Percutaneous coronary interventions in the real world : lessons from the nineties

Percutaneous Coronary Interventions in the Real World:

Lessons From the Nineties

Bart Robbert Gustav Brueren

Lay-out: PFHM van Dessel & BRG Brueren

ISBN.....

Percutaneous Coronary Interventions in the Real World:

Lessons From the Nineties

PROEFSCHRIFT

ter verkrijging van de graad van Doctor aan de
Technische Universiteit Eindhoven, op gezag van de
Rector Magnificus, prof. dr. R.A. van Santen,
voor een commissie aangewezen door het College voor Promoties,
in het openbaar te verdedigen op
donderdag 19 mei 2005 om 16.00 uur

door

Bart Robbert Gustav Brueren

Geboren te Tegelen in 1968

Promotores:	prof. dr. N.H.J. Pijls prof. dr. H.W.M. Plokker
Co-promotor:	dr. J.M.P.G Ernst
Kerncommissie:	prof. dr. P.J. de Feyter prof. mr. dr. B.A.J.M. de Mol prof. dr. F. Zijlstra
Overige promotieleden	dr. J.J.R.M. Bonnier prof. dr. H.H.M. Korsten

Contents

Chapter 1

Introduction

Historical background:

Percutaneous transluminal coronary angioplasty was introduced in the late seventies as a treatment to relieve angina pectoris due to coronary stenosis (1). This treatment was introduced by Grüntzig in 1977, and expanded to the Netherlands soon thereafter (St. Antonius Hospital April 1980; Catharina Hospital September 1980). In the thesis by Bonnier, written in 1992, lessons in interventional cardiology learned in the eighties were summarized (2). In those days the techniques and possibilities for the interventional cardiologist were far less than nowadays. In the nineties, many new techniques were introduced, and even three vessel disease or left main stem stenosis became part of the domain of the interventional cardiologist. Initially a few hundreds of procedures were performed annually in each center; currently the figure exceeds 2500 PTCA procedures/year in each of the centers mentioned above. The majority of the data presented in this thesis are derived from a database, developed and used in the St. Antonius Hospital from January 1990. These data have been extended by a second database, containing the key data of all patients undergoing PCI in the Catharina Hospital in 1993 and 1997, as collected by Liistro et al.

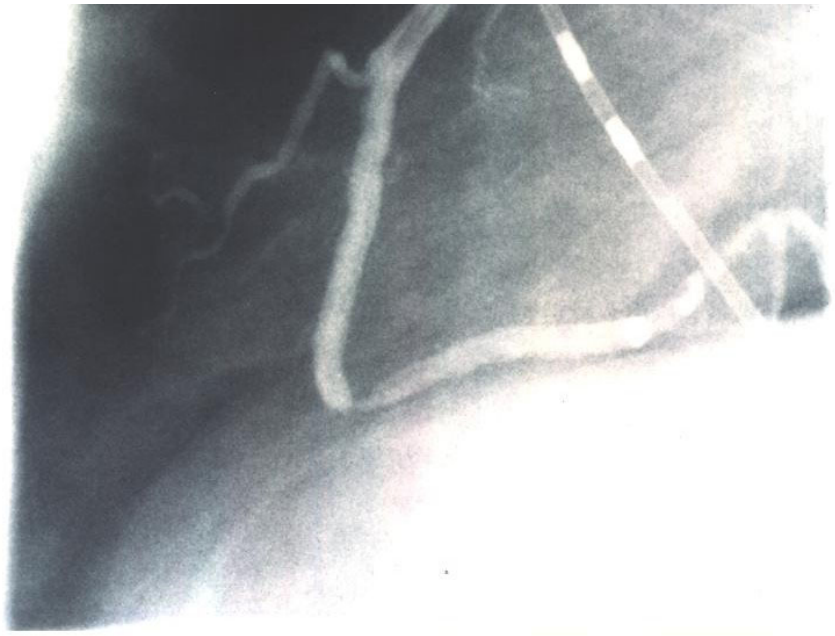


Figure 1. Images from first patient undergoing PTCA in september 1980 in the Catharina Hospital. Angiographic severity of stenosis prior to angioplasty.

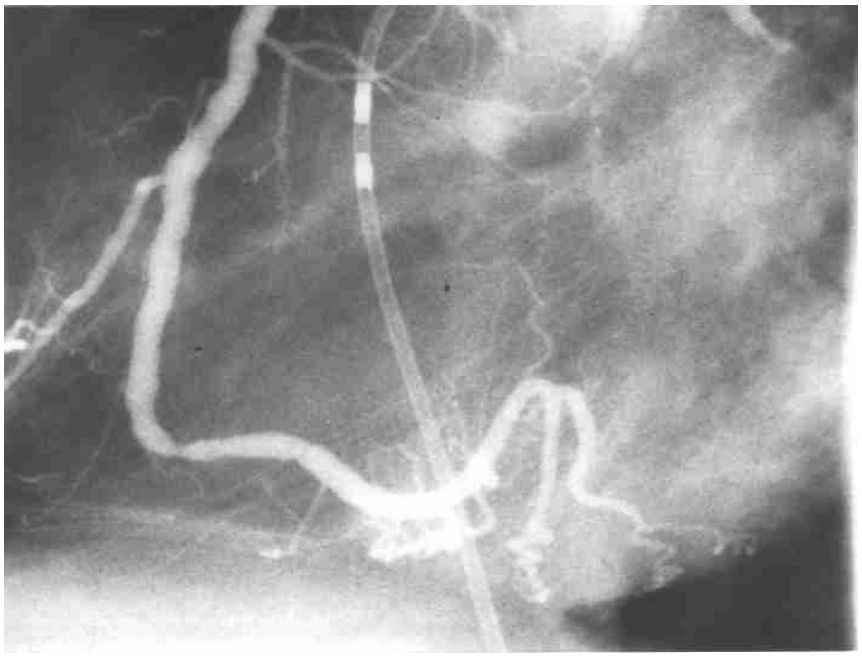


Figure 2. Same patient as in figure 1. Angiographic severity of stenosis post angioplasty.

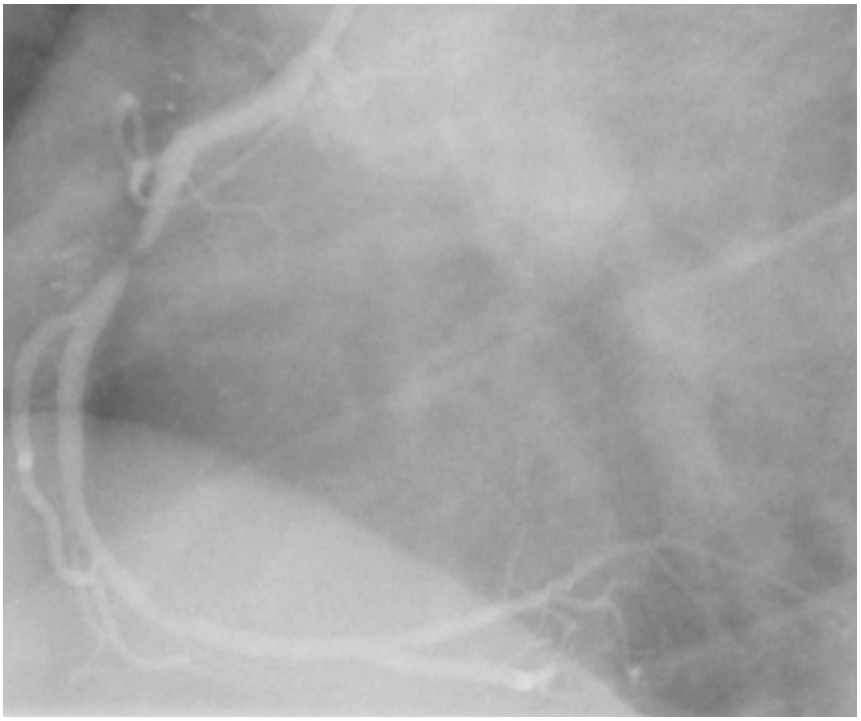
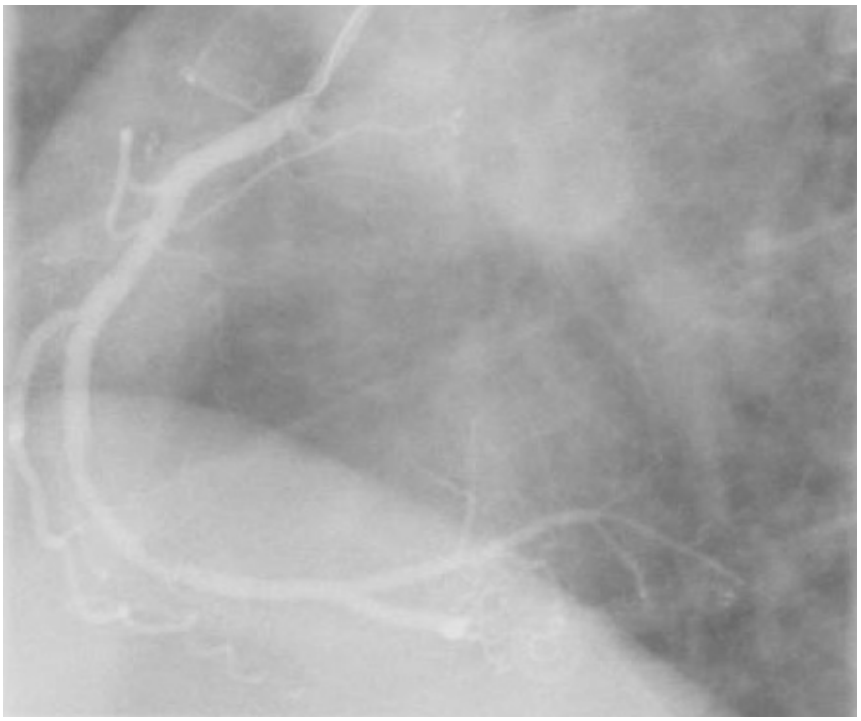


Figure 3. Images from patient undergoing PTCA in September 2004 in the Catharina Hospital. Angiographic severity of stenosis prior to angioplasty.



.
Figure 4. Same patient as in figure 1. Angiographic severity of stenosis post angioplasty.

The database as a tool for clinical scientific research

Any database derives its strength from the quality of data entered. Research based on databases is generally of retrospective nature and differs of course considerably from prospective randomised clinical research. On one hand, a publication which is based on facts from a database provides retrospective information. Among others, one can start with a clinical endpoint, e.g. a group of patients with a certain disease, coronary anatomy, particular treatment, or complication and look for outcome, associations, and other factors which can explain the longitudinal clinical course of patients or occurrence of events. On the other hand, a complete database can also contribute to prospective research, because the majority of the data to be entered is defined beforehand. Once the data to be collected are defined, results of treatment, occurrence of complications, and events are studied prospectively. Moreover, in sharp contrast to most randomized studies, a good and fair database includes *all* the patients and *all* treatments during a particular period of time. Therefore, if adequately used, conclusions from such database can be extremely valuable to acquire insight into 'real world medicine' instead of small subsets of patients as is often the case in prospective randomised trials. Consequently, from the databases mentioned above, we tried to learn lessons from the nineties in the real world of percutaneous coronary intervention (PCI).

'The Real World': what does it mean? Is it represented by the large trials?

Obviously, our clinical daily practice is based on evidence based medicine which is obtained by large prospective randomised trials. But at the same time, our practice is based upon our own experience which is reflected by the everyday population in our own hospitals. In the real world, it is often difficult to fit our individual patients into the framework of prospective randomised clinical trials. There is a difference between the average trial patient and the patient we are actually treating. For example, the patient is too old, has the female gender, has or has not certain risk factors, has a different type of coronary anatomy, etc. It turns out that in many of the prospective trials, all together the basis of evidence based medicine, the

population is not very representative for the everyday patient. This can be caused by several factors:

A. Only a minority of the eligible patients was asked for the study.

An example of such a type of shortcoming of a prospective study is the TIMI IIb trial (3). In this study, performed in the late eighties, and considered as a cornerstone of thrombolytic therapy, 3,262 patients were randomised in 50 centres. In spite of the very large number of patients, it ultimately turned out that only a minority of the eligible patients had been asked to participate in the study for various reasons, as was the case in many studies in acute myocardial infarction in those days. Similar shortcomings were applicable to the BARI trial (4), one of the landmark studies comparing CABG and PCI in multivessel disease (see below). Notwithstanding the great value of such studies for the evaluation of interventional cardiology, it is clear that significant bias might be present in the conclusion of this type of studies.

B. Inclusion criteria in the randomised study were too strict to represent a majority of patients.

An example of such a study is the BARI study (Bypass Angioplasty and Revascularisation Investigation) (4), performed between August 1988 and August 1991 in 18 centers. In this study, PTCA was investigated as alternative method for bypass surgery in patients with coronary artery disease, and thus compared PTCA and CABG. During the inclusion period, 25,200 patients were screened. Of these, almost 50% was not eligible on clinical or angiographic exclusion criteria. Out of the 12,530 patients clinically eligible for this study, only 4,110 were eligible after having screened for all the exclusion criteria, of whom ultimately 3,842 participated in the study. Finally, only 1,829 patients were randomised (5)!

C. Patients, eligible for a study refuse to participate.

An example of such a study is the ARTS trial (coronary artery bypass surgery and stenting for multivessel disease) (6), performed between April 1997 and June 1998 in 1205 patients in 67 centers in Europe and the United States. In that study, patients with multivessel disease were randomly assigned to be treated by multivessel stenting or bypass surgery. Although the inclusion criteria in this study were very reprensen-

tative for general multivessel population in the majority of the centers in the western world, many of the patients who were eligible, refused to participate (7). These patients were followed in the so-called ARTS registry. There were significant differences in outcome between the ARTS study itself and the ARTS registry; questioning the applicability of the conclusion of the ARTS study for a general population. A similar restriction was also present in the BARI trial, already mentioned above. Of those 3,842 patients fulfilling all the inclusion criteria of that study, only 1,829 consented to participate and 2,013 patients refused.

D. Publication bias.

It is clear that studies with positive findings are more easily published than studies with negative findings (8-9). This is specifically the case for more rare conditions as for example left main balloon angioplasty. In the second half of the nineties numerous small series have been published in the literature on this issue (10-19). Almost none of these studies contained more than fifty patients. According to stochastic principles, several of such studies will yield better than average results, other ones will have worse outcome (Gaussian distribution). Because the positive studies are published and the negative studies are not, there will be bias towards better outcome in such conditions as is truly the case in a ´real world population´.

It will be clear that those specific shortcomings of randomised studies are not present in a complete and well defined database. Therefore, such a database has additional value, and may better represent practice and outcome of percutaneous transluminal coronary interventions in every day practice.

Therefore, the aims of setting up and analysing the databases mentioned above and reflected in this thesis, were to obtain a complete and a valid view upon:

- The number and characteristics of various interventional procedures in a given time period.
- Outcome of all such procedures.
- The incidence of complications, including mortality, in all patients.
- Influence of new techniques on efficacy and safety.

- And finally, as a consequence of the above mentioned issues, to serve as an instrument of quality control and tool for clinical scientific research.

Literature

(1) Grüntzig A.R. Transluminal dilatation of coronary artery stenosis. Lancet 1978;1:263.

(2) Bonnier, J.J.R.M. Thrombolysis and interventional cardiology; experiences from the 80's. Thesis Oktober 1992.

(3) The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction. Results of the Thrombolysis in Myocardial Infarction (TIMI) Phase II trial. N Engl J Med 1989;320:618-27.

(4) The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. N Engl J Med 1996;335:217-25.

(5) Bourassa M.G., Roubin G.S., Detre K.M, et al. Bypass angioplasty revascularization investigation: patient screening, selection and recruitment. Am J Cardiol 1995;75:3C-8C.

(6) Serruys P.W., Unger F., Sousa J., et al. Comparison of coronary artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344:1117-24.

(7) Personal communication.

(8) Dickersin K., Rennie D. Registring clinical trials. JAMA 2003;290:516-23.

(9) Olson C.M., Rennie D., Cook D., et al. Publication bias in editorial decision making. JAMA 2002;287:2825-8.

(10) Tommasso C.L., Vogel J.H.K., Vogel R.A. for the national registry of elective supported angioplasty. Coronary angioplasty in high-risk patients with left main coronary stenosis: results from the national registry of elective supported angioplasty. Cath Cardiovas Diagnosis 1992;25:169-173.

(11) Keeley E.C., Aliabadi D., O'Neill W.W., et al. Immediate and long-term results of elective and emergent percutaneous interventions on protected and unprotected severely narrowed left main coronary arteries. Am J Cardiol 1999;83:242-246.

(12) Chauhan A., Zubaid M., Ricci D.R., et al. Left Main Intervention Revisited: Early and Late Outcome pf PTCA and Stenting. Catheterization and Cardiovascular Diagnosis. 1997; 41:21-29.

(13) Silvestri M., Barragan P., Sainsous J., et al. Unprotected left main coronary artery stenting: immediate and medium term outcomes of 140 elective procedures. J Am Coll Cardiol 2000;35:1543-50.

(14) Ellis S.G., Tamai H., Nobuyoshi M., et al. Contemporary percutaneous treatment of unprotected left main coronary stenoses. Initial results from a multi center registry analysis 1994-1996. Circulation 1997;96:3867-3872.

(15) Park S-J., Park S-W., Hong M-K., et al. Stenting of unprotected left main coronary stenoses: immediate and late outcomes. J Am Coll Cardiol 1998;31:37-42.

(16) Wong P., Wong V., Tse K-K., et al. A prospective study of elective stenting in unprotected left main coronary disease. Cathet Cardiovasc Intervent 1999;46:153-159.

(17) Laruelle C.J.J., Brueren G.B.R., Ernst S.M.P.G., et al. Stenting of "unprotected" Left Main Coronary Artery Stenoses: Early and Late Results. Heart. 1998;79:148-152.

(18) Karam C., Fajadet J., in patients at high surgical risk. Am J Cardiol 1998;82:975-978.

(19) Tan W.A., Tamai H., Park S-J., et al. for the ULTIMA investigators. Long-term clinical outcomes after unprotected left main trunk percutaneous revascularization in 279 patients. Circulation 2001; 104: 1609-1614.

Chapter 2

One year outcome of coronary angioplasty in patients with diabetes compared with non-diabetics.

B.R.G Brueren, J.M. ten Berg, J.C. Kelder, M.J. Suttorp, E.G. Mast, E.T. Bal, J.M.P.G. Ernst, H.W.M. Plokker.

Department of Cardiology, St Antonius Hospital, Nieuwegein.

This study was supported by a grant (94138) from the Netherlands Heart Foundation.

Published in the Netherlands Heart Journal 2004;12:144-150.

Abstract

Background. Some reports indicated that in patients with diabetes mellitus and multivessel disease, coronary artery bypass surgery is preferred over coronary angioplasty. We retrospectively compared outcome of coronary angioplasty in diabetic and non-diabetic patients.

Methods. Ninety-seven diabetics and 971 non-diabetics were included in the within the Balloon Angioplasty and Anticoagulation Study (BAAS), where patients were randomized before coronary angioplasty to aspirin alone or aspirin plus coumadin. Fifty diabetics and 481 non-diabetics underwent follow-up angiography. The primary end point comprised of all cause mortality, myocardial infarction or target-vessel revascularization.

Results. The baseline characteristics were similar between the groups except for significantly more males and smokers among the non-diabetics. The diabetics had significantly more previous strokes, more left anterior descending coronary artery disease as well as more restenotic lesions and multivessel disease. At 30 days, the primary end point occurred in 5 diabetics (5.2%) and 47 non-diabetics (4.9%), (p=0.8) and at 1-year in 17 (17.5%) and in 165 (17.1%), respectively (p=0.9). Event-free survival remained comparable during long-term follow-up (4 years). Multivariate analysis showed a hazard ratio of 1.036 for diabetes versus non-diabetes for the occurrence of any event (p=0.9; 95% CI, 0.6-1.7). At 6 months, the minimal luminal diameter was significantly smaller in the diabetics (1.55±0.76mm versus 1.78±0.66-mm; p=0.01). Diabetics also had more restenosis (41% versus 23%; p=0.003).

Conclusion. Despite angiographical differences at 6 months between the diabetics and non-diabetics, both short-term and long-term clinical follow-up appeared to be similar.

Introduction

The optimal treatment for patients with diabetes mellitus who need coronary revascularization is still a subject under debate. The prospective randomized Bypass Angioplasty Revascularization Investigation (BARI) study showed a significant higher 5-year mortality rate after Percutaneous Coronary Intervention (PCI) than after Coronary Artery Bypass Surgery (CABG) for diabetics with multivessel disease (1). On the other hand, these differences in outcome were less obvious in the registry of the BARI study as well as in a large observational report (2,3). Nevertheless, diabetics have a higher restenosis rate after PCI than non-diabetics, which seem to make PCI a less suitable treatment for diabetics (4-6). Until now, in our department the decision between CABG and PCI has not been based on the presence of diabetes and neither have the procedural methods been influenced. The therapy of choice was based solely on the suitability of the lesions for either way of revascularization. The present study was to analyse whether early and long-term outcome after PCI in diabetics is indeed worse than in non-diabetics in a selected group of patients.

Methods

The methods of the BAAS have been described previously (7). In short, all consecutive patients planned to undergo PCI from 7 referring centres between March 1996 and November 1997 were enrolled in the BAAS trial. Patients were part of the routine decision making process in which cardiologists and cardiothoracic surgeons decide which revascularization therapy to choose. BAAS randomized 1,058 patients before PCI to aspirin alone or aspirin plus coumarins and studied the effect of six-month coumarins treatment on one-year outcome. Exclusion criteria were acute myocardial infarction, contraindications to the use of coumarins or aspirin, target lesion in a bypass graft, and unwillingness or inability to provide written informed consent to participate in the trial. There was a 1:1 subrandomization to clinical follow-up alone or clinical and angiographic follow-up at six months. A policy of provisional stenting was used. No platelet glycoprotein IIb/IIIa-receptor blockers were administered.

Diabetics in the BAAS trial were identified by treatment with insulin or oral hypoglycemic medication. Acute myocardial infarction was defined as prolonged chest pain with new Q-waves of > 0.04 second in 2 or more contiguous leads or a new left bundle branch block, or a rise in creatine phosphokinase (CPK) rise to at least 3 times the normal upper limit after the procedure or to 2 times during follow-up. ECG and CPK were evaluated before and after PCI as well as on the next day. Reintervention was based on both angiographic restenosis and recurrent chest pain with ECG or scintigraphic evidence of ischaemia. Events were classified as early (day 0-30 after PCI) or late (day 30-365) and were reviewed at regular intervals by a safety committee. Quantitative coronary analysis was performed by an independent core laboratory (Prof Reiber, Heart Core, Leiden, The Netherlands). Follow-up angiography was performed in 50% of the patients, selected at random.

Primary End Point

The primary end point comprised of all cause mortality, myocardial infarction or target-vessel revascularization.

Statistics

The two groups were compared by the Student's *t*-test for continuous variables and the chi-square test, or when appropriate, Fisher's exact test for discrete variables. Discrete variables were compared in terms of relative risks with 95% CI. Event-free survival was calculated by the Kaplan-Meier method. Differences in survival times were assessed by the logrank test. A P-value less than 0.05 was considered significant.

Results

There were 97 (9.2%) diabetics and 961 non-diabetics in the BAAS trial. This percentage of diabetes is lower than in most US patients' populations, but normal in our country. Of these 97 diabetics 35 patients were treated with insulin. The clinical and angiographic baseline characteristics of the diabetic and non-diabetic patients are shown in table 1 and 2. There were no statistically significant differences between the diabetics and non-diabetics with respect to the use of stents or antithrombotic medication. But the non-diabetics were significantly more often males and smokers

and had significantly more often a lesion in the left anterior descending (LAD) coronary artery or a restenotic lesion. In contrast, the diabetics more often had a previous stroke and multivessel disease.

