the present study, the estimated 5 year survival was 87%. Thus the annual mortality is 3%, which is higher than the annual mortality reported in other studies (table 6). In the other studies annual mortality after balloon angioplasty ranged from 0.4% to 1.0%, which is lower than the reported annual mortality rate of 1.0% to 2.0% after bypass surgery. The difference in annual mortality between our study and earlier ones is probably the result of differences in sample size and the duration of follow up. Long-term event free survival, which was 50% in our study, is predominantly determined by a high need for repeat revascularisation, either by bypass surgery or by repeat balloon angioplasty (table 6). In addition, many patients sustained an acute myocardial infarction. These combined data may indicate that coronary atherosclerosis in young patients is indeed rapidly progressive. This is highlighted by the observation that in other studies intervention was performed because of progression of disease and not because of restenosis in 14-53% of the patients requiring redilatation.⁹⁻¹¹ In our study, four (22%) of the 18 patients underwent angioplasty of a newly acquired lesion. Because most of the follow up information was obtained by contacting the referring physician, some events may not have been identified and the reported event rate may underestimate the real incidence of events in the follow up period.

Our study has two main limitations. Its design does not allow a direct comparison of medical, surgical, and angioplasty treatments in young patients with coronary artery disease, and it may have been too small to identify all the independent predictors of long-term mortality and/or event-free survival. We now manage young patients with symptoms by intensive risk factor modification in combination with balloon angioplasty. Though this approach effectively relieves symptoms but the need for repeat revascularisation is high. Furthermore, it does not seem to improve the outcome in this group of patients.

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