Table 1. Clinical Characteristics of Diabetic and Non-diabetic Patients

	Diabetic patients (N=97)	Non-diabetic patients (N=961)	P-value
Age (yr)	61.8 ± 9.4	59.9 ± 10.1	0.08
Male sex (%)	64.9	78.9	0.003
Other Risk factors (%)			
Hypertension	28.9	20.4	0.07
Cholesterol> 5 mmol/l or lipid lowering	77.3	81.2	0.73
Smoking in preceding half year	18.6	32.5	0.004
Clinical features (%)			
Previous myocardial infarction	42.3	38.6	0.51
Previous angioplasty	16.5	14.8	0.22
Previous stroke	5.2	1.7	0.036
Angina class (CCS*)			
I	0	1.8	
II	30.9	29.9	
III	41.2	45.6	
IV	27.8	22.8	0.44
IV and ST-T changes	16.5	11.2	0.19
Number of diseased vessels (%)			
1	59.8	68.1	
2	34.0	30.0	
3	6.2	1.8	0.32
Ejection fraction < 50 % (%)	24.7	18.1	0.15
Stent implantation (%)	35.1	34.7	1.0
Bail out stenting (%)	8.8	8.7	1.0
Coumarin treatment (%)	52.6	49.8	0.67
Ticlopidine treatment	47.1	36.0	0.26

Continues variables are mean ± SD. CCS indicates Canadian Cardiovascular Society classification.

Table 2. Baseline Angiographic Characteristics of Diabetic and Non-diabetic Patients

	Diabetics lesions (N=141)	Non-diabetics lesions (N=1,388)	P-value
Target vessel (%)			
Left anterior descending	34.0	47.5	
Left circumflex	28.4	22.0	
Right coronary artery	36.9	30.3	
Left main	0.7	0.1	0.03
Restenotic lesion (%)	12.6	4.8	0.004
Ostial location of lesion (%)	9.9	15.0	0.13
Bifurcation lesion (%)	1.4	9.1	0.001
Moderate/severe calcification (%)	27.0	23.2	0.35
Angulation > 45 degrees (%)	27.7	20.2	0.05
Eccentric lesion (%)	66.7	65.6	0.92
Occluded lesion (%)	7.8	8.9	0.76
Lesion length (mm)	11.5 ± 6.0	11.9 ± 6.0	0.63
Stenosis (% of luminal diameter)	66.6 ± 14.8	65.8 ± 15.8	0.73
Balloon size (mm)	3.04 ± 0.42	3.06 ± 0.45	0.25
Maximal inflation pressure (atm)	12 ± 3.3	12 ± 3.4	0.84
Lesions treated per patient (No.)	1.45	1.44	0.9
Stented lesions (%)	29.1	29.1	1.0

Continues variables are means ± SD.

The angiographic success rate was 99.3% for the diabetics and 98.7% for the non-diabetics (p=1.0). The follow-up was 100% complete at 1 year. At 30 days, the primary end point occurred in 5 diabetics (5.2%) and 47 non-diabetics (4.9%) (p=0.8). At 1-year there was no significant difference in the primary end point for the diabetics and non-diabetics (17.5% vs. 17.1%; p=0.9) (table 3). The individual event rates during follow-up also did not differ significantly between the two groups (table 3). At 1-year, target-lesion revascularization was performed in 11 diabetics (11.5%) and 120 non-diabetics (12.5%) (p=0.9). Event-free survival remained comparable during long-term follow-up (fig 1). There was no difference in event-free survival between the insulin-dependent diabetics and diabetics treated with oral antiglycemic medication (fig 2).

Table 3. Procedural Outcomes and Clinical Events up to one year

	Diabetic patients (N=97)	Non-diabetic patients (N=957)	P-value
Early primary end points (0-30 days)			
Death	1 (1.0)	4 (0.4)	0.4
Myocardial infarction	2 (2.1)	33 (3.4)	0.8
Q-wave	1 (1.0)	10 (1.0)	
Non-Q-wave	1 (1.0)	23 (2.4)	
Acute coronary artery bypass grafting	2 (2.1)	4 (0.4)	0.1
Acute repeat angioplasty	2 (2.1)	34 (3.5)	0.8
Stroke	1 (1.0)	0 (0.0)	0.1
Any event	5(5.2)	47 (4.9)	0.8
Late primary end points (30-365 days)			
Death	1 (1.0)	6 (0.6)	0.5
Myocardial infarction	0 (0.0)	0 (0.0)	
Target lesion revascularization	11 (11.5)	120 (12.5)	0.9
Target lesion coronary artery bypass grafting	2 (2.1)	13 (1.4)	0.6
Target lesion angioplasty	9 (9.4)	107 (11.2)	0.7
Stroke	0 (0.0)	5 (0.5)	1.0
Any event	12 (12.5)	127 (13.3)	1.0
All primary end points (0-365 days)			
Death	2 (2.1)	10 (1.0)	0.3
Myocardial infarction	2 (2.1)	33 (3.4)	0.8
Q-wave	1 (1.0)	10 (1.0)	
Non-Q-wave	1 (1.0)	23 (2.4)	
Target lesion revascularization	14 (14.4)	150 (15.6)	0.9
Target lesion coronary artery bypass grafting	4 (4.1)	17 (1.8)	0.2
Target lesion angioplasty	11 (11.3)	136 (14.2)	0.5
Stroke	1 (1.0)	5 (0.5)	0.9
Any event	17 (17.5)	165 (17.2)	0.9

Multivariate analysis

The univariate hazard ratio for the primary composite end point was 1,031 for diabetes versus no diabetes (p=0.9; 95% CI 0.6-1.7). Since there were significant differences in the baseline characteristics among the study groups, a multivariate analysis was performed to adjust for the observed differences (sex, smoking, previous stroke, LAD lesion, restenotic lesion and multivessel disease). Only the presence of a LAD lesion was a significant predictor of the endpoint with a hazard ratio 1.486

(p=0.01; 95% CI 1.1-2.0). In the multivariate analysis, the hazard ratio hardly changed to 1.036 for diabetes versus no diabetes (p=0.9; 95% CI 0.6-1.7). Controlling for receiving a stent also did not change the hazard ratio for diabetes: 1.026 (p=0.9; 95% CI 0.6-1.7).

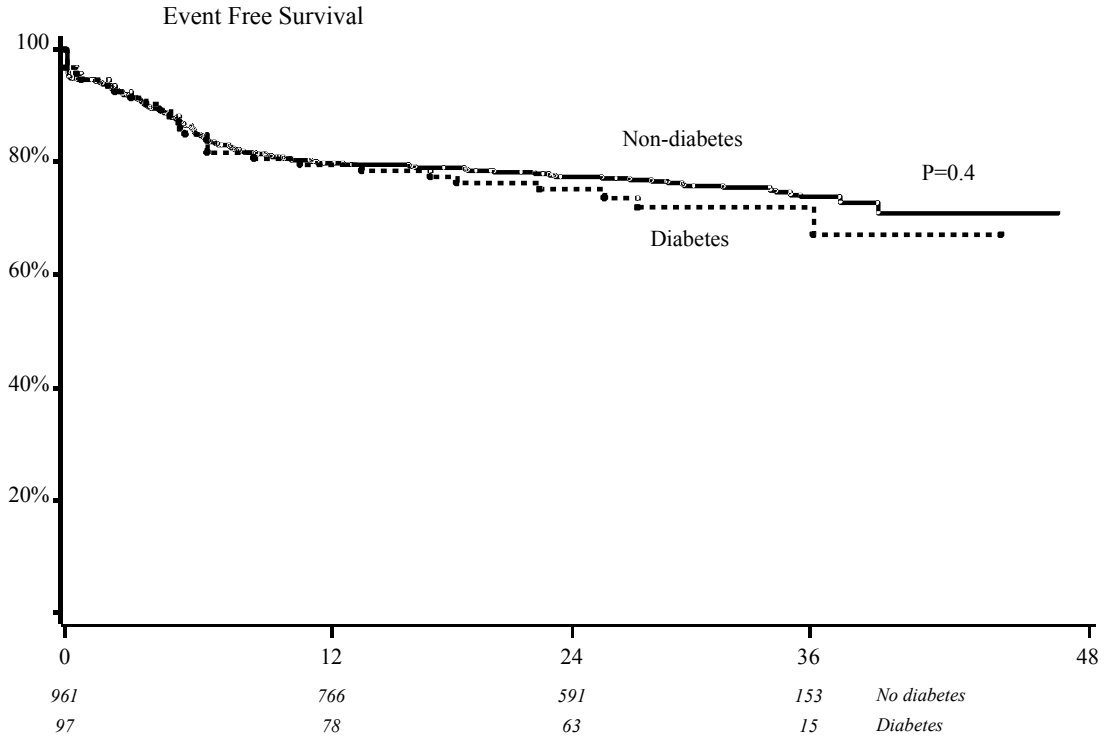


Figure 1. Event-free survival in weeks after coronary angioplasty in patients with diabetes compared with patients without diabetes.

Angiographic results

In the diabetic group 50 patients and in the non-diabetic group 481 patients were randomized to undergo follow-up angiography. Five diabetic patients (10%) did not undergo follow-up angiography because of death (1 patient); failed PCI (1); administrative fault (1); groin complication after PCI (1) and refusal (1). In the non-diabetic group 32 patients (6.7%) did not undergo follow-up angiography due to death (4); failed PCI (5); administrative faults (5); groin complications (5) and refusal (14).

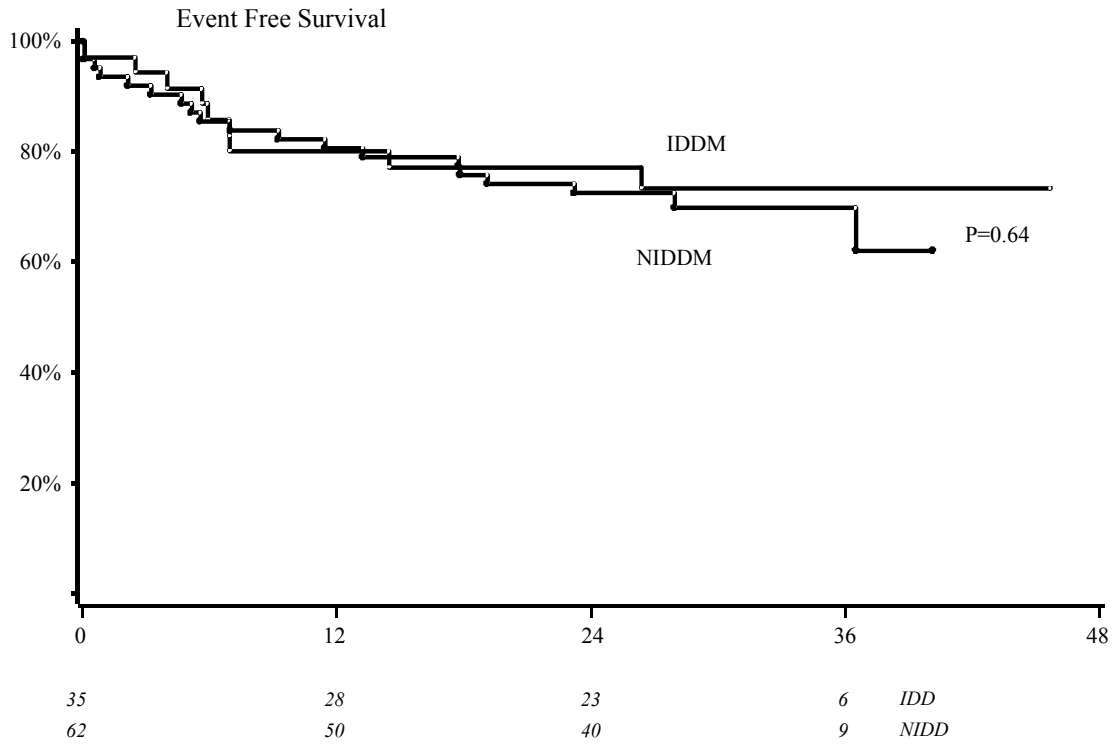


Figure 2. Event-free survival in weeks after coronary angioplasty in patients with insulin-dependent diabetics compared with diabetic patients treated with oral anti glycaemic medication.

The results of the 6-months angiographic follow-up are depicted in table 4. The reference diameter in the two groups did not differ significantly at any of the three time points studied. The minimal luminal diameter (MLD) at baseline and after the procedure did not differ significantly but at follow-up the MLD was significantly smaller in the diabetics (fig 3). In the diabetics the late loss was greater and the net gain significantly lowers. The diabetics had more restenosis by the >50% diameter stenosis criterion than the non-diabetics.

Table 4. Quantitative Angiographic Analysis of the Lesions

	Diabetic patients (N=56)	Non-diabetic patients (N=537)	P-value
Before the procedure			
Reference diameter (mm)	2.91 ± 0.60	2.96 ± 0.60	0.58
MLD (mm)	0.96 ± 0.51	0.99 ± 0.47	0.61
Diameter stenosis	66.9 ± 15.0	65.2 ± 16.5	0.21
Immediately after the procedure			
Reference diameter (mm)	3.13 ± 0.60	3.10 ± 0.57	0.67
MLD (mm)	2.30 ± 0.53	2.39 ± 0.59	0.30
Diameter stenosis	22.7 ± 14.0	23.7 ± 15.1	0.42
At 6 month follow-up			
Reference diameter (mm)	2.88 ± 0.64	2.87 ± 0.59	0.94
MLD (mm)	1.55 ± 0.76	1.78 ± 0.66	0.01
Diameter stenosis	39.1 ± 19.8	38.9 ± 19.0	0.71
Acute gain (mm)	1.34 ± 0.61	1.41 ± 0.64	0.46
Late loss (mm)	0.71 ± 0.63	0.61 ± 0.63	0.24
Loss index (mm)	0.45 ± 0.83	0.43 ± 0.58	0.78
Net gain (mm)	0.60 ± 0.58	0.79 ± 0.65	0.03
Diameter stenosis > 50 %	41.1 %	22.5%	0.003

MLD=Minimal lumen diameter. The values are expressed as means ± SD or as the percentage of the number of lesions.

Discussion

This study with over 1,000 patients demonstrated that in a broad spectrum of patients undergoing PCI, the angiographic outcome at 6 months was less favourable in diabetics compared with non-diabetics. In the subgroup with angiographic follow-up, diabetic patients more often developed restenosis due to a greater late loss. Our angiographic results corroborate those in the literature in which diabetes was frequently shown to be a risk factor for restenosis (4-6). Van Belle and colleagues compared the results of 300 consecutive patients who underwent single-vessel stenting

with those of 300 consecutive patients who underwent single-vessel balloon angioplasty. In the stent group there were 56 diabetics and in the balloon group 57 diabetics. In the balloon group the restenosis rate was almost twofold higher in diabetic than in non-diabetic patients (63% versus 36%; p=0.0002) due to both a greater late loss and more frequent late vessel occlusion. In the stent group, restenosis rates were similar in diabetics and non-diabetics (25% versus 27%, respectively) (6). Despite less favourable angiographic results our study showed that the clinical results were similar in the diabetics and non-diabetics. Most importantly, the late mortality rate was low and comparable in the two groups. Moreover the incidence of myocardial infarctions during the first 30 days after PCI was not higher in the diabetics than in the non-diabetics showing that PCI in diabetics is safe. There was also no difference in the target-vessel revascularization rate. Thus, despite a significantly smaller minimal luminal diameter, the diabetics did not undergo more ischaemia driven target lesion revascularizations.

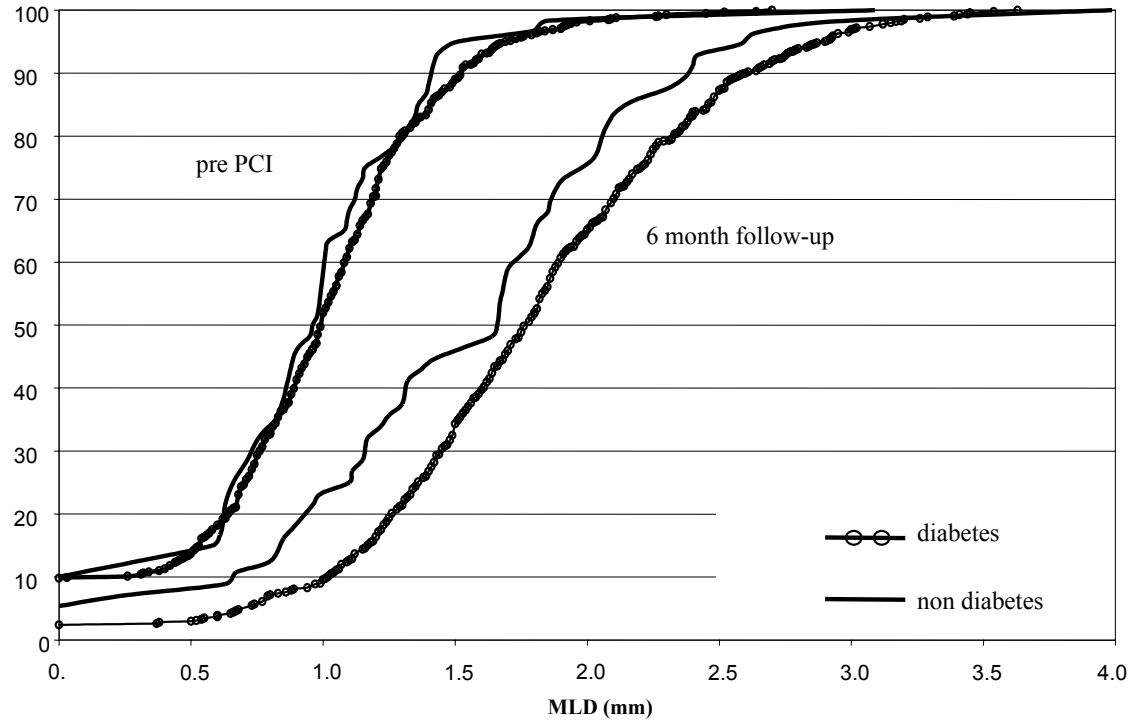


Figure 3. Minimal lumen diameter (MLD) at base line and after the procedure.

Angioplasty or Surgery

Our results appear to be in contrast with the general opinion that angioplasty is not inferior to bypass surgery with respect to survival in patients with diabetes. This opinion stems foremost from the results of the BARI (Bypass Angioplasty Revascularization Investigation) trial, which randomized 1,829 patients with multivessel disease to balloon angioplasty or CABG from 1988 to 1991 (8). A total of 353 patients were diabetics and in this subgroup the late survival was significantly better after CABG than after balloon angioplasty (1,9). Based on the BARI trial, the National Heart, Lung, Blood Institute issued a clinical alert to notify that CABG should be preferred in diabetics with multivessel disease (10). However, the BARI trial reported on a selected group of patients with multivessel disease, which is not a representation of the usual patient population referred for PCI. Of all patients, basically eligible for that trial, only 50.3 % of them were actually embedded, which can have induced bias. As compared with our study group, the BARI patients had more extensive coronary artery disease: triple vessel disease in 45% of the patients, a mean of 3.5 significant lesions and 2.9 grafts per patient and at least one occluded vessel in 38% of the patients. In contrast, our study population represents the current clinical practice with 1.45 treated lesions per patient. Our results are corroborated by a recent report on two randomized studies (ERACI and ERACI-II [three-year follow-up of the Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease]). In these studies 577 patients with multivessel coronary disease were randomized either to PCI or CABG. Of these patients 90 had diabetes. Coronary stents were used in 86.4% of the diabetic patients randomized to PCI. At 1-year the incidence of death, myocardial infarction and new revascularization procedures was not significantly different between the two diabetic study groups (22.7% in the PCI group versus 19.5% in the CABG group; p=ns) (11). Thus, also in these ERACI studies it was shown that coronary angioplasty in diabetics were safe and that the short term follow-up was good. The higher late mortality rate after PCI observed in the BARI trial is most likely due to progression of coronary artery disease as many patients initially randomized to PCI need CABG several years later (9). For the patients initially randomized to CABG, part of this

progression would probably be covered by the bypasses. It is interesting to note in this context that 1) even in patients with more extensive multivessel disease, it has been shown recently that one-or two vessel PCI of culprit lesions only selected by coronary pressure measurement, yields a similar favourable outcome on CABG of all angiographic lesions, and 2) that PCI of a physiologically non-significant stenosis is counter effective (12). This might explain the worse outcome in the BARI trial (where all angiographic lesions were treated by PCI) in the PCI group compared to CABG.

In conclusion, our results do not disprove those from the BARI trial. We also consider CABG the best revascularization method for patients with extensive coronary artery disease, but in diabetics with suitable lesions for PCI as in this study, the CABG procedure can safely be replaced by PCI.

Stents and platelet glycoprotein IIb/IIIa-receptor blockers

The present study was performed before the era of drug-eluting stents and large-scale use of GP IIb/IIIa antagonists. In selected patients stents reduce restenosis (13,14). Van Belle and colleagues studied the effect of stenting in diabetics and showed that diabetics who receive a stent have a similar restenosis rate as non-diabetics with a stent; the late loss and the rate of late vessel occlusion did not differ significantly between the diabetic and non-diabetic patients (6). Also others have found that stenting improves acute and mid-term outcome in diabetics compared with balloon angioplasty (15-17). Still, we have to notice that in most of these studies the outcome of the insulin dependent patients was worse compared with the non-insulin dependent patients (16,17). Thus, it is plausible that our results would further improve if more diabetic patients were to be treated with a stent. Especially the use of drug eluting stents is promising (21) but further investigation is warranted.

The same holds true for the use of GP IIb/IIIa-receptor blockers. Abciximab has been shown to convey a positive effect after stenting especially in diabetics (18). In the EPISTENT trial (Effect of Abciximab on Angiographic Complications during Percutaneous coronary Stenting in the Evaluation of platelet IIb/IIIa inhibition in stenting trial) 2,399 patients randomly received stent-plus-abciximab, stent-plus-placebo or balloon-plus-placebo (19). The results of the prospectively defined subgroup of 491 diabetic patients were reported separately and showed a significant

reduction of the composite end point consisting of death, myocardial infarction or target-vessel revascularization of 13% in the stent-plus-abciximab group versus 25.2% in the stent-plus-placebo group and 23.4% in the balloon-plus-abciximab group (p=0.005). There was a significant reduction in the 6-month target-vessel revascularization rate as well as a greater angiographic net gain in the stent-plus-abciximab group (18). At the time of our study abciximab was not used mainly because of economic reasons, and its use could again have further improved our results.

Limitations

This study does not describe the results of PCI in all diabetics referred to our hospital for undergoing revascularization. The results are biased due to a selection of only those lesions suitable for PCI: our heart-team decided whether lesions were suitable for PCI. And although diabetes is not a discriminator for the decision between CABG and PCI, bias could have played a role in the selection of the revascularization method. Nevertheless, there were no major differences between the basic characteristics of the diabetics and the non-diabetics, which shows that our study group is a representation of patients undergoing PCI in a high volume centre.

The one year follow-up in our study might be too short to observe differences in outcome between the diabetics and the non-diabetics. The BARI trial showed a sharp rise in the number of CABG procedures in the fifth and six years of follow-up for the diabetics initially treated with PCI.

Our study group may not be comparable to patients in the USA, as in our country a smaller group of patients undergoing PCI is affected by diabetes (12). Also the effectiveness of the treatment of the patients' glycemic state could be of influence on long-term outcome, on which neither our data nor the BARI or EAST data provide information.

Conclusion

Despite angiographical differences between the diabetics and non-diabetics six months after PCI of one or two arteries, both short-term and long-term clinical follow-up appeared to be similar.

References

(1) The BARI Investigators. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease. Circulation 1997;96:1761-9.

(2) Detre K.M., Guo P., Holubkov R., et al. Coronary revascularization in diabetic patients. A comparison of the randomized and observational components of the Bypass Angioplasty Revascularization Investigation (BARI). Circulation 1999;99:633-40.

(3) Weintraub W.S., Stein B., Kosinski A., et al. Outcome of coronary bypass surgery versus coronary angioplasty in diabetic patients with multivessel coronary artery disease. J Am Coll Cardiol 1998;31:10-9.

(4) Rensing B.J., Hermans W.R.M., Vos J., et al. Luminal narrowing after percutaneous transluminal coronary angioplasty: a study of clinical, procedural, and lesional factors related to long-term angiographic outcome. Circulation 1993;88:975-85.

(5) Weintraub W.S., Kosinski A.S., Brown C.L., et al. Can restenosis after coronary angioplasty be predicted from clinical variables? J Am Coll Cardiol 1993;21:6-14.

(6) Van Belle E., Bauters C., Hubert E., et al. Restenosis rates in diabetic patients. A comparison of coronary artery stenting and balloon angioplasty in native coronary vessels. Circulation 1997;96:1454-60.

(7) ten Berg J.M., Kelder J.C., Suttorp M.J., et al. Effect of coumarins started before coronary angioplasty on acute complications and long-term follow-up: a randomized trial. Circulation 2000;102:386-91.

(8) The BARI Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. N Engl J Med 1996;335:217-25.

(9) The BARI Investigators. Seven-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI) by treatment and diabetic status. J Am Coll Cardiol 2000;1122-1129.

(10) Ferguson JJ. NHLBI BARI clinical alert on diabetics treated with angioplasty. Circulation 1995;92:3371.

(11) Bech G.J., De Bruyne B., Pijls N.H., et al. Fractional flow reserve to determine the appropriateness of angioplasty in moderate coronary atenosis: a randomised trial. Circ 2001;103:2928-34.

(12) Pereira C.F., Bernardi V., Martinez J., et al. Diabetic patients with multivessel disease treated with percutaneous coronary revascularization had similar outcome than those treated with surgery: one year follow-up results from two Argentine randomized studies (ERACI-ERACI II). J Am Coll Cardiol 2000;35:3A.

(13) Serruys P.W., Jaegere de P., Kiemeneij F., Macaya C., Rutsch W., Heyndrickx G., et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coranary artery disease. NEJM 1994;331(8):489-95.

(14) Fischman DL, Leon MB, Baim DS, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. NEJM 1994;331(8):496-501.

(15) Savage M.P., Fischman D.L., Slota P., et al. Coronary intervention in the diabetic patient: improved outcome following stent implantation versus balloon angioplasty. J Am Coll Cardiol 1997;29:188A.

(16) Thierry J., Fajadet J., Jordan C., et al. Coronary stenting in diabetics: Immediate and mid-term clinical outcome. Cathet Cardiovasc Intervent 1999;47:279-84.

(17) Abizaid A., Mehran R., Bucher T.A., et al. Does diabetes influence clinical recurrence after coronary stent implantation. J Am Coll Cardiol 1997;29:188A.

(18) Marso S.P., Lincoff M., Ellis S.G., et al. Optimizing the percutaneous interventional outcomes for patients with diabetes mellitus: results of the EPISTENT (Evaluation of the Platelet IIb/IIIa Inhibitor for Stenting Trial) diabetic substudy. Circulation 1999;100:2477-84.

(19) Lincoff A.M., Califf R.M., Moliterna D.J., et al. Complementary clinical benefits of coronary-artery stenting and blockade of platelet glycoprotein IIb/IIIa receptors. NEJM 1999;341(5):319-27.

(20) Kornowsky R., Lansky A.J. Current perspectives on interventional treatment strategies in diabetic patients with coronary artery disease. Catheter Cardiovasc Interv 2000;50: 245-54.
(21) Morice M.C., Serruys P.W., Sousa J.E., et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularizition. NEJM 2002;346(23):1773-80.
(22) King S.B. 3rd, Kosinski A.S., Guyton R.A., et al. Eight-year mortality in the Emory Angioplasty versus Surgery Trial (EAST). J Am Coll Cardiol 2000;35:1116-21.

Chapter 3

Are there differences in late outcome after PTCA for angina pectoris after non-Q wave vs. Q wave myocardial infarction?

B.R.G. Brueren, M.P.P. Rosseel, E.T. Bal, E.G. Mast, J.M.P.G. Ernst, M.J. Suttorp, J.C. Kelder and H.W.M. Plokker.

Department of Cardiology, St. Antonius Hospital, Nieuwegein, The Netherlands;

Department of Cardiology, Aalster Stedelijk Ziekenhuis, Aalst, Belgium.

Published in part in the European Heart Journal 1997;18:1903-1912.

Abstract

Background. Revascularization is thought to improve prognosis more if ischaemia persists after so-called non-Q wave myocardial infarction, than after Q-wave myocardial infarction, because it is assumed that prognosis is better when there is less loss of left ventricular function. This study evaluates the differences in clinical outcome between patients with Q wave and those with non-Q wave myocardial infarction who underwent percutaneous transluminal coronary angioplasty (PTCA) because of recurrent ischaemia.

Methods. We retrospectively analysed two consecutive groups of patients who underwent PTCA for ischaemia after either a non-Q wave (n = 175) or a Q wave (n = 175) myocardial infarction. The follow-up was 4 years.

Results. Initial angioplasty success rates were similar in both groups. At 44 months of follow-up there were no significant differences between the two patient groups in rates of death (9 % vs. 11 %, P=ns), myocardial infarction (3 % vs. 7 %, P=ns) and target vessel revascularization by repeat PTCA (11 % vs. 15 % P=ns) or coronary bypass surgery (both 7 %).

Conclusion. We conclude that the benefit of elective coronary angioplasty in patients with angina pectoris after non-Q wave myocardial infarction is not more than after Q wave myocardial infarction. Thus, management strategies after myocardial infarction should not be based on the absence or presence of Q waves on the electrocardiogram.

Introduction

Natural history studies have suggested that patients have a more favourable prognosis after a non-Q wave myocardial infarction due to less necrosis and better preserved left ventricular function (1-6) compared to patients after a Q wave myocardial infarction. However, this has been disputed in some other studies; although there was a higher incidence of unstable angina and recurrent ischaemia in these studies, there was no improvement of late prognosis after PTCA for non-Q wave myocardial infarction (3,4,7).

This being the case, one might expect to prevent recurrent ischaemia or myocardial infarction after non-Q wave myocardial infarction by target vessel revascularization. However, few data are available on the immediate and long-term results of PTCA after non-Q wave myocardial infarction.

Therefore, we studied retrospectively the initial results and late outcome of PTCA in a consecutive group of patients with recurrent ischaemia after Q wave versus non-Q wave myocardial infarction.

Methods

Patients who underwent percutaneous transluminal coronary angioplasty in our centre in 1991 were studied. These comprised the first 175 patients with symptoms and/or signs of ischaemia after Q wave myocardial infarction and the first 175 with symptoms and/or signs of ischaemia after non-Q wave myocardial infarction. Q wave myocardial infarction was defined as prolonged (>30 minutes) chest pain characteristic of acute myocardial infarction, the appearance of new Q waves of at least 40 ms in duration and 2 mm in depth in at least two contiguous leads of the electrocardiogram, together with specific cardiac enzyme elevation defined as an increase in serum creatine kinase levels to at least twice the normal level. Non-Q wave myocardial infarction was defined in this study as prolonged (>30 minutes) chest pain characteristic of acute myocardial infarction, and specific cardiac enzyme elevation without the appearance of new pathological Q waves, as described above.

Prior to balloon angioplasty, all patients underwent coronary angiography and left ventricular angiography. The ventriculogram was evaluated using the Coronary Artery Surgery Study CASS system. This left ventricular function score provides a quantitative assessment of the segmental abnormalities of left ventricular function.

Procedural success was defined as a >20 % increase in luminal diameter by visual examination, with the final diameter stenosis <50 % and without the occurrence of death, acute myocardial infarction, or the need for repeat angioplasty or emergency bypass operation within the first 48 hours.

All patients were followed-up at our outpatient clinic, or by the referring cardiologist. If additional information was required, patients were interviewed by telephone. The following events were taken into account during follow-up: death (cardiac or non-cardiac death), myocardial infarction, re-intervention either for restenosis or progression of disease elsewhere, and coronary bypass grafting. Follow-up was 44 ± 2 months.

Statistical analysis

Continuous data are presented as means ± standard deviations and when appropriate the median. Categorical data are presented as percentages. For the comparison of categorical data the Chi-square test or when appropriate the Fisher exact test was used. Normally distributed data were compared by means of the Student t-test A P-value of 0.05 was considered statistically significant. For the comparison of right censored end-point data, the Kaplan-Meier method was used to draw the survival curves. Statistical comparison of the Kaplan-Meier curves was performed by means of the long-rank test. The hazard ratios were calculated by means of the Cox proportional hazard model, univariately and multivariately, with corresponding 95 % confidence intervals for the indication of precision. This study has a power of more than 80 % to reveal a 6 % cumulative survival difference at follow-up.

Table 1. Clinical characteristics

	Q wave (%)	Non-Q wave (%)	P-value
Number (patients)	175 (100)	175 (100)	
Age (years) SD	60.0 (11.6)	59.9 (9.9)	0.905
Female gender	28 (16)	35 (20)	0.40
Time from myocardial infarction to PTCA	8 (5)	11 (6)	
<24 h	43 (25)	52 (30)	
>24 h	124(71)	112(64)	0.38
>6 weeks			
Thrombolysis			
None	110 (63)	120(69)	
IC/IV	65 (37)	55 (31)	0.311
Number previous CABG			
0	151 (86)	158 (90)	
1	22 (13)	14 (8)	
2	2 (1)	3 (2)	0.34
Number previous PTCA			
0	150 (86)	144 (82)	
1	23 (13)	28 (16)	
2	2 (1)	3 (2)	0.67
AP class after myocardial infarction			
I	8 (5)	5 (3)	
II	48 (27)	40 (23)	
III	58 (33)	54 (31)	
IV	54 (31)	71 (41)	
Silent ischaemia	7 (4)	5 (3)	0.38

SD = standard deviation; CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty; AP = angina pectoris; IC/IV = intracoronary/intravenous; Ml = myocardial infarction.

Results

Baseline characteristics

The baseline characteristics were comparable in both groups (Table 1). Age, sex, time between myocardial infarction and percutaneous transluminal coronary angioplasty, thrombolysis, previous coronary artery bypass surgery, and the duration of follow-up there were not significantly different between the two groups (Table 1).

Table 2. Angiographic data

	Q wave (%)	Non-Q wave	P-value
Collaterals			
Yes	168 (63)	171 (68)	
No	97 (37)	80 (32)	0.03
CASS score for LV function			
Good	126	143	
Moderate	30	15	
Unknown	19	17	0.02
Calcifications			
No	194 (73)	195 (78)	
Yes	71 (27)	56 (22)	0.26
Number of diseased vessels			
1	86 (49)	94 (54)	
2	72(41)	70 (40)	
3	17 (10)	11 (6)	0.43
Main stem stenosis	4 (2)	3 (2)	
Stenosis diameter pre-PTCA (%)			
50-70	24 (9.1)	27 (10.8)	
70-90	107 (40.4)	122 (48.6)	
90-99	83 (31.3)	73 (29.1)	
100	51 (19.2)	29 (11.6)	0.06
Localization myocardial infarction			
Anterior	73 (42)	76 (43)	
Other	102 (58)	99 (57)	0.75

PTCA = percutaneous transluminal coronary angioplasty; CASS = Coronary Artery Surgery Study; LV = left ventricular.

Angiographic data

The number of patients with or without collaterals was the same in both groups, with a P value of 0.267. Stenosis severity prior to percutaneous transluminal coronary angioplasty was not statistically significantly different between the two groups on a categorial basis (P=0.057) when categorized as percentages documented between 50-70 %, 70-90 %, 90-99 %, and 100 %. In Table 2, the CASS classification of left ventricular function is shown. Only three non-Q wave myocardial infarction patients had a poor left ventricular function (Coronary Artery Surgery Study score 18 or 19), and one Q wave myocardial infarction patient had a poor left ventricular function (Coronary Artery Surgery Study score 18). Because of the small number of patients in

these categories, these patients were classified in the group with moderate left ventricular dysfunction.

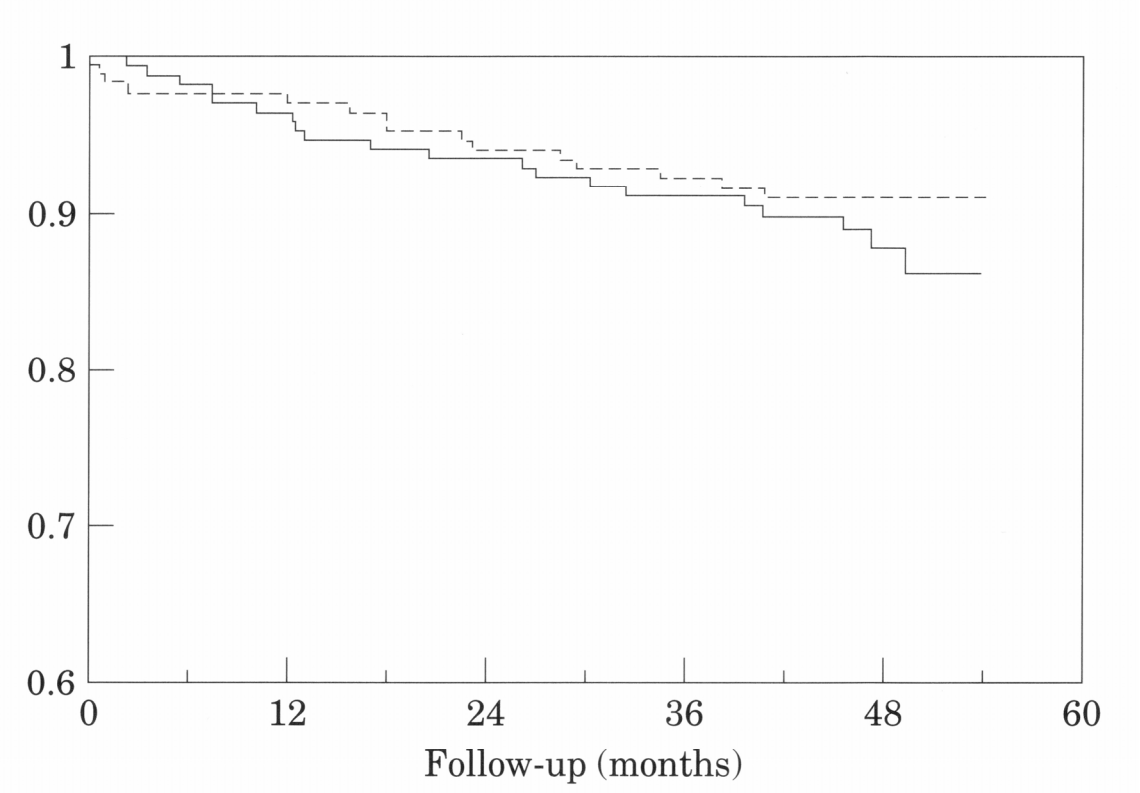


Figure 1. Freedom from all-cause mortality after PTCA for post infarct myocardial ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines.

The CASS score for ventricular function was assessed and found to be significantly different for the Q wave myocardial infarction patients as compared to the non-Q wave myocardial infarction patients (p=0.016). Fifteen of the 175 non-Q wave myocardial infarction patients had moderate left ventricular function as opposed to 30 in the Q wave myocardial infarction patients. The Cox proportional hazards model showed virtually identical hazards ratios for the Q wave and non-Q wave myocardial infarction patients when age, gender and left ventricular function score were incorporated in the model as compared to the univariate analyses. Only univariate hazard ratios are shown in Fig. 1.

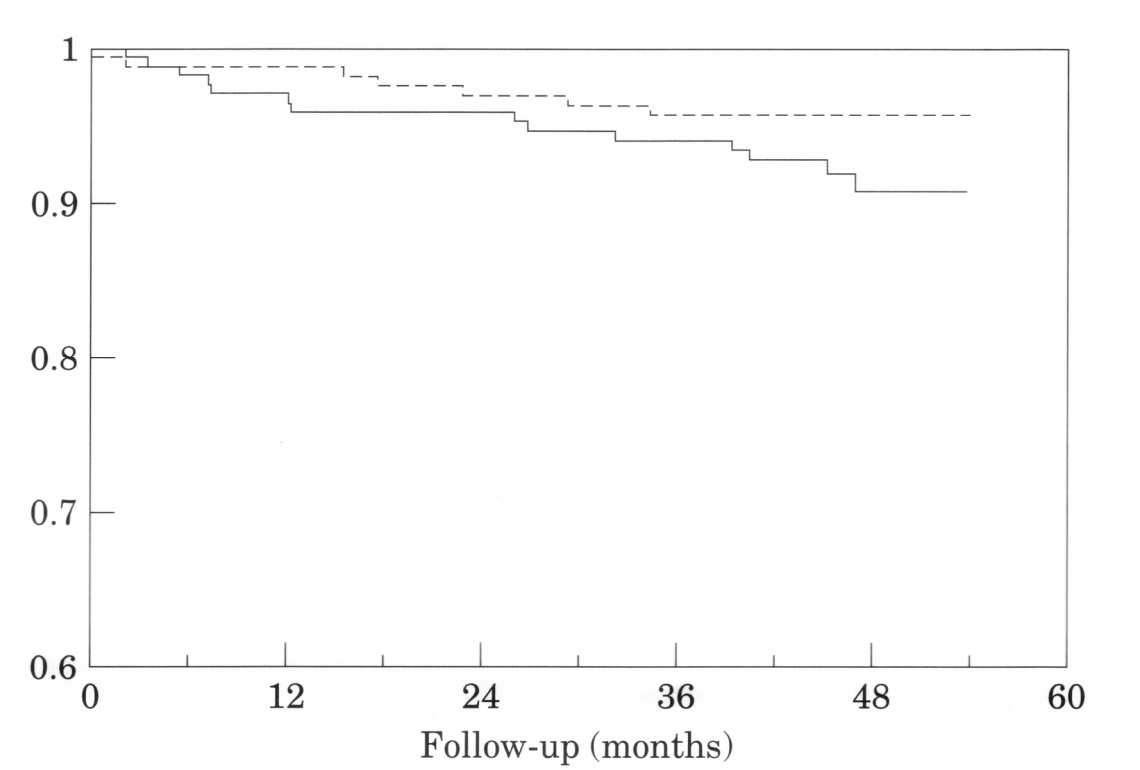


Figure 2. Freedom from cardiac death after PTCA for post infarct myocardial ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines. Symbols as in Fig. 1.

There were significantly more total occlusions with a P value of 0.02 in the Q wave patients (51 %) as compared to the non-Q wave patients (29 %). Other angiographic data including calcifications, number of diseased vessels and the localization of the myocardial infarction are given in Table 2.

Procedural results

In the 175 patients who underwent PTCA for angina pectoris after Q wave myocardial infarction, 265 lesions were dilated (1.5 lesions/patient). In the group with a non-Q wave myocardial infarction, 251 lesions were treated (1.4 lesions/patient). Success rates per patient in the Q wave group was 94 % (164/175), and in the non-Q wave myocardial 97 % (169/175) (P=0.21). No patient died or needed emergency bypass surgery in the first 48 hours (Table 3). Myocardial infarction as a complication of the angioplasty procedure occurred in 10 (5.7 %) of the Q wave myocardial

infarction patients and in 13 (7.4 %) of the non-Q wave myocardial infarct patients, P=0.52. Six patients from the Q wave group needed acute redilatation, vs. three in the non-Q wave group (P=0.5).

Table 3. Initial results (first 24 hours)

	Q wave (%)	Non-Q wave (%)	P-value
Dilated lesions	265	251	0.76
Lesions per patient	1.51	1.43	
Success rates	164(94)	169 (97)	0.21
Stenosis pre-PTCA SD	85 (12.6)	82 (11.8)	
Stenosis post-PTCA SD	14 (21.7)	11 (17.8)	
Complication <48 h			
Death	0	0	
Myocardial infarction	10	13	0.7
Bypass surgery	0	0	
PTCA	6	3	0.5

PTCA = percutaneous transluminal coronary angioplasty; SD = standard deviation.

Table 4. Long-term follow-up

	Q wave (%)	Non-Q wave (%)	P value
Mean follow-up (months)	43.32	45.02	0.83
No event	114	101	0.54
Event	61	74	0.40
Cardiac death	14(8)	7 (4)	0.12
Non-cardiac death	6 (3)	8 (5)	0.59
re-infarction related to the PTCA vessel	5 (3)	6 (3)	
re-infarction not related to the PTCA vessel	0(0)	7 (4)	0.76
Repeat PTCA			
Related vessel	13 (7)	19 (11)	0.27
Not related vessel	6 (3)	9 (5)	0.43
Bypass surgery	13 (7)	12 (7)	0.84

MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Follow-up

Mean follow-up was 44 ± 2 months in both groups (fig.3). During follow-up, 114 out of 175 patients in the Q wave group had remained free from any event (65.1

%), compared to 101 in the non-Q wave group (57.8 %), p=0,54. Angina pectoris recurred in 15 patients in the Q wave group and in 14 patients in the non-Q wave group (P=0-85). Twenty patients died in the Q wave group, of whom 14 for cardiac reasons; 15 died in the non-Q wave group, of whom 7 for cardiac reasons (P=0.53). Myocardial infarction related to the vessel in which PTCA was performed occurred in six patients in the non-Q wave group and in five patients in the Q wave group (P=0.76). Myocardial infarction not related to the vessel in which percutaneous transluminal coronary angioplasty was performed was only seen in the non-Q wave myocardial infarction group (n=7) (Fig 4, Table 4).

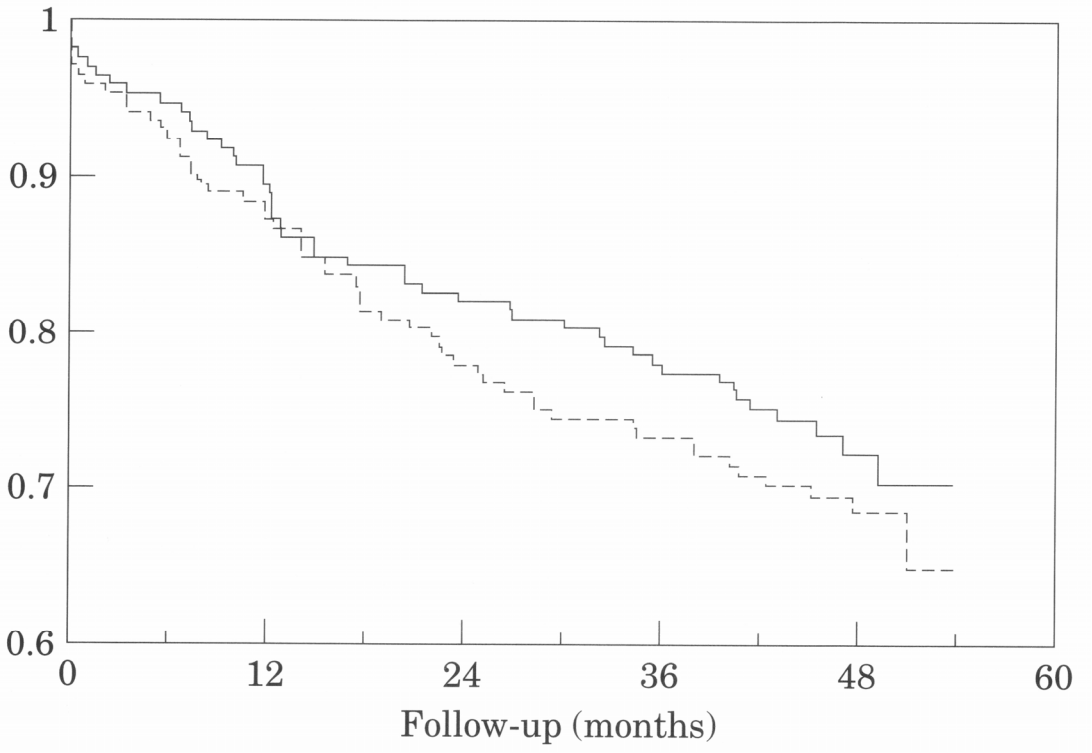


Figure 3. Freedom from death, myocardial infarction (MI), coronary artery bypass grafting (CABG), or related percutaneous transluminal coronary angioplasty (PTCA) after PTCA for post myocardial infarction ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines. Symbols as in Fig 1.

Bypass surgery was performed in 13 patients (7 %) in the Q wave group, and in 12 patients (7 %) of the non-Q wave group (fig 5). Repeat coronary angioplasty was performed in 13 patients (7 %) in the Q wave group, and in 19 (11 %) patients of the

non-Q wave group (fig. 6). Coronary angioplasty not related to the previous myocardial infarction area was performed in 6 patients (3 %) in the Q wave group, and in 9 patients (5 %) of the non-Q wave group (Table 4). Freedom from CABG or related PTCA is depicted in figure 7.

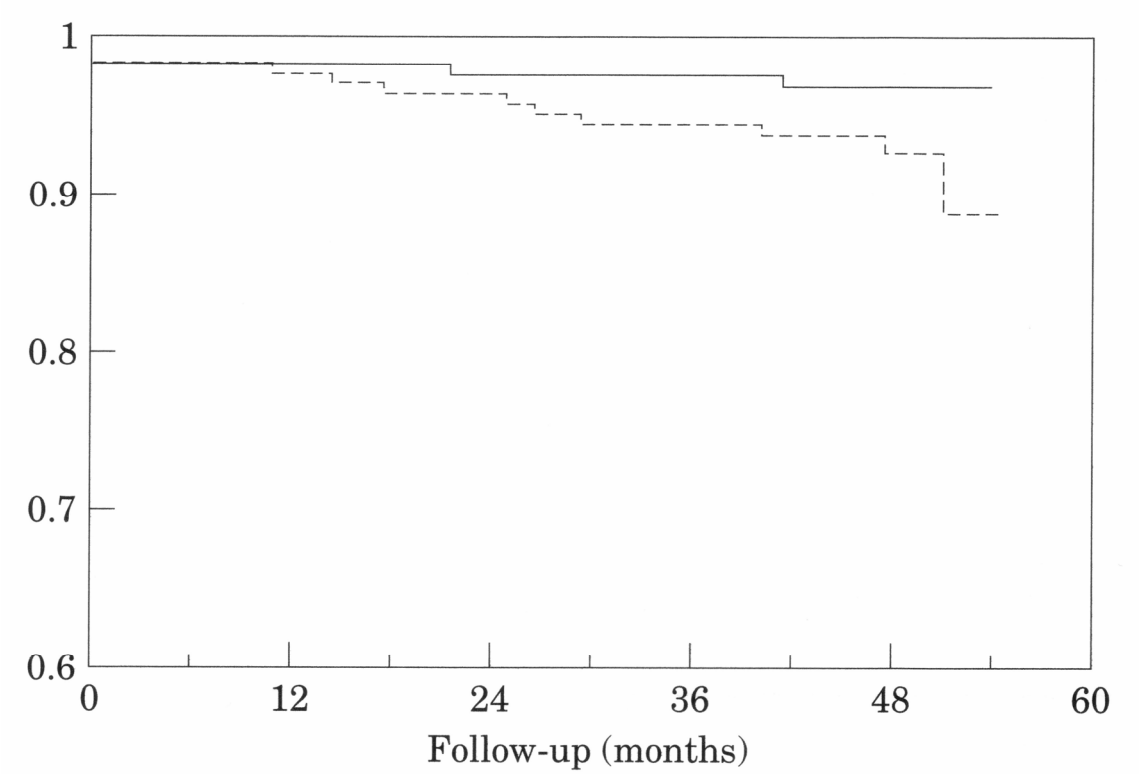


Figure 4. Freedom from myocardial infarction after PTCA for post myocardial infarction ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines. Symbols as in Fig. 1.

Discussion

Our results indicate that the initial and long-term outcome after PTCA for post-infarct angina pectoris is similar in patients who suffered from non-Q wave myocardial infarction or a Q wave myocardial infarction.

The literature on outcome after Q wave and non-Q wave myocardial infarction is, in many respects, conflicting.

In a non-selected group of patients with acute myocardial infarction, the incidence of a non-Q wave myocardial infarction is probably much higher than

previously reported (9,10). This may be due to better recognition of myocardial infarction, by the more sensitive creatine-kinase-MB assay, or to better medical treatment, specifically thrombolytic therapy, leading to early reperfusion (4,9,10-12).

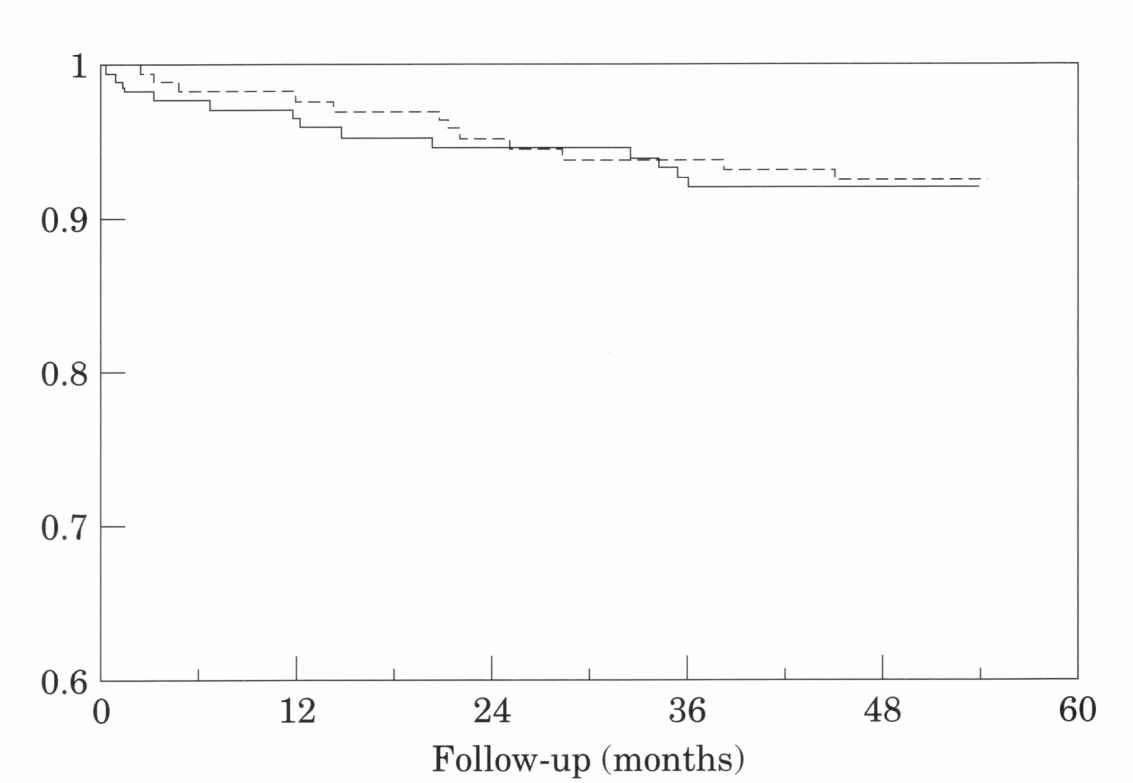


Figure 5. Freedom from CABG after PTCA for post myocardial infarction ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines. Symbols as in Fig. 1.

Non-Q wave myocardial infarction is more likely to affect an older population, with a higher proportion of women, more previous coronary events (9). In our patients, age and percentages of women were equal in both groups. Aguirre et al showed that in non-Q wave, as opposed to Q wave patients there were more women and fewer anterior wall infarctions, and that the left ventricular function was better.

Non-Q wave myocardial infarction is usually characterized by partial perfusion of the infarct-related artery by either collateral or antegrade flow, and by a lower incidence of intracoronary thrombus than in Q wave myocardial infarction (4,14,15,18,19). At angiography following non-Q wave myocardial infarction, arterial occlusion is usually subtotal, probably because reperfusion has occurred (13,16,17).

The size of non-Q wave myocardial infarction is therefore generally less extensive than Q wave myocardial infarction, as was shown by enzymatic, scintigraphic and angiographic data (1,6,20).

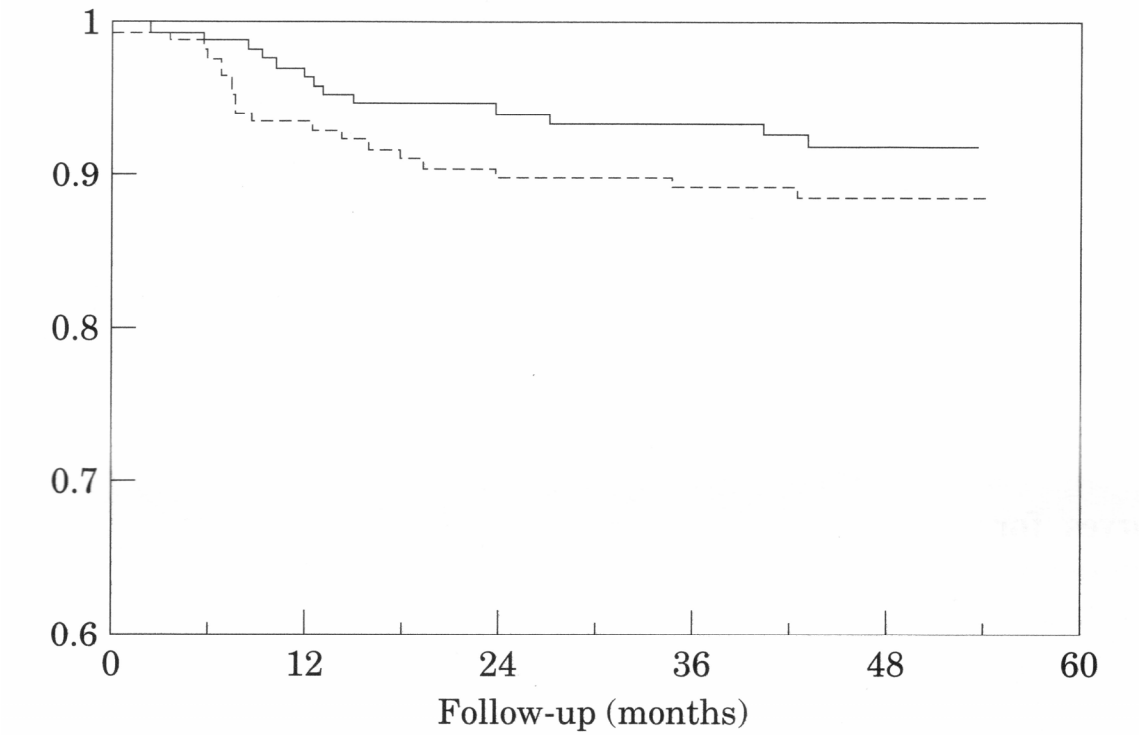


Figure 6. Freedom from related PTCA after PTCA for post myocardial infarction ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines. Symbols as in Fig. 1.

The same phenomenon of early reperfusion explains why the results of exercise stress testing and thallium myocardial scintigraphy suggest that residual myocardial ischaemia is more frequent and extensive after non-Q wave myocardial infarction (20). Long-term prognosis after non-Q wave myocardial infarction is also dependent on the amount of viable myocardial tissue at risk and the extent of collateral coronary circulation (20). So, although patients with non-Q wave myocardial infarction have a favourable short-term prognosis, late prognosis might be poorer due to a high incidence of recurrent unstable angina pectoris or myocardial infarction. Therefore, it is not surprising that mortality 1 year after the myocardial infarction was similar for both patients with Q wave and non-Q wave myocardial infarction (11,20,22-24). When infarction recurs after a non-Q wave myocardial infarction, this has a

deleterious effect on survival (3). Thus, is it possible to select and treat those patients who have an unfavourable long-term outcome? Post-infarction angina has been identified as an important risk variable for adverse long-term outcome in-patients with non-Q wave myocardial infarction (25,26). One study showed that only 25 % of the patients have angina pectoris after a non-Q wave myocardial infarction (27).

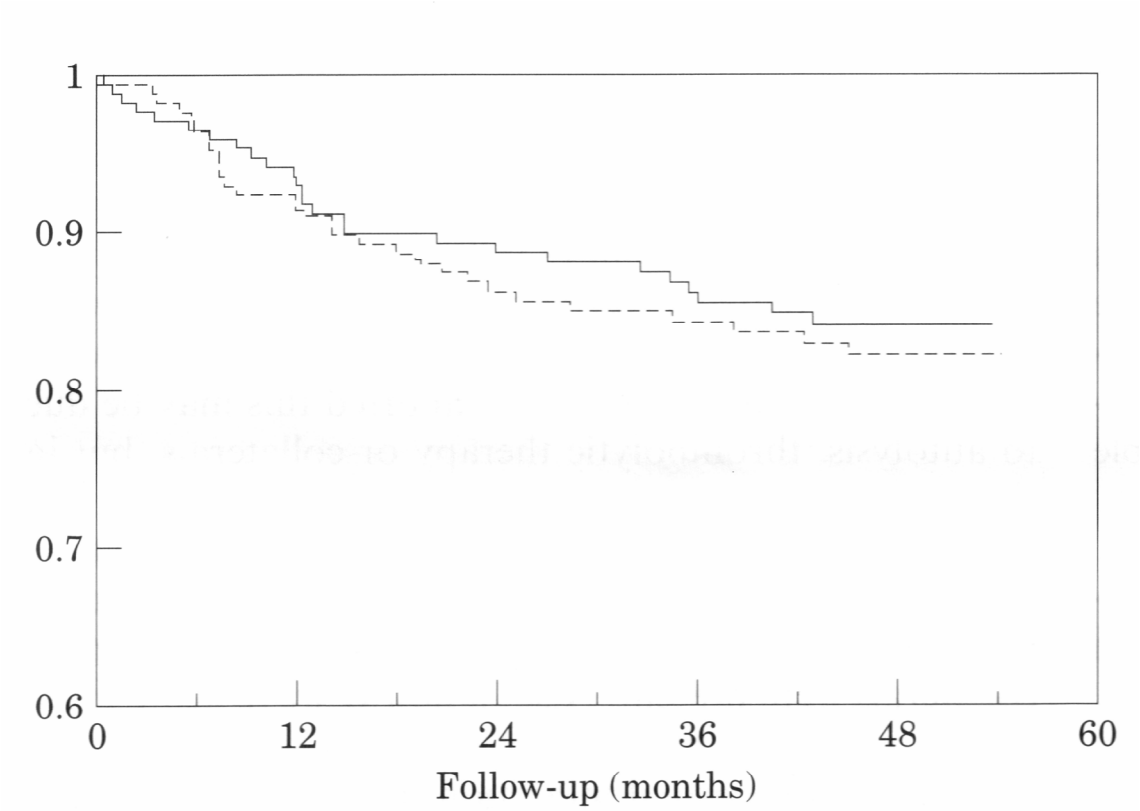


Figure 7. Freedom from CABG or related PTCA after PTCA for post myocardial infarction ischaemia. Non-Q wave myocardial infarctions are indicated by broken lines, Q wave myocardial infarctions by solid lines. Symbols as in Fig. 1.

Mickley et al (28) showed that in non-Q wave myocardial infarction the presence of ST segment depression on ambulatory electrocardiography recordings and exercise testing had a statistically significant predictive value for the development of future angina pectoris, whereas patients at increased risk for subsequent non-fatal reinfarction or cardiac death were not identified. Batalha et al (21) concluded from their study that it is not necessary to use invasive studies in every patient who has suffered a non-Q wave myocardial infarction without complications, since stress testing shows a high sensitivity (94.4 %) and specificity (75 %), and a high predictive

positive value (100 %) for predicting the risk of recurrent ischaemia. In patients with normal technetium-99m sestamibi stress testing, event rate was 12 % compared with 39 % of those with an abnormal test. Patients should be considered for angiography and revascularization when they continue to have anginal complaints, ischemic ECG abnormalities, or thallium perfusion defects on exercise especially if they already have reduced ventricular function (32).

Left ventricular function has an important influence on post infarct survival, particularly in (8,37,39) patients with more extensive coronary disease. In our study no significant difference in left ventricular function was present in each group which can explain the equal long-term outcome. It remains unclear whether complete revascularization is indicated for post myocardial infarction ischaemia. In our patients we tried to achieve complete revascularization as often as possible, as reflected by the number of 1.4-1.5 lesions dilated per patient. In a recent follow-up study, Weintraub et al. showed that associated significant disease in non-dilated segments was the strongest predictor of late events including death, myocardial infarction and need for a repeat revascularization (40). However others have indicated that patients are at an increased risk for recurrent ischaemia usually in the non-Q wave(41,42)myocardial infarction area.

Thus, although there is greater potential to salvage myocardium in patients with non-Q wave myocardial infarction, in our study group the clinical results after 4 years were not better in those patients than in the Q-wave myocardial infarction group. These somewhat surprising findings may, in part, be explained by careful patient selection, because PTCA was limited to lesions technically suitable for such procedure, and because patients were included on the basis of postinfarct ischaemia, either indicated by angina pectoris or positive functional testing. Our study was not randomized or compared to other treatments to resolve myocardial ischaemia.

Our data confirm that PTCA is an effective means for treating patients with ischaemia, both after non-Q wave and Q wave myocardial infarction. PTCA in such clinical setting provides not only a high primary success rate, but also a favourable outcome at 4 years, without differences between both groups.

In conclusion, PTCA for postinfarct angina pectoris or proven ischaemia has similar initial and long-term outcome in-patients with non-Q wave versus Q wave myocardial infarction. This indicates that revascularization strategies in case of residual post infarct ischaemia should not be based on the absence or presence of Q waves at the ECG.

References

(1) Keller K.B., Lemberg L. Q and non-Q wave myocardial infarctions. Am J Crit Care 1994; 3: 158-61.

(2) Finocchi G., Ometto R., La Vecchia L., et al. The clinical and prognostic significance of the infarct size in patients discharged after a myocardial infarction. Cardiologia 1991; 36: 563-8.

(3) Maisel A.S., Ahnve S., Gilpin E. et al. Prognosis after extension of myocardial infarction: the role of Q wave or non-Q wave infarction. Circulation 1985 71: 211-17.

(4) Goldberg R.J., Gore M., Alpert J.S., et al. Non-Q wave myocardial infarction: recent changes in occurrence and prognosis, a community wide perspective. Am Heart J 1987: 113: 273-9.

(5) Cannon D.S., Levy W., Cohen L.S. The short- and long-term prognosis of patients with transmural and nontransmural myocardial infarction. Am J Med 1976: 61: 452-8.

(6) Rigo P., Murray M., Taylor DR et al. Hemodynamic and prognostic findings in patients with transmural and nontrans mural infarction. Circulation 1975: 51: 1064-70.

(7) Nicholson M.R., Roubin G.S., Bernstein L., et al. Prognosis after an initial non-Q wave myocardial infarction related to coronary arterial anatomy. Am J Cardiol 1983; 52: 462-5.

(8) Mock M.B.. Ringqvist L., Fischer M.B. et al. Survival of medically treated patients in the coronary artery surgery study (CASS) registry. Circulation 1982: 66: 562-8.

(9) Andre-Fouet X., Pillot M., Leizoroviez A., et al. 'Non-Q-wave' alias nontransmural' myocardial infarction: A specific entity. Am Heart J 1989: 117: 893-902.

(10) Karlson B.W., Herlitz J., Richter A., et al. Prognosis in acute myocardial infarction in relation to development of Q-waves. Clin Cardiol 1991; 14: 875-80.

(11) Edlavitch S.A., Crow R., Burke G.L., et al. Secular trends in Q wave and non-Q wave acute myocardial infarction: The Minnesota Heart Survey. Circulation 1991; 83: 492-503.

(12) Huey B.L., Gheorghiade M., Crampton R.S. et al. Acute non-Q wave myocardial infarction associated with early ST segment elevation: evidence for spontaneous coronary reperfusion and implications for thrombolytic trials. J Am Coll Cardiol 1987; 9: 18-25.

(13) Aguirre F.V., Younis L.T., Chaitman B.R., et al. Early and 1 -year clinical outcome of patients' evolving non-Q-wave versus Q-wave myocardial infarction after thrombolysis. Results from The TIMI 11 study. Circulation 1995; 91: 2541-8.

(14) Sabia P.J., Powers E.R., Ragosta M., et al. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. N Engl J Med 1992; 327: 1825-31.

(15) Keen W.D., Savage M.P., Fischman D.L. et al. Comparison of coronary angiographic findings during the first six hours of non-Q-wave and Q-wave myocardial infarction. Am J Cardiol 1994; 74: 324-8.

(16) DeWood M.A., Stiffer W.F., Simpson et al. Coronary arterio graphy findings soon after non-Q-wave myocardial infarction. N Engl J Med 1986; 315: 417-23.

(17) Fuster V., Badimon L., Badimon J.J., et al. The pathogenesis of coronary artery disease and the acute coronary syndromes. N Engl J Med 1992; 326: 310-18.

(18) Schaper W., Frenzel H., Hort W. Experimental coronary artery occlusion 1. Measurement of infarct size. Basic Res Cardiol 1979; 74: 46-53.

(19) Reimer K.A., Jennings R.B. The 'wavefront phenomenon' of myocardial ischemic cell death 11. Transmural progression of necrosis within the framework of ischemic bed size (myocardium at risk) and collateral flow. Lab Invest 1979; 40: 633-44.
(20) Gibson R.S. Current problems in Cardiology. Chicago: Year book of cardiovascular medicine. 1988: 1-72.
(21) Gibson R.S., Curling R.M., Czaddock G.B. et al. Prevalence and clinical significance of residual myocardial ischaemia two weeks after acute non Q-wave infarction. Circulation 1983; 68 (Suppl): 111-30.
(22) Hollander G., Ozick H., Greengart A., et al. High mortality early reinfarction with first nontransmural myocardial infarction. Am Heart J 1984; 108: 1412-16.
(23) Krone R.J., Friedman E., Thanavaro S., et al. Long-term prognosis after first Q-wave (transmural) or non-Q-wave (nontransmural) myocardial infarction: analysis of 593 patients. Am J Cardiol 1983; 52: 234-9.
(24) Lekasis J., Katsoyanni K., Trichopoulos D., et al. Q- versus non-Q-wave myocardial infarction: clinical characteristics and 6-month prognosis. Clin Cardiol 1984; 7: '183-8.
(25) Boden W.E. Strategies for managing the patient with acute non-Q-wave myocardial infarction. Clinical Cardiology 1989; 12 (7 Suppl 3): 111 33-40.
(26) Larsson H., Areskog M., Areskog N-H. et al. The diagnostic and prognostic importance of ambulatory ST recording compared to a predischarge exercise test after an episode of unstable angina or non-Q wave myocardial infarction. Eur Heart J 1995; 16: 888-93.
(27) Bellamy G.R., McEniery P.T., Zaidi A.R., et al. Percutaneous transluminal coronary angioplasty after non-Q-wave infarction. Cleve Clin J Med 1989: 56: 141-5.
(28) Mickley H., Pless P., Nielsen J.R. et al. Residual myocardial ischaemia in first non-Q-wave versus Q-wave infarction: maximal exercise testing and ambulatory ST-segment monitoring. Eur Heart J 1993: 14: 18-25.
(29) Batalha V., Mourao L., Cunha J., et al. Risk stratification in non-Q-wave myocardial infarction. Rev Port Cardiol 1993; 12: 731-5.
(30) Stratmann H.G., Younis L.T., Wittry M.D., et al. Exercise technetium-99m myocardial tomography for the risk stratification of men with medically treated unstable angina pectoris. Am J Cardiol 1995; 76: 236-40.
(31) Gibson R.S. Management of acute non-Q-wave myocardial infarction: role of prophylactic pharmacotherapy and indications for predischarge coronary arteriography. Clin Cardiol 1989; 12 (7 Suppl 3): 11126-32.
(32) Cheitlin M.D. Non-Q-wave infarct: diagnosis, prognosis and treatment. Adv Intern Med 1988; 33: 267-94.
(33) Alfonso F., Macaya C., Iniquez A., et al. Percutaneous transluminal coronary angioplasty after non-Q-wave acute myocardial infarction. Am J Cardiol 1990; 65: 835-9.
(34) Suryapranata H., Beatt K., De Feyter P.J., et al. Percutaneous transluminal coronary angioplasty for angina pectoris after a non-Q-wave acute myocardial infarction. Am J Cardiol 1988; 61: 240-3.
(35) Safian R.D., Snijder L.D., Snijder B.A., et al. Usefulness of percutaneous transluminal coronary angioplasty for unstable angina pectoris after non-Q-wave acute myocardial infarction. Am J Cardiol 1987; 59: 263-6.
(36) Williams D.B., Ivey T.D., Bailey W.W., et al. Post-infarction angina: results of early revascularization. J Am Coll Cardiol 1983; 2: 859-64.
(37) Mundth E.D., Austen W.G. Surgical measures for coronary heart disease. N Engl J Med 1975; 293: 13-19.
(38) Le Feuvre C., Bonan R., Cote G., et al. Five- to ten-year outcome after multivessel percutaneous transluminal coronary angioplasty. Am J Cardiol 1993; 71: 1153-8.
(39) Sanz G., Lastanar A., Betriu A., et al. Determinants of prognosis in survivors of myocardial infarctions. A prospective clinical angiography study. N Engl J Med 1982; 306: 1065-70.
(40) Weintraub W.S., Ghazzal Z.M.B., Cohen C.L., et al. Clinical implications of late proven patency after successful coronary angioplasty. Circulation 1991; 84: 572-82.
(41) Bisset J.K., Matts J., Sharma B. Residual myocardial jeopardy in patients with after Q-wave and non-Q-wave infarction. Br Heart J 1987; 58: 460-4.

(42) Marmor A., Sobel B.E., Roberts R. Factors presaging early recurrent myocardial infarction ('extension'). Am J Cardiol 1981; 48: 603-10.

Chapter 4

Percutaneous transluminal coronary angioplasty in patients with acute myocardial infarction: towards a regional infarction center.

B.R.G. Brueren, M.J. Suttorp, M.A.J. Landman, E.G.Weijers, A.C. Bredero, H.W.M. Plokker.

Department of Cardiology, St Antonius Hospital, Nieuwegein.

Published in part in Cardiologie 2001;8:104-9.

Abstract

Background. PTCA (percutaneous transluminal coronary angioplasty) is often performed for acute myocardial infarction as primary (instead of thrombolysis) or rescue procedure (after failure of thrombolysis). This study describes the results of all 173 patients who were referred to the St. Antonius Hospital for PTCA for acute myocardial infarction from the Utrecht/Nieuwegein region in 1997.

Methods. One-hundred and fifty-three patients underwent PTCA within six hours after the onset of symptoms; 27 patients underwent a rescue PTCA.

Results. Angioplasty was performed in the LAD in 69%, in the RCA in 22%, in the RCX in 5%, and in the bypass graft in 3% of the cases. Thirteen patients (7.5%) required intra-aortic balloon pumping, and in 27 patients (16%) one or more stents were used. The procedure was successful in 169 patients (98%), and myocardial infarction could be prevented completely in 32 patients (19%). In 115 patients (16%) only a non-Q-wave myocardial infarction occurred. Urgent bypass surgery was required in one patient. Nine patients (5%) died in the acute phase, and nine patients died in the follow-up period of one year (5%). Three patients had a recurrent myocardial infarction within 6 months, five patients underwent repeat PTCA because of restenosis, and 7 patients underwent an elective bypass surgery.

Conclusion. In patients who are admitted with acute myocardial infarction, good results can be achieved by referring those patients for PTCA, even in the higher-risk groups. Therefore we plead for regional myocardial infarction centers.

Introduction

During acute myocardial infarction (MI), early reperfusion of the occluded coronary artery is of paramount importance to preserve myocardium and to reduce mortality and complications (1-7). Prognosis is determined to a large degree by early opening of the infarct related artery.

It has been recognized more and more that primary percutaneous coronary intervention (PCI) is at least as good as thrombolytic therapy during acute MI (2,4,5,8-25). The advantage of the so-called rescue PCI (after failed thrombolysis), has not been clearly established yet (3,4,10-12).

Performing primary PCI during acute infarction is associated with a number of logistic and infrastructural problems. Only few hospitals have the possibilities to perform primary PCI around the clock.

In the present study, we investigated the feasibility of performing primary PCI in an urban area with an optimum cooperation between referring hospitals, ambulance services, and the primary PCI center, and a transportation delay of a maximum of 45 minutes between different hospitals.

Patients and Methods

All patients were studied who were admitted either to the primary PCI center or to one of the referring hospitals during the year 1997 and who were treated by PCI either primary or as rescue procedure. Indications for primary PCI were anterior wall myocardial infarction, or inferior wall infarction with right ventricular involvement and/or hemodynamic instability, a new developing left bundle branch block, or contraindications for thrombolytic therapy. Only patients who presented less than six hours after the start of symptoms were included. Also patients referred for rescue PCI after failed thrombolytic therapy were included, if the criteria mentioned above were fulfilled.

During the transportation, aspirin and nitrate were started and at the start of the procedure, heparin was administered according to routine at that time.

Stents were used according to the routine of 1997, i.e. in case of suboptimal result of balloon angioplasty. Intraaortic balloon counter pulsation was used in case of cardiogenic shock, defined as systolic blood pressure below 80 mmHg.

PCI was considered successful if a residual stenosis of less than 30% was achieved by visual estimation. Clinical follow-up was performed after 48 hours and after 1 year.

Results

A total of 173 patients were included in the study, of whom 146 underwent primary PCI and 27 rescue PCI after failed thrombolysis. Of these, 103 patients were referred from the adjacent hospitals and 70 patients presented at the primary PCI center itself.

The average time delay between the first ECG made in the hospital and the opening of the infarct related artery was 81 minutes for the primary PCI group, and 104 minutes for the rescue group. A total of 201 coronary arteries were dilated (1.16 per patient).

Table 1. Patient characteristics

Number of patients	173
Presentation in peripheral hospital	103 (60 %)
Presentation in St Antonius Hospital	70 (40 %)
Number of lesions	201 (1,16 pp)
Female	27 (16 %)
Age	59 ± 16
Time AMI – PCI	
<6 hours	153 (88 %)
>6 and < 24 hours	20 (12 %)
Mean delay ECG – open vessel (rescue PCI)	104 min
Mean delay ECG – open vessel (primary PCI)	81 min
Thromobolytic therapy in these 27 pts receiving rescue PCI	
Anterior	14 (52 %)
Inferior	12 (44 %)
Lateral	1 (4 %)

AMI = Acute myocardial infarction; PCI = Percutaneous coronary intervention.

Average age of the patients was 51 years. Baseline characteristics are mentioned in Table 1. Of those patients undergoing rescue PCI, 14 experienced an anterior wall myocardial infarction, and 12 patients had an inferior wall myocardial infarction. In one patient a lateral infarction was present. In 140 patients (80%), the infarct related artery was occluded. One hundred six patients had one vessel disease, 40 two-vessel disease, and 27 patients three-vessel disease (61 %, 23 %, and 16 %, respectively).

Table 2. Angiographic data

	N (%)
Number of diseased vessel	
1-vessel	106 (61)
2-vessel	40 (23)
3-vessel	27 (16)
Complete revascularization	
No	128 (74)
Yes	45 (26)
Infarct related vessel	
RCA	38 (22)
RDA	120 (69)
RCX	10 (6)
Grafts	5 (3)
IABP placed	13 (8)
Stents	27 (16)
Thrombolysis IC	3 (2)

RCA = Right coronary artery; RCX = Ramus circumflexus; RDA = Ramus descendus anterior; IABP = Intra aortic balloon pump; IC = Intracoronary.

The infarct related artery was the left anterior ascending artery in 69% of the patients, the right coronary artery in 22%, and the circumflex artery in 6%. In 3% of the patients, the infarct related artery was a bypass graft (Table 2). Angiographic technical successful PCI could be performed in 169/173 patients (98%). In 32 patients no enzymes elevation or Q- wave developed.

Of those 146 patients undergoing primary PCI, 9 patients (5%) died within 48 hours because of cardiogenic shock in 7 patients, 1 patient because of a severe cerebrovascular accident, and one patient because of multi organ failure. Of those 27 patients with a rescue PCI, 1 patient died within 48 hours (Table 3).

Table 3. Success and complications

	N (%)
Primary procedures	**146 (84)**
Success	
Yes	143 (98)
No	3 (2)
Myocardial infarction	
None	27 (19)
Q-wave	95 (65)
Non-Q-wave	24 (16)
Emergency redilatation	1 (0.6)
Emergency CABG	1 (0.6)
Death	9* (5)
Rescue procedures	27 (16)
Success	
Yes	26 (96)
No	1 (4)
Myocardial infarction	
None	5 (19)
Q-wave	20 (74)
Non-Q-wave	2 (7)
Redilation or CABG	0 (0)
Death	1 (4)

* *In 3 patients the procedure was not successful. CABG = Coronary artery Bypass Grafting.*

Complete follow-up was obtained in 96% of the patients (Table 4). During 1-year follow-up, another 9 patients died (5.2%), and therefore, total survival after 1 year was 89.8%. During follow-up 5 patients (3%) underwent re-PCI, and 7 patients underwent bypass surgery. In 9.8% of the patients, angina pectoris re-occurred. The 1-year-survival is presented in figure 1.

Discussion

The major goal in patients with acute myocardial infarction is early reperfusion of the treated myocardium and preservation of left ventricular function (25). This goal can be achieved either by thrombolytic therapy or primary PCI. With the first treatment, a maximum of 70% of the patients achieves early reperfusion. Of these patients, in large meta analysis, about 10% of the patients dies within the first 2 months after infarction.

Table 4. 12-month follow-up

	N (%)
Lost to follow-up	7 (4)
No complaints	113 (69)
Recurrence of angina pectoris	
NYHA I	4
NYHA II	8
NYHA III	2
NYHA IV	2
Positive Thalliumscan without angina pectoris	2
Treatment of recurrent AMI	
Conservative	1 (0.6)
Alteplase	1 (0.6)
Streptokinase	1 (0.6)
Re-PCI	
Same lesion	1 (0.6)
Other segment	4
Elective CABG	7 (4)
Heart failure	
NYHA I	2 (1.2)
NYHA IV	6 (3.7)
Acute heart failure	2 (3.7)
Death	
Pneumonia and septic shock	1 (0.6)
Failed thrombolysis	1 (0.6)
Cardiogenic shock	5 (3.1)
OHCA	1 (0.6)
Unknown	1 (0.6)

NYHA = New York Heart Association; PCI = Percutaneous coronary intervention; CABG = Coronary artery bypass grafting; OHCA = Out-of-hospital cardiac arrest.

From literature, it is known that a reperfusion rate of more than 90% can be achieved with primary PCI. Also, mortality data in these patients indicate a favorable outcome compared to thrombolysis (3,4,8,11-17,19-22,25-29). Those mortality data, however, are from studies including all patients with PCI including those with small myocardial infarctions. In our present study, it should be noted that the average patient was a high risk patient. And therefore, the mortality rate is not completely comparable with the larger studies often referred to in literature.

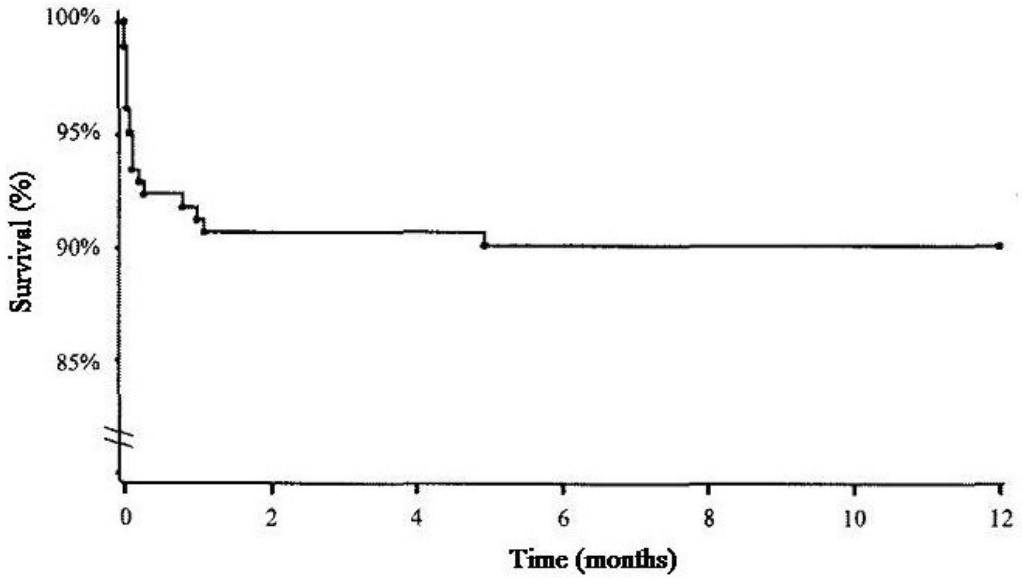


Figure 1. 1-year survival.

Our present strategy is that patients with extensive myocardial infarction, are transferred to the heart center as early as possible to undergo primary PCI. In this group of patients, the achieved early reperfusion rate was 98% of the cases. Nevertheless, the 48 hours mortality in this group was approximately 5% and another 5% mortality was observed in the first year. Compared to the literature in similar patient groups with a high risk, these numbers seem to be favorable. From large randomized studies, it is still not clear if rescue PCI after failed thrombolysis, decreases mortality or severe congestive heart failure (4,10). But in many of those studies, the rescue PCI is performed rather late (up to 12 hours). The proportion of patients with rescue PCI in the present study, is too small to draw conclusions in this field. Nevertheless, the outcome of these patients was favorable compared to literature, and our data even suggest that after failed thrombolysis and ongoing ischemia, rescue PCI makes sense, especially in those high risk patients as included in this study.

In the PRAGUE study, 3 different strategies to treat acute myocardial infarction were investigated:

A. Patients receiving thrombolysis in the referring hospital.

B. Patients receiving thrombolysis in the referring hospital, with immediate transportation to the heart center for PCI in case of failed thrombolysis.

C. Patients not receiving thrombolysis but transported directly to the heart center for primary PCI.

This study showed that transferring patients from community hospitals to a tertiary angioplasty centre in the acute phase is feasible and safe. This strategy is associated with a significant reduction in the incidence of reinfarction and the combined clinical end-point of death/reinfarction/stroke at 30 days when compared to standard thrombolytic therapy at the community hospital.

A fourth strategy, so-called facilitated PCI, was not investigated in that study. Another option, performing PCI in the referral center, was not investigated either. The latter option doesn't seem realistic nor optimum in a country like The Netherlands. To run a PCI center, a service around the clock and around the year, is necessary and sufficient experience outside the setting of acute AMI is mandatory too. Moreover, as we showed in this study, only little time was lost by transporting the patients from the referring hospital to the PCI center.

Summary and Conclusion

From this study, it can be concluded that it is feasible within The Netherlands to organize the care for patients with acute myocardial infarction in a heart center clustered way, similar to the situation for elective PCI and bypass surgery. Patients can be admitted to the nearest hospital and receive thrombolytic therapy or transported directly to the regional heart center in case of high risk (large anterior wall infarctions or RCA occlusions with right ventricular involvement and/or hemodynamic instability).

The logistic consequences should not be underestimated because this means a 24-hours availability of a team of 4-5 specialists/technicians, adequate training and organization of emergency and coronary care departments in the referring hospitals and ambulance services. If organized in a proper way as described here, from our study it can be concluded that even in these patients with high risk, 48 hours mortality can be reduced to approximately 5% with another 5% during the first year.

The present management of patients with acute myocardial infarction in the Eindhoven area is formulated in chapter 10.

References

(1) Anderson J.L., Karagounis L.A., Becker L.C., et al. TIMI perfusion grade 3 but not grade 2 results in improved outcome after thrombolysis for myocardial infarction. Ventriculographic, enzymatic, and electrocardiographic evidence from the TEAM-3 Study. Circulation 1993;87:1829-39.

(2) Simes R.J., Topol E.J., Holmes D.R., et al. Link between the angiographic substudy and mortality outcomes in a large randomised trial of myocardial perfusion. Importance of early and complete infarct artery reperfusion. GUSTO-1 Investigators. Circulation 1995;91:1923-8.

(3) Fibrinolytic Therapy Trailists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1000 patients. Lancet 1994;343:311-22.

(4) Michels K.B., Yusuf S. Does PTCA in acute myocardial infarction affect mortality and reinfarction rates? A quantitative overview (meta-analysis) of the randomized clinical trials. Circulation 1995;91:476-85.

(5) The GUSTO Angiographic Investigators. The effect of tissue plasminogeen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. N Engl J Med 1993;329:1615-22.

(6) Kleiman N.S., White H.D., Ohman E.M., et al. GUSTO Investigators. Mortality within 24 hours of thrombolysis for myocardial infarction. The importance of early reperfusion. The GUSTO Investigators, Global Utilization of Streptokinase and Tissue Plasminogeen Activator for Occluded Coronary Arteries. Circulation 1994;90:2658-65.

(7) Simoons M.L., Serruys P.W., van den Brand M., et al. Early trombolysis in acute myocardial infarction: limitation of infarct size and improved survival. J am Coll Cardiol 1986;7:717-28.

(8) Zahn R., Schuster S., Schiele R., Seidl K., et al. Comparison of primary angioplasty with conservative therapy in patients with acute myocardial infarction and contraindications for trombolytic therapy. Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Study Group. Catheterization and Cardiovascular interventions 1999;46:127-33.

(9) Califf R.M., Topol E.J., Stack R.S., et al. Evaluation of combination trombolytic therapy and timing of cardiac cathererization in acute myocardial infarction: results of thrombolysis and angioplasty in myocardial infarction-phase 5 randomized trail. TAMI Study Group, Circulation 1991;83:1543-56.

(10) Abbotthsmith C.W., Topol E.J., George B.S., et al. Fate of patients with acute myocardial infarction with patency of the infarct-related vessel achieved with successful thrombolysis versus rescue angioplasty. J Am Coll Cardiol 1990;16:770-8.

(11) Mc Kendall, Forman S., Sopko G., et al. Value of rescue percutaneous transluminal coronary angioplasty following unsuccessful thrombolytic therapy in patients with acute myocardial infarction. Thrombolysis in Myocardial Infarction Investigators. Am J Cardiol 1995;76:1198-11.

(12) Grines C.L., Browne K.F., Marco J., et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The Primary Angioplasty in Myocardial Infarction Study Group. N Engl J Med 1993;328:637-9.
(13) Zijlstra F., De Boer M.J., Hoorntje J.C., et al. A comparison of immediate coronary angioplasty with intraveneous streptokinase in acute myocardial infarction. N Engl J Med 1993;328:680-4.
(14) Gibbons R.J., Holmes D.R., Reeder G.S., et al. immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. The Mayo Coronary Care Unit and Catheteriztion Laboratory Groups. N Engl J Med 1993;328:685-91.
(15) De Boer M.J., Suryapranata H., Hoorntje J.C., et al. Limitation of infarct size and preservation of left ventricular function after primary coronary angioplasty compared with intravenous streptokinase in acute myocardial infarction. Circulation 1994;90:753-61.
(16) Brodie B.R., Grines C.L., Ivanhoe R., et al. Six-month clinical and angiographic follow-up after direct angioplasty for acute myocardial infarction. Final results from the Primary Angioplasty Registry. Circulation 1994;90:156-62.
(17) De Boer M.J., Reiber J.H., Suryapranata H., et al. Angiographic findings and catheterization laboratory events in patients with primary coronary angioplasty or streptokinase therapy for acute myocardial infarction. Eur Heart J 1995;16:1347-55.
(18) De Boer M.J., Hoorntje J.C., Ottervanger J.P., et al. Immediate coronary angioplasty versus intravenous streptokinase in acute myocardial infarction: left ventriculair ejection fraction, hospital mortality and reinfarction. J Am Coll Cardiol 1994;23:1004-8.
(19) O'Keefe J.H. Jr, Rutherford B.D., McConahay D.R., et al. Early and late results of coronary angioplasty without antecedent thrombolytic therapy for acute myocardial infarction. Am J Cardiol 1989;64:1221-30.
(20) O'Keefe J.H. Jr, Baily W.L., Rutherford B.D., et al. Primary angioplasty for acute myocardial infarction in 1,000 consecutive patients. Results in an unselected population and high-risk subgroups. Am J Cardiol 1993;72:107G-15G.
(21) Lee L., Bates E.R., Pitt B., et al. Percutaneous transluminal coronary angioplasty improves survival in acute myocardial infarction complicated by cardiogene shock. Circulation 1988;78:1345-51.
(22) Weaver W.D., Litwin P.E., Martin J.S. Use of direct angioplasty for treatment of patients with acute myocardial infarction in hospitals with and without on-site cardiac surgery. The Myocardial Infarction, Triage, and Intervention Project Investigators. Circulation 1993;88:2067-75.
(23) Topol E.J., Califf R.M., George B.S., et al. A randomized trail of immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. N Engl J Med 1987;317:581-8.
(24) Zijlstra F., Hoorntje J.C., Boer M.J. de, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1999;341:1413-9.
(25) Stampfer M.J., Goldhaber S.Z., Yusuf S., et al. Effect of intravenous streptokinase on acute myocardial infarction:pooled results from randomized trails. N Engl J Med 1982;307:1180-2.
(26) Ellis S.G., da Silva E.R., Heyndrickx G.R., et al. Final results of the RESCUE study evaluating PTCA after failed thrombolysis for patients with anterior infarction [abstract]. Circ 1993;88(supp):1106.
(27) Ellis S.G., da Silva E.R., Heyndrickx G.R., et al. Randomized comparison of rescue angioplasty with conservative management of patients with early failure of thrombolysis for acute anterior myocardial infarction. Circulation 1994;90:2280-4.
(28) Widimsky P., Groch L., Zelizko M., et al. Multicentre randomized trail comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J 2000;21:823-31.
(29) Vermeer F., Oude Ophuis A.J., Berg E.J. van de, et al. Prospective randomised compartison between thrombolysis, rescue PTCA, and primary PTCA inpatients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart 1999;82:426-31.

Chapter 5

How good are experienced cardiologists in predicting the hemodynamic severity of coronary stenoses when taking fractional flow reserve as the gold standard.

B.R.G. Brueren, J.M. ten Berg, M.J. Suttorp, E.T. Bal, J.M.P.G. Ernst, E.G. Mast, H.W.M. Plokker.

Published in part in The International Journal of Cardiovascular Imaging 2002:18;73-76.

Presented in part on the XXII Congress of the European Society of Cardiology, August 26-30, 2000.

Abstract

Background**.** Coronary angioplasty should be based on documented ischemia. However, in daily clinical practice the indication for angioplasty is often based on eyeball assessment of the severity of the stenosis. This study was performed to assess the accuracy of eyeball estimation of coronary stenosis when taking fractional flow reserve (FFR) as gold standard.

Methods**.** Lesions were studies where no mutual agreement on the severity of the stenosis was obtained. The procedure consisted of a repeat control angiogram, FFR measurement and in case of FFR<75% Percutaneous Trans Coronary Angioplasty. The eyeball assessment of the stenosis was written down before further execution of the procedure. FFR was measured with a pressure monitoring guide. Maximal myocardial hyperemia was induced by intra venous adenosine infusion.

Results Fifty-two patients were studied. Agreement between eye ball assessment and FFR existed in a total of 36 cases (69.2%). Over estimation of hemodynamic severity occurred in 6 cases (11.5%) and under estimation in 10 cases (19.2%). Consequently, the positive predictive value of eyeball assessment for pressure-derived FFR was 63% and the negative predictive value 76%.

Conclusion: The assessment of the hemodynamic severity of intermediate coronary stenosis should not be based on eyeball assessment even by experienced interventional cardiologists.

Introduction

Decisions regarding coronary interventions should be based on objective evidence of ischemia on one hand and coronary angiographiy on the other hand (1). Evidence of ischemia may be obtained from non-invasive investigations, such as exercise tests, myocardial scintigraphy and stress echocardiography. It is not difficult to infer the physiological significance of angiographically severe stenoses (>80% diameter stenosis) or minimal disease (<30% diameter stenosis). However, angiographic interpretation of intermediate stenosis has had a poor correlation with actual measurements of blood flow (2). Thus, decisions to revascularize patients with intermediate lesions based on angiographic appearance are potentially fraught with a high degree of inaccuracy. However in many of such patients percutaneous transluminal coronary angioplasty (PTCA) is performed solely on angiography. A catheter-based alternative for ischemia detection is measurement of fractional flow reserve (FFR). FFR measures the consequence of the stenosis in terms of reduction of myocardial blood flow. FFR reliably identifies stenoses associated with inducible ischemia with an accuracy>90%, which is higher than for any other (non)invasive tests (3-6). An additional advantage of FFR is that it provides lesion specific information, contrary to non invasive techniques. Nevertheless, the decision for PTCA is often taken on the basis of eyeball estimation of stenosis only. This study was performed to assess the accuracy of eyeball estimation of coronary stenosis when taking FFR as gold standard in cases where the severity of a stenosis was disputable.

Methods

Patient population

This study was performed at one high volume center with 6 interventional cardiologists performing a total of 2,000 angioplasty procedures per year. Approximately 70% of the patients were referred from other hospitals. Diagnostic coronary angiograms were reviewed on a daily basis by the ‘heart-team’, in which cardiologists, thoracic surgeons and interventional cardiologists were represented.

Each case was discussed until the therapy of choice was mutually agreed. In case of disagreement on the severity of stenosis the patient was included in this study. From January 1999 until January 2000 fifty-two patients were included. Informed consent was obtained in all patients prior to the study.

Procedure

The procedure consisted of a repeat control angiogram, FFR measurement, and PTCA with or without placement of a stent, if FFR was ≤0.75. The procedure was carried out by means of 7F guiding catheters. Angiography was performed in at least two orthogonal projections. The eyeball assessment of the severity of target stenosis by the interventional cardiologist was written down on the study work sheet before further execution of the procedure. Subsequently, FFR (myo) was measured using a pressure monitoring guide wire (Pressure Guide, Radi Medical Systems, Uppsala, Sweden). Maximal myocardial hyperemia was induced by intra venous adenosine infusion. The infusion rate was 140-microgram/kg bodyweight per minute for a duration of 2-4 minutes. FFR (myo) was calculated by the ratio of distal coronary pressure (Pd) and aortic (Pa) during steady state hyperaemia following the formula: FFR(myo)=Pd/Pa (6).

Results

Baseline & angiographic characteristics

Fifty-two patients (42 men and 10 women) were studied. Eighty-one percent of the patients were male; seventeen patients (32.4%) had a previous myocardial infarction not related to the target lesion. Eight patients (15.4%) had a previous PTCA. All patients had stable angina pectoris according to the Canadian Cardiovascular Society classification. Most patients had 1-vessel disease located in the left anterior descending artery. Baseline characteristics are presented in table 1.

Table 1. Clinical and angiographic characteristics

Age	65.0 years +/- 10.9
Gender	Male: 42 (80.8%)
	Female: 10 (19.2%)
Risk factors	
Diabetes mellitus	10 (19.2%)
Hypertension	12 (23.1%)
Total cholesterol	39 (75%)
Smoking preceding half year	12 (23.1%)
Clinical features	
Previous MI	17 (32.7%)
Previous PTCA	8 (15.4%)
Angina pectoris	
I	1 (1.9%)
II	44 (84.6%)
III	2 (3.8%)
Statin	28 (53.8%)
Number of diseased vessels	
1	45 (86.5%)
2	2 (3.8%)
3	5 (9.6%)
LAD	34 (65.4%)
RCX	10 (19.2%)
RCA	8 (15.3%)

MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CCS = Canadian Cardiovascular Society Classification.

Procedural safety

Coronary pressure measurement and FFR could be successfully performed in all patients and no complication occurred in any of the patients related to the catheterization or coronary pressure measurement.

In table 2, the relation between eyeball assessment and FFR is presented. Agreement between both assessments existed in a total of 36 cases (69.2%); 17 of these were proper prediction of hemodynamically significant stenosis and in 19 cases the stenosis was indeed insignificant. Over estimation of hemodynamic severity occurred in 6 cases (11.5%) and under estimation in 10 cases (19.2%). Consequently, the positive predictive value of eyeball assessment for correct classification of a significant stenosis was 63%. In analogy, the negative predictive value for correct

classification of a non-significant stenosis was 76%, the sensitivity was 74% and the specificity 66%.

Table 2. Visual estimation of hemodynamic significance vs. FFR

	FFR <0.75	FFR>0.75	Total
Visually predicted ≤0.75	17	10	27
Visually predicted >0.75	6	19	25
Total	23	29	52

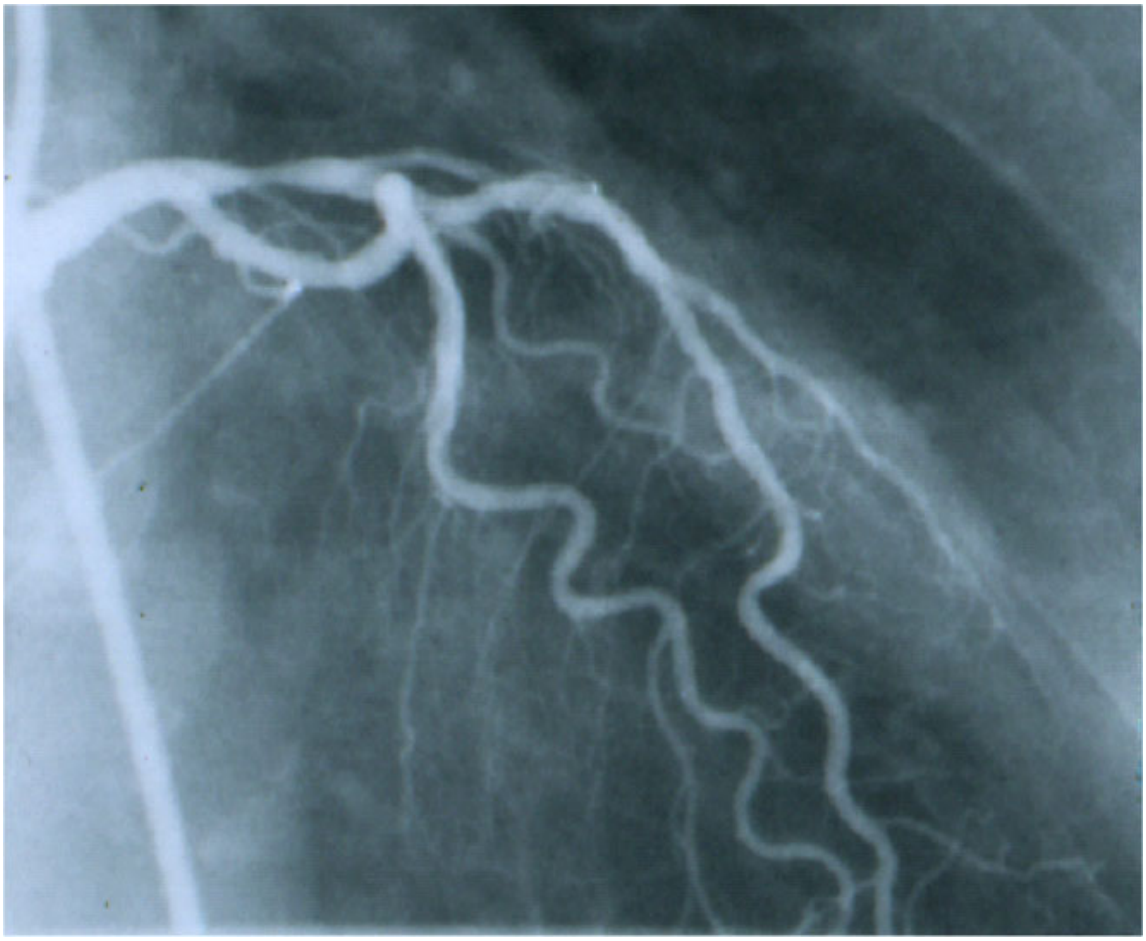


Figure 1. Intermediate stenosis of proximal RDA

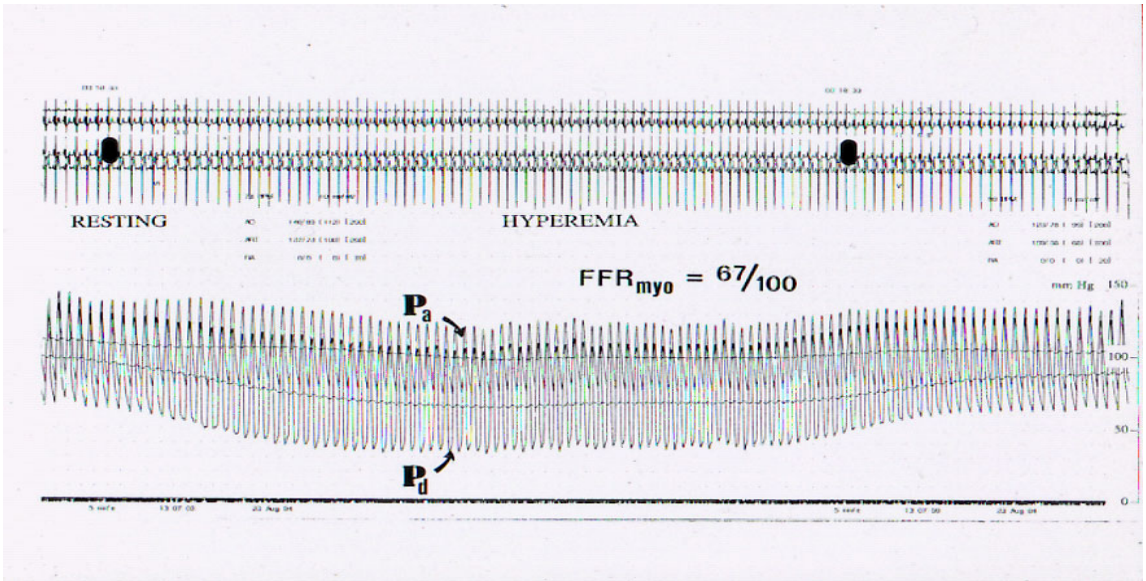


Figure 2. FFR measurement

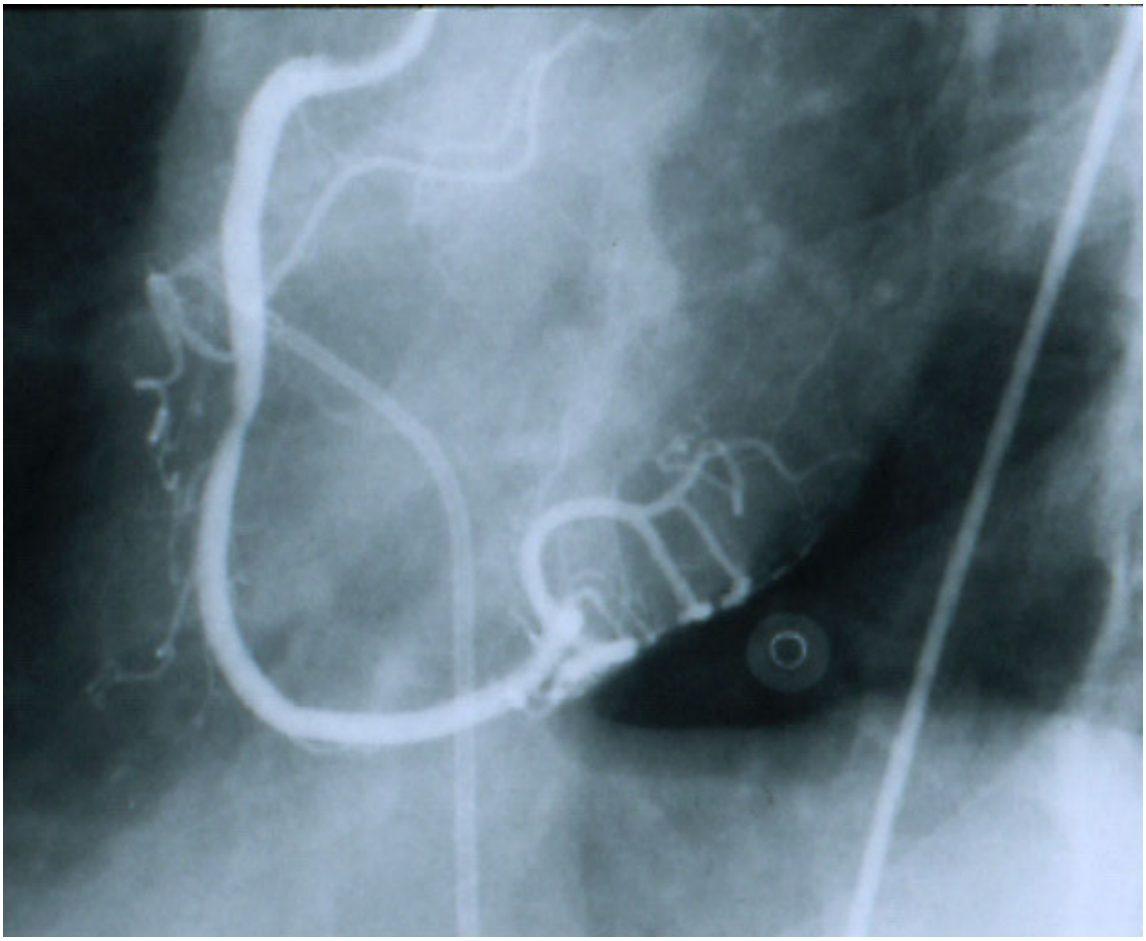


Figure 3. Intermediate stenosis of mid RCA.

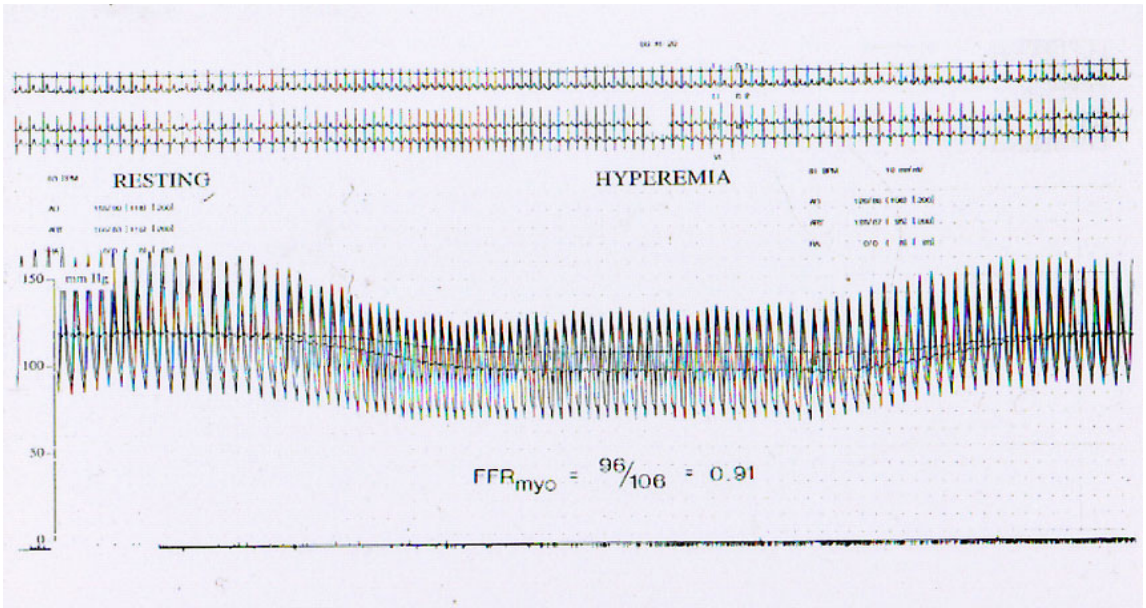


Figure 4. FFR measurement.

Discussion

In-patients with coronary artery disease, the decision to perform revascularization should be based not only on the coronary anatomy but also on objective proof of ischemia in the area of interest (1,8-11). However, the luminogram obtained during coronary angiography is a relative poor representation of coronary anatomy and has limited value for taking decisions with regards to revascularisation. Both over and under estimation of coronary stenosis occur frequently. Over estimation of functional stenoses severity may result in unnecessary intervention and in case of under estimation efficacious, revascularisation may be withhold. In addition, there is a significant intraobserver and interobserver variability in visual estimating stenoses severity (11). An alternative method for assessing severity of stenoses is QCA. Although interobserver variability is less with QCA, still only a poor correlation is present between QCA and functional stenoses severity (12).

In practice, in most cases proof of ischemia is based on classical exercise tests, in The Netherlands typically performed on a bicycle. Although this test is quite accurate in predicting significant coronary artery disease, conclusions on the distribution of myocardial ischemia cannot be made reliably (13,14). This can be accomplished by non-invasive stress echocardiography or myocardial scintigraphy. With both techniques the region of myocardial ischemia is determined and the relation with coronary stenoses can be inforced. However, these tests are demanding for the patient, relatively expensive, and not able to distinguish between several abnormalities within the same coronary artery or between focal and diffuse disease. For these reasons, invasive approaches to document ischaemia and which can be performed immediately during coronary angiography have been developed.

Fractional flow reserve

An alternative approach for non-invasive tests for detection of myocardial ischemia is an invasive assessment of the hemodynamic severity of a stenosis. FFR is defined as the ratio of maximum blood flow in as stenotic artery to normal maximum flow in the same vessel. Stated another way, maximum flow in the presence of the

stenoses is expressed as a fraction of the maximum flow in the hypothetical case that the epicardial artery is completely normal (7,15-18). This value can be obtained relatively easily and rapidly during cardiac catheterization. A major advantage of this method is that functional data are obtained which are specific for the lesion of interest, while the non-invasive tests provide only data on the entire vessel of interest.

It has been well established that the cut-off value of 0.75 discriminates reliable between functionally significant and nonsignificant stenosis (7,16). The sensitivity of FFR to detect significant stenoses is 90%, the specificity 100%.

Several studies demonstrated that more than 60% of coronary interventions are performed without evidence that the coronary stenosis is causing the symptoms of the patient (18,19). Our study shows that in-patients with intermediate stenosis unnecessary PTCA would have been performed in 11.5% of the cases when FFR would not have been measured. In addition, potentially beneficial PTCA would have been withheld in 19% of the patients without FFR measurement. In summary, eyeball estimation only would have resulted in a incorrect decision in more than 30% of the patients.

In conclusion, the assessment of the hemodynamic severity of coronary stenosis should not rely on eyeball estimation, even when performed by experienced cardiologists. Our study is a strong plea in favor of a more widespread application of FFR, in particular in case of doubt on the severity of stenosis.

References

(1) Ryan T.J., Baumann W.B., Kennedy J.W. et al. ACC/AHA guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Committee on Percutaneous Transluminal Coronary Angioplasty). J Am Coll Cardiol. 1993;22:2033-2054.

(2) White C.W., Wright C.B., Doty D. et al. Does visual interpretation of the coronary arteriogram predict the physiologic importance of a coronary stenosis? N Engl J Med. 1984;310:819-823.

(3) De Bruyne B., Bartunek J., Sys S.U., et al. Relation between myocardial fractional flow reserve calculated from coronary pressure measurements and exercise-induced myocardial ischemia. Circulation 1995;92:93-6.

(4) Scanlon P.J., Faxon D.P., Audet A.M.J., et al. ACC/AHA guidelines for coronary angiography: a report of the American College of Cardiology/American Heart Association Task Force on practical guidelines (Committee on Coronary Angiography) developed in collaboration with the Society for Cardiac Angiography and Interventions. J Am Coll Cardiol. 1999;33:1756-1824.

(5) De Bruyne B., Baudhuin T., Melin J.A., et al. Coronary flow reserve calculated from pressure measurements in Humans: validation with positron emission tomography. Circulation. 1994;89:1013-1022.
(6) Pijls N.H.J., Van Gelder B., Van der Voort P., et al. Fractional flow reserve: a useful index to evaluate the influence of an epicardial coronary stenois on myocardial blood flow. Circulation 1995;92:3183-3193.
(7) Pijls N.H.J., De Bruyne B., Peels K., et al. Measurement of fractional flow reserve to assess the functional severity of coronary artery stenoses. N Engl J Med 1996;334:1703-1708.
(8) Klocke F.J. Cognition in the era of technology: "seeing the shades of gray". J Am Coll Cardiol 1990;16:763-9.
(9) Ryan T.J., Faxon D.P., Gunnar R.M., et al. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart association Task Force on assessment of Diagnostic and Therapeutic Cardiovascular Procedures. (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). Circulation 1988;78:780-9 ACC/AHA guidelines and indications for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Coronary Artery Bypass Graft Surgery). Circulation 1991;83:1125-73.
(10) Zir L.M., Miller S.W., Dinsmore R.E., et al. Interobserver variability in coronary angiography. Circulation 1976;53:627-632.
(11) Bartunek J., Sys S.U., Heyndrickx G.R., et al. Quantitative coronary angiography in predicting functional significance of a stenoses in a unselected patient cohort. JACC 1995;26:328-334.
(12) De Bruyne B., Bartunek J., Sys S.U., et al. Simultaneous coronary pressure and flow velocity measurements in humans. Circulation 1996;94:1942-9.
(13) Topol E.J., Ellis S.G., Delos M., et al. Analysis of cornary angioplasty practice in the United States with an insurance-claims database. Circulation 1993;87:1489-97.
(14) Pijls N.H.J., van Son A.M., Kirkeeide R.L., et al. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. Circulation 1993;87:1354-67.
(15) Serruys P.W., Di Mario C., Meneveau N., et al. Intracoronary pressure and flow velocity with sensor-tip guidewires : a new methodologic approach for assessment of coronary hemodynamics before and after coronary interventions. Am J Cardiol 1993;71:41-53D.
(16) Kern M.J., De Bruyne B., Pijls N.H.J. From research to clinical practice: current role of intracoronary physiologically based decision making in the cardiac catheterization laboratory. J Am Coll Cardiol 1997;30:613-620.
(17) Pijls N.H.J., De Bruyne B. Coronary pressure measurement and fractional flow reserve. Heart 1998;80:539-542.
(18) Bech G.J.W., De Bruyne B., Bonnier H.J.R.M., et al. Long-term follow-up after deferral of percuraneous transluminal coronary angioplasty of intermediate stenosis on the basis of coronary pressure measurement. J Am Coll Cardiol 1998;31:841-7.

Chapter 6

How good are experienced interventional cardiologists in predicting the risk and difficulty of a coronary angioplasty procedure? A prospective study for optimum utilisation of surgical standby.

B.R.G. Brueren, E.G. Mast, M.J. Suttorp, J.M.P.G. Ernst, E.T. Bal, H.W.M. Plokker.

Department of Cardiology, St Antonius Hospital, Nieuwegein, The Netherlands.

Published in part in Catheterization and Cardiovascular Interventions 1999;46:257-262.

Abstract

Background. The prediction of the risk of a PTCA has either been based on coronary lesion morphology or on clinical parameters, but a combined angiographic and clinical risk assessment system has not yet been evaluated prospectively.

Methods. Five experienced interventionalists categorized 7,144 patients with 10,081 stenoses (1.4 lesion/patient) for both the risk and the difficulty of the procedure. Both for risk and difficulty, 3 categories were made. This division was made for PTCA planning purposes. Success was defined as a reduction of the degree of stenosis to less than 50%, without acute myocardial infarction, emergency redilatation, emergency bypass grafting, or death within 1 week.

Results. The procedure was not successful in difficulty category 1 in 1.6%, in category 2 in 3.5%, and in category 3 in 9.9%. Complications occurred in risk category 1 in 3.5%, in category 2 in 5.2%, and in category 3 in 12.4%. All differences were statistically significant ($P < 0.05$).

Conclusion. Experienced cardiologists can well predict the risk and success of a coronary angioplasty procedure. This study helps to optimize surgical standby, although even in the lowest-risk category complications can occur.

Introduction

There are various clinical and angiographic variables that contribute to the rate of complications during PTCA. The algorithms to predict complications during PTCA are often complex and not too specific. The guidelines defined by the American College of Cardiology/American Heart Association (ACC/AHA) task force subcommittee in 1988 and later updates in 1990 and 1992 do not provide hard data to predict clinical consequences, especially because the technical difficulty and the risk of procedural complications have been considered as one entity (See Table 1) (1-3). For instance, in type B lesions, the success rate should be between 60% and 85% with a moderate risk. However, important clinical variables such as the left ventricular function, renal function, age, diabetes, etc., are not taken into account. Thus, the ACC/AHA classification is not helpful in daily clinical practice when the interventional cardiologist tries to define the risk and difficulty of a PTCA procedure. Therefore a simple combined clinical and angiographic risk assessment system based on the clinical experience of over 17,500 PTCA procedures was developed and evaluated prospectively.

The purpose of this study was to investigate to what extent a strategy can be worked out to predict the risk of a PTCA procedure in order to optimize surgical standby and to inform the patient and the referring physician about the expected success rate and the risk of the procedure.

Patients and Methods

The study was performed in the patients who underwent PTCA in the St. Antonius Hospital, Nieuwegein, The Netherlands. In 1991 we started to stratify all the PTCA patients prospectively based on both clinical and angiographical data. From 1991 till 1995 all 7,144 consecutive patients who underwent PTCA for 10,081 lesions (1.4 lesion/patient) in our institution were included. For this prospective study only the patients with an acute myocardial infarction were excluded.

Table 1. Angiographic Characteristics of Lesions

Type A lesions (high success, >85%; low risk)
Discrete (< 10 mm length)
Concentric Readily accessible
Non-angulated segment, <45%
Smooth contour
Little or no calcification
Less than totally occlusive
Not ostial in location
No major branch involvement
Absence of thrombus
Type B lesions (moderate success, 60%-86%; moderate risk)
Tubular (10- to 20-mm length)
Eccentric Moderate tortuosity of proximal segment
Moderately angulated segment, >45%, <90%
Irregular contour Moderate to heavy calcification
Total occlusion <3 months
Ostial in location
Bifurcation lesions requiring double guidewires
Some thrombus present
Type C lesions (low success, <60%; high risk)
Diffuse (>2-cm length)
Excessive tortuosity of proximal segment
Extremely angulated segments >90%
Total occlusion >3 months
Inability to protect major side branches
Degenerated vein grafts with friable lesions

At least 2 out of a group of five interventional cardiologists, each with a experience of at least 1,000 cases and performing more than 350 cases per year, were asked to stratify intuitively the patients into categories for both risk and for difficulty in three categories (Table 2).

Table 2. Risk and Difficulty Categories

Risk	Difficulty
1. low	1. easy
2. moderate	2. moderate
3. high	3. difficult

In this risk category stratification, all possible clinical variables are to be taken into account, such as the amount of myocardium at risk, the risk of cardiogenic shock in case of abrupt closure, the presence or absence of collaterals and the personal experience of the panel. For instance, a coronary occlusion older than 6 months is considered to be difficult but to carry a low risk, whereas a type A lesion in a single remaining vessel carries a high risk (category 3). Therefore, whenever a patient is presented for an interventional procedure, the interventional cardiologist bases the difficulty and the risk of the procedure on both clinical and angiographical data. Technical difficulty is mainly based on angiographic features, as used in the ACC/AHA lesion classification.

The stratification for each patient was entered in a database before the procedure and was first of all made for PTCA planning purposes: We made 2 discriminations: **risk category** 1 patients were considered to undergo their PTCA procedure in the morning, when operating rooms for surgical standby are not available. Risk category 2 patients were planned at least in the first of our operating rooms when the surgical team becomes available within 1 hour (which in our hospital means after 11:00 AM when at least in one operating room the surgical team has finished their first operation). Risk category 3 patients required classical surgical standby.

Difficulty categories were introduced with a view to the availability of interventional cardiologists to assist each other. Difficulty category 1 represented single operator procedure at all times; category 2, second interventional cardiologist available for consulting; category 3, starting procedure with two interventional cardiologists.

Table 3. Number of Patients within ACC/AHA Classification

ACC/AHA classification	Number of patients
A	1,093
B	3,897
C	2,154

In order to make some comparison possible, the lesions were also classified according to the ACC/AHA guidelines (Table 3). Success was defined if luminal narrowing was reduced to less than 50% without complications. Complications were defined in an hierarchical order as death of the patient, acute myocardial infarction (pain, on the electrocardiogram ST-segment elevation and/or intraventricular conduction disturbances, and enzyme elevation), emergency coronary artery bypass grafting directly from the cath lab, or emergency re-PTCA.

Data were prospectively entered into a database. Discontinuous variables were analyzed as percentages and compared by chi-square test. Differences were considered statistically significant if $P < 0.05$.

Results

All 7,144 patients were included, among them 5,482 men and 1,662 women (23.3%). Mean age was 60 years. In these patients, 10,081 lesions were dilated (1.4 lesion per patient). For 155 patients (2.2%), the procedure was performed for angina pectoris class I, for 1,912 patients (26.8%) for angina pectoris class II, for 2,841 patients (39.8%) for class III, and for 2,236 patients (31.2%) angina pectoris class IV (Table 4).

Table 4. Clinical data

Number of patients	7,144
Number of lesions	10,081 (1.4 lesion per patient)
Mean age (years)	60.4
Angina pectoris (NYHA)	
Class I	155 (2.2%)
Class II	1,912 (26.8%)
Class III	2,841 (39.8%)
Class IV	2,236 (31.2%)

NYHA = New York Heart Association.

In 4,251 patients (60%) there was one-vessel disease, in 2,459 patients (34%) two vessel disease and in 365 patients (5%) three vessel disease. The left ventricular function was normal in 2,906 patients (41%). A chronic total occlusion was present in

1,123 patients (16%). In 550 patients a stent (8%) was used, as usual at the time this study was performed, (Table 5).

Table 5. Angiographic Data

Number of diseased vessels		
1	4,251	(60%)
2	2,459	(34%0
3	365	(5%)
Left ventricular function normal	2,906	(41%)
Total occlusion (100% stenosis)	1,123	(16%)
Lesions		
Left main	95	(1%)
Left anterior descending	3,274	(46%)
Right coronary artery	2,095	(29%)
Ramus circumflexus	1,388	(19%)
Grafts	288	(4%)
Left internal artery mammaria	4	
Number of stents placed	550	(8%)

According to the morphological characteristics from the ACC/AHA guidelines, 1,093 patients (15.3%) had a class A lesion, 3,897 patients (54.5%) class B, and 2,154 patients (30.1%) class C lesion (Table 3). Success was achieved in difficulty category 1 in 98.4% of the cases (77/4,954), in category 2 in 96.5% (137/3,863), and in category 3 in 90.1% (125/1,264). The differences between the three groups are statistically significant (Table 6). All P-values were less than 0.005.

Table 6. Angiographic Success Rates according to difficulty category (10,081 stenoses)

	Number of lesions in every difficulty category	Success rate	Percentage
Difficulty category 1	4,954	4,877	98.4
Difficulty category 2	3,863	3,726	96.5
Difficulty category 3	1,264	1,139	90.1

Total number of lesions = 10,081; P < 0.005.

Complications (any event) occurred in risk category 1 in 3.5%, in risk category 2 in 5.2%, and in risk category 3 in 12.4% (Table 7). Death following the procedure occurred in risk category 1 in 0.3%, in category 2 in 0.2%, and in category 3 in 1.9%. An acute myocardial infarction occurred in 2.1% in risk category 1, in 3.1% in category 2, and in 7.8% in category 3. Coronary bypass grafting was needed in category 1 in 0.3%, in category 2 in 0.9%, and in category 3 in 2.9%. The need for redilatation in risk category 1 was 1.1%, in category 2 1.4%, and in category 3 1.5%. (Table 7). All P differences were significant. There were no statistically significant operator differences with respect to referral for emergency coronary bypass grafting.

Table 7. Complications in Each Risk Category

	All events (%)	Death (%)	AMI (%)	CABG (%)	Re-PTCA (%)
Risk category 1 N=2,045	71 (3.5)	6 (0.3)	43 (2.1)	6 (0.3)	23 (1.1)
Risk category 2 N=4,363	225 (5.2)	9 (0.2)	135 (3.1)	39 (0.9)	62 (1.4)
Risk category 3 N=413	51 (12.4)	8 (1.9)	32 (7.8)	12 (2.9)	6 (1.5)
P-value	<0.005	<0.005	<0.005	<0.005	<0.005

AMI = acute myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass grafting. Note: in the first column patients are mentioned, in the 2nd, 3th, 4th and 5th events.

Discussion

In our scoring system, we tried to incorporate the knowledge, experience, and intuition of experienced interventional cardiologists to attempt to predict the risk and outcome of a PTCA procedure, trying not only to rely on angiographic but also clinical criteria.

We found that a small subgroup of patients can be discriminated beforehand with a high complication rate, but that the majority of events occur in patients not indicated as particularly difficult or riskful beforehand. These data indicate that, at least at the time of this study, surgical stand-by was a requisite to perform lege artis PTCA.

At the time of writing this thesis, PTCA has become safer on one hand by the large-scale use of stents but more dangerous on the other hand by the greater complexity of patients. Both effects, most likely, have counterbalanced each other and there are no reasons to suggest that predicting complications has become easier nowadays. Therefore, it can be concluded that surgical stand-by remains mandatory.

In the discussion about the risk of a PTCA procedure and more specifically about the question of surgical standby (in the same institution or at a distance), in most of the literature, this risk is only related to the lesion-specific stratification by the ACC/AHA task force subcommittee on guidelines for PTCA of 1993 (Table 1) (1,2). These guidelines reflect experience on angioplasty between 1986 and 1988; only small modifications were made by Ellis et al. (2) based on further experience between 1986 and 1987, and by Myler et al. (3) based on experience between 1990 and 1991. These classification schemes are outdated and need to be changed for application in current angioplasty practice. Tan et al. (4) suggested that analyzing specific lesion morphology characteristics rather than applying a simple overall lesion classification when evaluating angioplasty outcome may be more useful because it provides a more precise profile of the lesion and allows better patient stratification and selection. Lesion characteristics are associated with unfavorable results, as has been identified in population studies, but for a specific patient the risk and success rate is hard to predict (5,6); although Ellis et al. (2) and Myler et al. (3) identified some lesions with intermediate or high risk of abrupt closure. This occurs approximately in 4%-7% of cases when elective PTCA was performed, before the use era of coronary stenting (7-12). Most closure events become apparent before the patient leaves the cardiac catheterization laboratory, although a small number occurs later (within 24 hour).

Table 8 shows that there are major differences when scoring lesions according to our scoring system or the system of the ACC/AHA. For instance, most of the patients in our group 1 have type B lesions.

Table 8. Difference ACC/AHA vs. St Antonius Hospital Score

	1		2		3	
A	13/1,463	(2.8%)	18/582	(3.1%)	2/48	(4.2%)
B	70/1,426	(4.9%)	149/2,254	(6.6%)	22/217	(10. 1)
C	16/579	(2.8%)	99/1,388	(7.1%)	25/187	(13.4%)

The number of patients with a complication divided by the total number of patients in this group.

In the age of stenting, PTCA can be performed with less complications, especially because a bailout device is available for failed angioplasty (8,13,14). In our series only 550 patients (8%) received a stent almost invariably for bailout purposes. Despite improvements in angioplasty equipment, the final acute occlusion rate has remained stable due to considerable widening of the range of indications for angioplasty (8,15,16). Although "stent-by" is a highly effective treatment of subacute closure after coronary angioplasty, surgical "standby" remains certainly mandatory despite challenge of it by some authors (10). Klepzig et al. (17) showed that immediate surgical support should be available for patients with reduced exercise tolerance (<75 Watt) and no visible collaterals to the target vessel when angioplasty is performed.

Although Vogel (18) and Kuntz et al. (7) argue that active surgical standby can be markedly reduced with new technologies (stents, coronary atherectomy), attempts to establish risk factors and classify potential referrals for emergency surgery has not been successful so far (15,19-24).

In our study we have demonstrated that experienced interventional cardiologists are capable of predicting the high risk of a PTCA, which is necessary for the organization of the daily clinical practice. On the other hand, the majority of complications occurred in those patients assessed as having only a small or intermediate risk beforehand.

One major problem remains: What are the success and complication percentages worth for the individual patient? Our data indicate that in "easy" cases with a low risk, the complication rate is 3.5%, with a need for acute reangioplasty of

1.1%, a risk for coronary artery bypass grafting of 0.3%, and a risk of death of 0.3%. Although small, these numbers are not negligible and indicate that even the best operator in the cath lab has a surgical emergency complication every now and then. For the difficult and high-risk cases, the need for emergency bypass surgery increases to almost 3%.

These figures should be taken into account when the need for surgical standby is being questioned, even in the age of stenting. In New York State, both hospital angioplasty volume and cardiologist angioplasty volume are significantly inversely related to in-hospital mortality rate and same-stay bypass surgery rate for patients undergoing PTCA (25). There is a significant relation between operator volume and outcomes in PTCA; high-volume operators are more successful and encounter fewer adverse outcomes (26). But even in our institution with a case load of more than 350 per interventional cardiologist per year, there remains the need for surgical standby, even in the lowest-risk groups. Selection of patients without risk is in our opinion impossible, so cardiac surgery and interventions should not be separated.

We found that experienced operators are able to select a small subgroup of patients with a high risk for peri-procedural events, but that only the minority of all adverse events 51/6,809 (0.75%) occurred in those patients scheduled as high risk. Even in those patients, classified beforehand as low risk, adverse events occurred in 3.5%.

Experienced interventional cardiologists are very capable in predicting the success and the risk of a PTCA; however, the numbers of complications and need for coronary artery bypass grafting, even in the lower-risk groups, make it dangerous to perform PTCA without surgical standby.

References

(1) Ryan T.J., Faxon D.P., Gunnar R.M., et al. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association task force on assessment of diagnostic and therapeutic cardiovascular procedures (subcommittee on percutaneous transluminal coronary angioplasty). Circulation 1988;12:486-502.

(2) Smith S.C. Jr, Dove J.T., Jacobs A.K., et al. ACC/AHA guidelines for percutaneous coronary interventions (revision of the 1993 PTCA guidelines)-executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and Interventions. Circulation 2001;19:3019-41.

(3) Myler R.K., Shaw R.E., Stertzer S.H., et al. Lesion morphology and coronary angioplasty: current experience and analysis. J Am Coll Cardiol 1992;19:1641-1652.

(4) Tan K., Sulke N., Taub N., et al. Clinical and lesion morphologic determinants of coronary angioplasty success and complications: current experience. JACC 1995:25;855-865.

(5) Savage M.P., Goldberg S., Hirshfeld J.W., et al. M-HEART Investigators: clinical and angiographic determinants of primary coronary angioplasty success. J Am Coil Cardiol 1991;17:22-28.

(6) Hermans W.R.M., Rensing B.J., Foley D.P., et al. Therapeutic dissection after successful coronary balloon angioplasty: no influence on restenosis or on clinical outcome in 693 patients-the MERCATOR Study Group. J Am Coil Cardiol 1992;20:767-780.

(7) Kuntz R.E., Piana R., Pomerantz R.M., et al. Changing incidence and management of abrupt closure following coronary intervention in the new device era. Cathet Cardiovasc Diagn 1992;27:183-190.

(8) Scott N.A., Weintraub W.S., Carlin S.F., et al. Recent changes in the management and outcome of acute closure after percutaneous transluminal coronary angioplasty. Am J Cardiol 1993;71:1159-1163.

(9) Buffet P., Juilliere Y., Cherrier F. Complications de I'angioplastie coronaire. Presse Medicale 1993;22:870-875.

(10) Stauffer J.C., Eeckhout E., Vogt P., et al. Stand-by versus stent-by during percutaneous transluminal coronary angioplasty. Am Heart J 1995;130:21-26.

(11) Roubin G.S., Cannon A.D., Agrawal S.K., Macander P.J., Dean L.S., Baxley W.A., Breland J. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal coronary angioplasty. Circulation 1992; 85:916-927.

(12) Baims D.S. Interventional catheterization techniques: percutaneous transluminal angioplasty, valvuloplasty, and related techniques. In: Braunwald E, editor. Heart disease, 4th ed. Philadelphia, PA: W.B. Saunders; 1992:1365-1381.

(13) Mehl J.K., Schieman G., Dittrich H., Buchbinder M. Emergent saphenous vein graft stenting for acute occlusion during percutaneous transluminal coronary angioplasty. Cathet Cardiovasc Diagn 1990;21:266-270.

(14) Altmann D.B., Racz M., Battleman D.S., et al. Reduction in angioplasty complications after the introduction of coronary stents: results from a consecutive series of 2242 patients. Am Heart J 1996;132:503-507.

(15) King S.B. Prediction of acute closure in percutaneous transluminal coronary angioplasty. Circulation 1990;81 (suppl):IV5-IV8.

(16) Wang N., Gundry S.R., Van Arsdell G., et al. Percutaneous transluminal coronary angioplasty failures in patients with multivessel disease: is there an increased risk? J Thoracic Cardiovasc Surg 1995;110:214-221.

(17) Klepzig H. Jr, Kober G., Satter P., et al. Analysis of 100 emergency aortocoronary bypass operations after percutaneous transluminal coronary angioplasty: which patients are at risk for large infarctions? Eur Heart J 1991;1:946-951.

(18) Vogel J.H. Changing trends for surgical standby in patients undergoing percutaneous transluminal coronary angioplasty. Am J Cardiol 1992;69:25F-32F.
(19) Hasdai D., Berger P.B., Bell M.R., et al. The changing face of coronary interventional practice: the Mayo Clinic experience. Arch Int Med 1997; 157:677-682.
(20) Klinke W.P., Hui W. Percutaneous transluminal coronary angioplasty without on-site surgiacla facilities. Am J Cardiol 1992;70:1520-1525.
(21) Richardson S.G., Morton P., Murtagh J.G., et al. Management of acute coronary occlusion during percutaneous transluminal coronary angioplasty: experience of complications in hospitals without on site facilities for cardiac surgery. Br Med J 1990;300:355-358.
(22) Hannan E.L., Arani D.T., Johnson L.W., et al. Percutaneous transluminal coronary angioplasty in New York State: risk factors and outcome. JAMA 1992;268:3092-3097.
(23) Iniguez A., Macaya C., Hernandez R., et al. Comparison or results of percutaneous transluminal coronary angioplasty with and without selective requirement of surgical stand-by. Am J Cardiol 1992;69:1161-1165.
(24) Feldman R.L. Is short-stay coronary angioplasty safe? Clin Cardiol 1991; 14:119-123.
(25) Hannan E.L., Racz M.J., Ryan T.J., et al. Coronary angioplasty volumeoutcome relationships for hospitals and cardiologists. JAMA 1997;277:892-898.
(26) McGrath P.D., Wennberg D.E., Malenka D.J., et al. Operator volume and outcomes in 12,988 percutaneous coronary interventions. J Am Coll Cardiol 1998;3:570-576.

Editorial Comment - Risky Business

Peter C. Block, MD Providence Heart Institute, Portland, Oregon

How do we identify which patients are likely to have a complication during interventional procedures? Selecting the variables for a database to assess risk is difficult. An ideal database is large enough to include the pertinent data elements but small enough so that data collection takes little time. Inclusion of elements not directed toward the goal of the database simply increases data collection and entry time without adequate return. It is critical to define the purpose of a database from the outset even though the purpose may evolve, making the addition of new elements imperative. Elements that assess risk need to be the "right" or "correct" elements. Lastly, all data elements need to be relatively rigidly defined so that results can be compared.

In cardiac surgery, a minimum cardiac surgical data set has been defined and evaluated by testing it against multiple national databases (1). Similarly, in a more recent article, a minimum data set for interventional cardiology has been reported, which uses the same methodology to identify the 30 most important data elements from eight large respected databases (2). The American College of Cardiology has developed a database that goes beyond simple risk assessment and is therefore larger. An important part of all these efforts was defining the data elements as rigorously as possible to minimize "gaming." For example, angina classification into "mild," "moderate,- or "severe" categories is subjective enough to make "gaming" possible. If outcomes in one institution are worse than another, the inclusion of "severe" angina into every patient's record would make the poor outcomes appear more readily explainable. On the other hand, a Canadian classification of angina is more rigid and less subjective.

Because of all of these issues, choosing a set of data elements to define risk is difficult and demands multiple elements to complete an overall picture of risk for each individual patient. Database detractors might scoff at the need for having a large number of data elements to define what, for all of us, seems intuitively obvious. Somehow,

when we evaluate a patient, we put together in our own minds a risk profile that is constructed from many sources-the patient's history, the way a patient “looks”, comorbidity characteristics (renal failure, liver failure, pulmonary function abnormalities, etc.), and laboratory data. Individual cardiologists vary in their ability to predict risk, but, overall, most of us appear to do this fairly well. In the BARI database, the catheterizing physician's “sense” of a patient's risk correlated well with outcome. In this issue, Brueren et al. report that a subjective “score” of 1-3, with 1 denoting an “easy” lesion and 3 denoting a "difficult” lesion, correlated well with complications of 3.5%, 5.2%, and 12.4% in each of the three risk categories, respectively. All differences were significant at the $P < 0.05$ level. The report unfortunately tells us nothing about how the judgements of low, intermediate, and high risks were made.

Experience, patient appearance, operator confidence, and other similar nebulous factors all play a role in clinical judgement. This is not to argue that the authors of the report are not able to predict outcomes-quite the contrary. However, we cannot duplicate their methods. Would the same judgements be made in a smaller-volume institution, or by lower-volume operators, or in a laboratory where stents are placed more than 8% of the time? Databases must be used to compare results-peer vs. peer, individual vs. group, institution vs. institution, etc. Uniformly defining variables across databases is the only way to allow valid comparisons and avoid the "apples and oranges" problem. Clinical judgement is not definable, cannot be exported, and thus defies comparison. As a database variable, it is useless, and using it in a database is risky business.

Or is it? Just because we do not understand clinical judgement should not make us disregard it. What we learn from Brueren et al. is that clinical judgement can help predict outcome. Therefore, our charge should be to dissect and define the parts of

judgement that we can. That is no minor task--clinical judgement is a dynamic process that depends on recent experience and uses numbers of variables that would make database managers cringe. Some parts might be relatively easy and may already reside in most databases (ventricular function, acuity, etc.), but others may force us to add more variables (better lesion-specific lesion descriptors, myocardium at risk). Still others may be impossible (a patient's "grit"). What we collect in our databases needs to be evaluated prospectively to determine if more or fewer variables are needed. Variables will change with the questions asked, but if we include “clinical judgement” let us define what we mean. Only then can databases be used to best advantage. Therein lies the challenge.

References

(1) Jones RH, Hannan EL, Hammermeister KE, DeLong ER, O'Connor GT, Luepker RV, Parsonnet V, Pryor DB. Identification of preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. J Am Coll Cardiol 1996;28:1478-1487.

(2) Block PC, Peterson EC, Krone R, Kesler K, Hannan E, O'Connor GT, Detre K. Identification of variables needed to risk adjust outcomes of coronary interventions: evidence-based guidelines for efficient data collection. J Am Coll Cardiol 1998;32:275-82.

Chapter 7

Stenting of 'unprotected' left main coronary artery stenoses: early and late results.

B.R.G. Brueren, J.M.P.G. Ernst, M.J. Suttorp, J.M. ten Berg, B.J.W.M. Rensing, E.G. Mast, E.T. Bal, A.J. Six, H.W.M. Plokker.

From the department of Cardiology, St Antonius Hospital, Nieuwegein, The Netherlands.

Published in part in Heart 2003;89:1336-9.

Abstract

According to the ACC/AHA guidelines, left main coronary artery (LMCA) stenosis is a contraindication for percutaneous coronary interventions (PCI), and coronary artery bypass surgery (CABG) is the treatment of choice. However, PCI of the left main is sometimes performed under exceptional circumstances. Retrospectively, we found 71 patients (0.4%) with non-bifurcational LMCA stenosis in our database out of 17,683 PCI procedures (0.4%) who underwent an elective PCI between 1991 and 2001.

The age ranged from 26.7-86.5 years. Severe concomitant disease was the most frequently used argument for choosing PCI instead of CABG. PCI consisted of balloon angioplasty only in 24 cases (33.8%). A stent was used in 47 cases (66.2%).

Average follow-up was 43 months (range: 0-121 months). One patient died one day after the procedure. Total one year survival was 70/71 (98.6%). Seven patients died during the follow-up period, mostly because of non cardiac reasons. The annual mortality rate was 2.5%. Recurrent elective PTCA for restenosis of the LMCA was performed in 1 patient (1.4%), 6 weeks after the initial procedure. CABG was required in 13 patients (18.3%) throughout the follow-up period.

Based on our results, we believe that elective PCI of the non-bi-furcational LMCA can be performed safely, in selected patients.

Introduction

Since its introduction in 1977 (1) the number of percutaneous coronary intervention (PCI) has been increased steadily and today basically all manifestations of artherosclerotic coronary artery disease can be treated percutaneously. One of the few remaining contraindications is stenosis of the left main coronary artery. This condition is considered too dangerous due to the expected high mortality expected in case of acute closure. Therefore, coronary artery bypass surgery (CABG), which can be performed with a risk less than 5% is usually performed (2). Consequently left main stenosis has been excluded in most clinical trials and should be avoided according to the present guidelines for PCI (3). However, PCI of the left main has been practiced under special circumstances, such as in case of protection by means of a bypass graft, in the setting of acute myocardial infarction or in case of acute closure due to catheter manipulation during diagnostic or therapeutic catheterization. Due to the experience with PCI of the LMCA under special circumstances, this treatment is carefully extended now to broader categories of patients. In this study, we present the outcome of patients who underwent elective PCI of the unprotected left main coronary artery in our hospital during the last 10 years.

Methods

Patient selection

Between January 1990 and July 2001, 17,683 PCI procedures were performed in our hospital. A database of relevant patient characteristics and procedural data was maintained. PCI of the non-bifurcational left main was performed in a total of 218 cases (1.2 %). In 104 cases this concerned PCI of the unprotected left main coronary artery. Twenty-four of these patients (23.1%) were excluded for this study due to the setting of acute myocardial infarction. Nine other cases (8.7%) were excluded, as this procedure concerned an emergency treatment due to dissection during coronary angiography. Consequently, this analysis contains 71 patients with elective PCI of the unprotected left main, representing 0.4% only of the total PCI population.

Only stenosis proximal to the bifurcation was considered suitable for catheter interventions. In contrast, we always considered PCI in a short LMCA and with stenosis involving the bifurcation to be contraindicated.

Major adverse events

The endpoints in this study, were defined in our hierarchical order as death from any cause, myocardial infarction, bypass surgery, or repeated PCI. One-year follow-up was obtained in all but one patient. Acute myocardial infarction was defined as clinical documentation including typical electrocardiographic changes and/or elevated cardiac enzymes. Repeated PCI was defined as any catheter based intervention occurring more than one hour after the index procedure. LV function was classified semi-quantitatively based on pre-treatment LV-angiography.

Statistics

Data are presented as percent incidence, mean ± SD, or median and interquartile range as appropriate. Total and event-free survival were determined using Kaplan-Meier statistics.

Results

Patients

Patient characteristics are given in table 1. The age of the patients ranged from 26.7-86.5 years at the time of procedure. Ten patients (14.1%) had a previous myocardial infarction, 6 patients (8.5%) had undergone a PCI previously. Angiographic data are presented in Table 2. In 49.3% percent of the cases, the patient had left main stenosis only, while the other 50.7% had an additional significant stenosis in one or more of the branches of the coronary tree. The average stenosis-diameter as assessed by QCA was 69%. Twenty-one patients (29.6%) had only minimal calcifications. In six patients (8.5%) excellent collaterals to the perfusion area of the LMCA were noted. LV function was normal in 43 patients (60.6%), slightly diminished in 13 patients (18.3%), and moderately to severely impaired in 12 patients (16.9%). In 3 patients (4.2%) data on LV function were not available.

Table 1. Patient characteristics

Total PCI population	17,683
Left main PCI	218 (1.2%)
Unprotected, elective left main PCI	71 (0.4%)
Age (mean+/- SD)	60.4 +/- 12.6
Male gender	43 (60.1%)
Risk factors	
Smokers	22 pts (31.0%)
Known hypercholesterolemia	28 pts (39.4%)
Diabetes	5 pts (7.0%)
Family history of CAD	21 pts (29.6%)

CAD: coronary artery disease.

Indications

Severe concomitant disease was an argument for choosing PCI instead of CABG in 37 (51.1%) of the cases. Very severe peripheral arterial occlusive disease was present in 19 patients (26.8%), severe chronic obstructive pulmonary disease (with reduced pulmonary capacity) in 6 patients (8.5%), cardiomyopathy in 4 patients (5.6%), recent myocardial infarction in 4 patients (5.6%), severe renal insufficiency in 3 patients (4.2%) and malignant tumors 1 patient (1.4%). In 34 (47.9%) of the cases the decision to perform PCI was based on the combination of patient preference and feasible anatomy, without clear medical contraindication for CABG. In all cases the elevated risk of the procedure was carefully considered, discussed with the referring cardiologist and explained clearly to the patient.

Table 2. Baseline angiography

Coronary stenosis	
left main only	35 (49.3%)
left main plus:	
1 vessel	10 (14.1%)
2 vessel	24 (33.8%)
3 vessel	2 (2.8%)
Calcification	21 pts (29.6%)
Collaterals to LMCA	6 pts (8.5%)

LMCA: Left Main Coronary Artery.

Medical treatment

All but one patient were on aspirin. All patients received heparin during the procedure. All stent patients had either Ticlopidine or Clopidrogel after stenting, and 21 patients were treated with oral anticoagulants.

Procedural and in-hospital complications:

PCI consisted of balloon angioplasty only in 23 cases (32.4%). A stent was used in 46 cases (64.4%). In one case a cutting balloon was used. In one other case a rotablator was applied. An intra aortic balloon pump was not routinely used.

Complications are summarised in table 3. One patient died one day after the procedure; an AVE 3.5-16 mm stent was used. In this patient, only heparin and aspirin had been used as concomitant anti thrombotic medication. At that point in time (1993) clopidogrel and ticlopidine were not yet commercially available. Urgent coronary angiography revealed massive thrombus formation in the left coronary artery. Redilatation was not technically possible. This patient died in cardiac shock during the second procedure.

During the procedure dissection of the left main occurred in 11 patients. In 1 patient (1.4%) urgent coronary bypass surgery was required as a bailout procedure because of a dissection extending into the LAD and RCX. The further clinical course was uncomplicated.

In one patient, repeat balloon angioplasty within 30 minutes was needed because of acute closure and a bail out stent was placed. No enzyme elevation or new Q-waves developed in this patient. This patient underwent elective CABG 10 months later. In one other patient, acute lateral ischemia occurred within one hour after the procedure. At angiography, the stent placed during the index procedure appeared to be patent. However, thrombus formation was seen in another branch. Dilatation was performed successfully. Cardiac enzymes did not rise.

Table 3. Complications during the procedure

Dissection	11 pts (15.3 %)
Urgent CABG	1 pt (1.4%)
Urgent angiography	2 pts (2.8 %)
Peri-procedural death	1 pt (1.4 %)

CABG: Coronary Artery Bypass Grafting.

Long term follow-up

Average follow-up was 43 months, ranging from 0-121 months. One other patient died during the first year follow-up due to pulmonary malignancy 11 months after the PCI. The total survival after one year was 70/72 (97.2%).

Long term survival by Kaplan-Meier curves is given in figure 1. Seven patients died during the follow-up period. The annual mortality rate was 2.5%. Most of these patients died from non-cardiac causes, such as cancer (2), renal insufficiency (1) and cerebro-vascular accident (2). One other patient died due to a car accident. Recurrent elective PTCA for restenosis of the LMCA was performed in 1 patient, 6 weeks after the initial procedure.

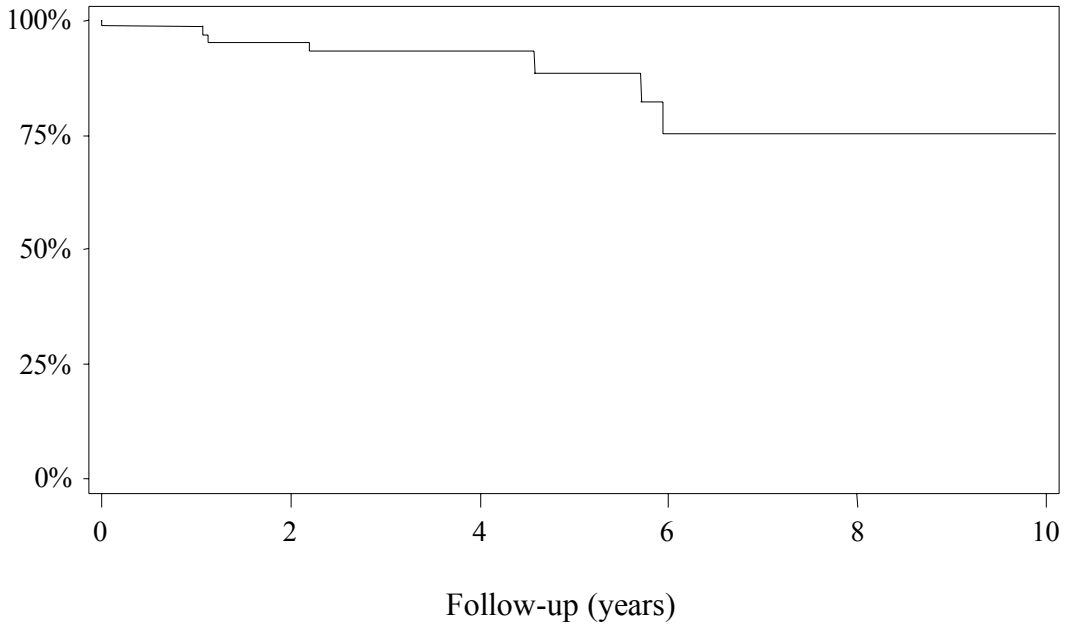


Figure 1. Freedom from all cause mortality following unprotected elective PCI of the left main stem.

Event free survival is presented in figure.2. After one year, 93 percent of the patients were alive and free from death, AMI, repeat PTCA or CABG. CABG was required in 13 patients throughout the follow-up period, in 1 case due to restenosis and in 12 cases due progression of stenosis elsewhere. Freedom from CABG is given in figure 3.

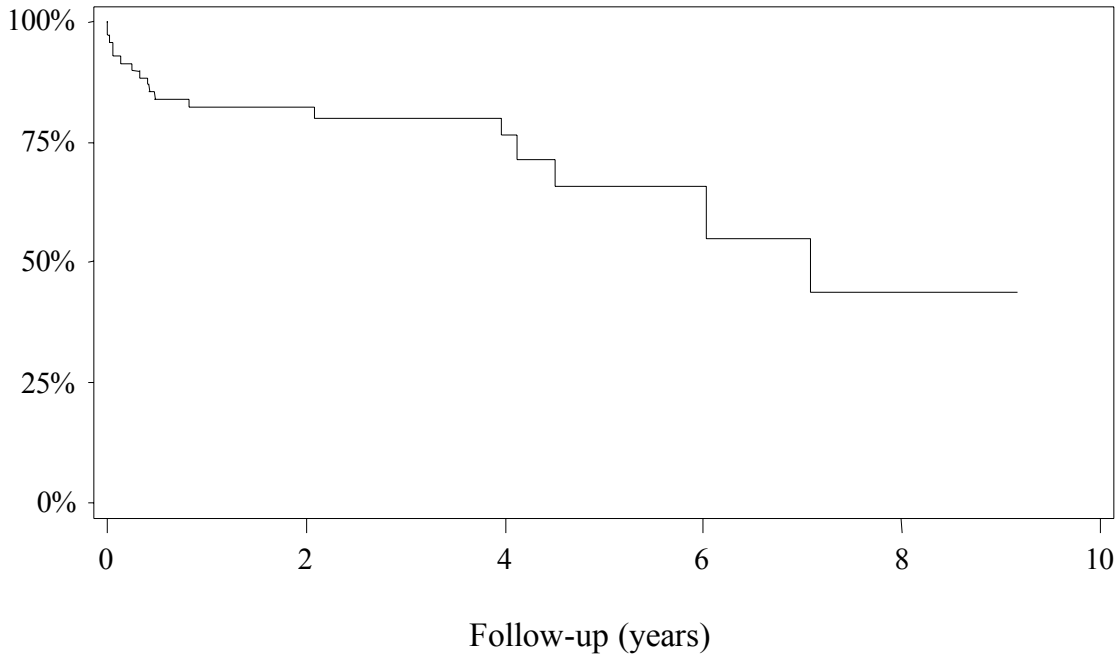


Figure 2. Freedom from all cause mortality, AMI, repeat PTCA or CABG.

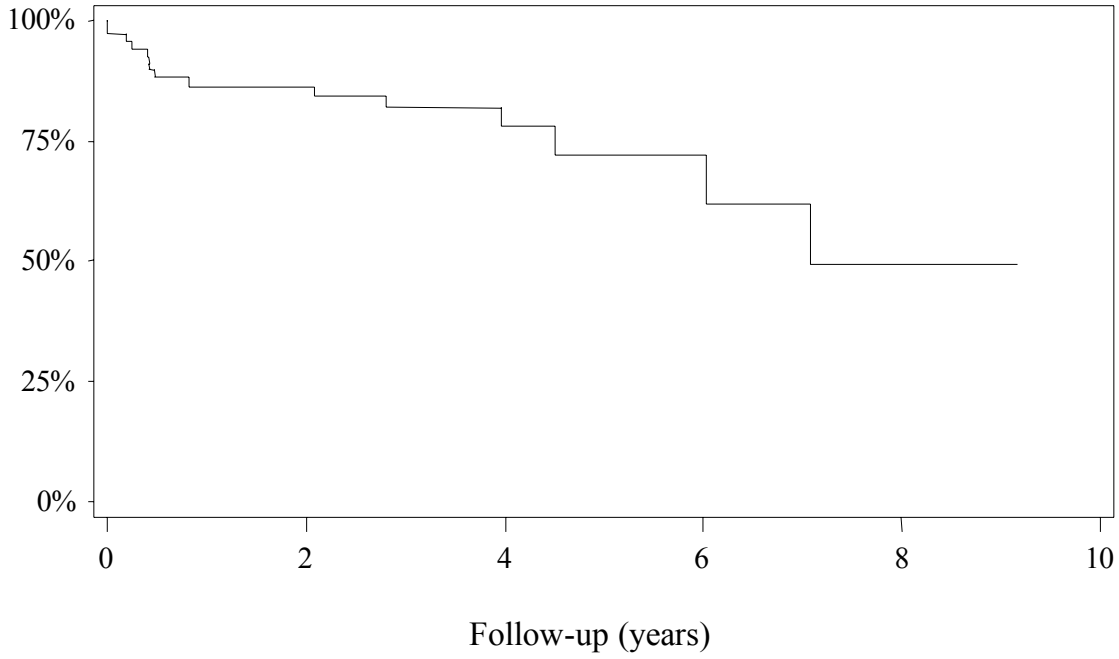


Figure 3. Freedom from CABG.

Discussion

PCI of the unprotected left main coronary artery has been discouraged by the ACC/AHA (3). Therefore, there is only limited experience with elective PCI of

unprotected left main stenosis, reflected by only 10 publications on studies involving >10 patients (4-13). These studies report an average peri-procedural mortality of 8.8% (range 0-36%) in a total of 799 patients. So it is clear that PCI of a significant stenosis of the left main coronary artery carries significant risks. The three-year mortality rate in case of left main stenosis treated with drugs only may be at least 50% according to various publications in the seventies (14-17). Acute closure of this vessel may result in immediate mortality, whilst bypass surgery in these patients can be performed at amore acceptable risk (18-19). It should be emphasised that the study population in the publication mentioned above, most likely were very different.

Initial experience in the eighties with PCI for left main stenosis was indeed quite discouraging. O'Keefe reported a 9.1 % procedural death rate in 1989 (20). In the early series published by Tomasso, Keeley and Chauhan et al. in-hospital mortality rates of 14%, 5% and 36% respectively (4-6). These rates have gradually decreased to 0-13.7% in more recent studies (7-13). The well-documented registry by Silvestri et al. reports a relatively favorable short-term outcome in terms of an in hospital mortality of 3% in 140 patients treated between 1993 and 1998 at one single site (7). However, in this series the 1-year mortality was rather high, i.e. 13%. Ellis (8) reports unfavorable early results as demonstrated by an in hospital mortality of 12% in 91 patients, and by a 6 month mortality risk of 30%. The smal studies by Park and Wong (9,10) report 100% early survival, but long-term figures are lacking. The recently published multi center registry of 279 patients by Tan et al. (13), reports in-hospital mortality of 13.7% and of 26.8% at one year.

In fact, the average early mortality of 8.8 % in the 10 recently published major studies, as mentioned in the introduction of this paper, is a truly strong argument in favor of CABG in patients with left main stenosis. Only in case of severe concomitant disease, when the risk of bypass surgery is considered unacceptably high, the risk-benefit ratio may be in favor of angioplasty. Also in our hospital the number of patients involving PCI of LMCA is very low (0.4%). Initially, we only treated patients with severe co-morbidity, which was present in 52 (73.2%) patients of the study population. With the safety of the procedure increasing and with improvement of procedural techniques, drugs and experience of the operators, we have gradually come

to consider PCI of LMCA as a non-obsolete alternative for bypass surgery. When the patient is well informed and prepared to make his own decision, based on risk stratification, we are willing to consider PCI of the LM artery, especially if contraindications for CABG are present.

The in-hospital mortality was 1.4% in our series. More importantly, long term follow up results in our patients, both those treated without stents in the early days and those treated with stents, were excellent. Our Kaplan Meier analysis shows event rates, which are comparable to the results of CABG in-patients with severe coronary artery disease. Three patients died due to end-stage conditions of concomitant diseases, such as metastasised cancer or renal insufficiency. Meanwhile, these patients held significant medical benefit from the cardiac intervention, being free of severe angina pectoris and myocardial infarction. It should be stressed that concomitant disease were reason for the unusual interventional approach, whilst in randomised trials such patients are typically excluded. In the literature there is only limited information on long-term follow-up after LM angioplasty. Only Keeley (5) provides follow-up data longer than 2 years. However, that study combines elective, emergent, protected and unprotected cases. Detailed information on the subgroups is not provided. Therefore, that study does not provide a clear view on the prognosis of patients undergoing elective PCI of the unprotected left main.

The favorable results in our study require further explanation. One explanation is the angiographic selection criteria: in our study, the procedure was only performed in non-bifurcational lesions in relatively long LMCA and not in case of a short LMCA and/or atherosclerotic stenosis involving the bifurcation. We believe that in particular PCI of LM bifurcation lesion is associated with an unacceptably high risk. This is explained by the fact that even in the area of stenting, bifurcational lesions have a particularly high recurrence rate. The relatively good results in our study group may also be explained in part by higher success rates in more experienced hands, illustrated by an annual volume of more than 500 PCI's per interventional cardiologist at our site. This finding in PCI in general may hold true in particular for technically difficult or risky procedures such as PCI of the left main (20). In the light of the study period 1990-2001, it is not surprising that the number of stents used (66.2%) is relatively low.

In todays practice basically all patients would receive a stent. The advantages and disadvantages of drug eluting stents are under study.

Our study does not include any kind of control group. A prospective randomized comparison would be desirable. A comparison with drug therapy only, would be unethical due the very poor prognosis of medically treated LMCA stenosis. Randomization versus CABG could be a demanding but challenging option. Due to the selection criteria (non-bifurcational) it would take a very long time to include a large number of patients. In the view of a procedural risk of 1.4% and a CAD-related annual mortality of just 1% a large number of patients would have been necessary to show a benefit of either treatment.

In conclusion we believe that it is time to reconsider their recommendations for PCI in-patients with LMCA stenosis. Based on our results retrieved from historical data, elective PCI of the non-bifurcational LMCA should not be principally avoided, at least not in experienced hands and a favourable morphology of the stenosis.

References

(1) Gruentzig A.R. Transluminal dilatation of coronary artery stenosis. Lancet 1978;1:263.

(2) d'Allonnes F.R., Corbineau H., Le Breton H., et al. Isolated left main coronary artery stenosis : long term follow-up in 106 patients after surgery. Heart 2002;87:544-8.

(3) ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines-Executive summary. A report of the American College of Cardiology/American Heart Association Task Force on practical guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). JACC 2001;37:2215-38.

(4) Tommasso C.L., Vogel J.H.K., Vogel R.A. for the national registry of elective supported angioplasty. Coronary angioplasty in high-risk patients with left main coronary stenosis: results from the national registry of elective supported angioplasty. Cath Cardiovas Diagnosis 1992;25:169-173.

(5) Keeley E.C., Aliabadi D., O'Neill W.W., et al. Immediate and long-term results of elective and emergent percutaneous interventions on protected and unprotected severely narrowed left main coronary arteries. Am J Cardiol 1999;83:242-246.

(6) Chauhan A., Zubaid M., Ricci D.R., et al. Left Main Intervention Revisited: Early and Late Outcome pf PTCA and Stenting. Catheterization and Cardiovascular Diagnosis. 1997; 41:21-29.

(7) Silvestri M., Barragan P., Sainsous J., et al. Unprotected left main coronary artery stenting: immediate and medium term outcomes of 140 elective procedures. J Am Coll Cardiol 2000;35:1543-50.

(8) Ellis S.G., Tamai H., Nobuyoshi M., et al. Contemporary percutaneous treatment of unprotected left main coronary stenoses. Initial results from a multi center registry analysis 1994-1996. Circulation 1997;96:3867-3872.

(9) Park S-J., Park S-W., Hong M-K., et al. Stenting of unprotected left main coronary stenoses: immediate and late outcomes. J Am Coll Cardiol 1998;31:37-42.

(10) Wong P., Wong V., Tse K-K., et al. A prospective study of elective stenting in unprotected left main coronary disease. Cathet Cardiovasc Intervent 1999;46:153-159.

(11) Laruelle C.J.J., Brueren G.B.R., Ernst S.M.P.G., et al. Stenting of "unprotected" Left Main Coronary Artery Stenoses: Early and Late Results. Heart. 1998;79:148-152.
(12) Karam C., Fajadet J, in patients at high surgical risk. Am J Cardiol 1998;82:975-978.
(13) Tan W.A., Tamai H., Park S.J., et al. for the ULTIMA investigators. Long-term clinical outcomes after unprotected left main trunk percutaneous revascularization in 279 patients. Circulation 2001; 104: 1609-1614.
(14) Bruschke A.V.G., Proudit W.L., Sones F.M., et al. Progress study of 590 consecutive nonsurgical cases of coronary disease followed 5 to 9 years. Circulation 1973;47:1147-53.
(15) Lim J.S., Proudit W.L., Sones F.M., et al. Left main coronary arterial obstruction : long-term follow-up of 141 nonsurgical cases. Am J Cardiol 1975;36:131-5.
(16) Cohen M.V., Gorlin R. Main left coronary artery disease: clinical experience from 1964 to 1974. Circulation 1975;52: 275-85.
(17) Conley M.J., Ely R.L., Kisslo J., et al. The prognostic spectrum of left main stenosis. Circulation 1978;57:947-52.
(18) Varnanskas E., for the European Coronary Surgery Study Group, twelve year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med 1988; 319: 332-7.
(19) Caracciolo E.A., Davis K.B., Sopko G., et al. Comparison of surgical and medical group survival in patients with left main coronary artery disease. Long-term CASS Experience. Circulation 95; 91: 2325-2334.
(20) O'Keefe J.H., Hartsler G.O., Rutherford B.D., et al. Left main coronary angioplasty: early and late results of 127 acute and elective procedures. Am J Cardiol 1989;64:144-147.
(21) Serruys P.W., Unger F., Sousa J.E., et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344:1117-24.

Chapter 8

Emergency PCI for unprotected left main stenosis: immediate and long term follow-up.

B.R.G. Brueren, J.M.P.G. Ernst, M.J. Suttorp, J.M. ten Berg, B.J.W.M. Rensing, E.G. Mast, E.T. Bal, A.J. Six, H.W.M. Plokker

From the department of Cardiology, St Antonius Hospital, Nieuwegein, The Netherlands.

Published in part in Heart. 2004; 90: 1067 - 1068.

Abstract

Introduction. Significant disease of LMCA is considered as a contra-indication for PCI. Acute occlusion of the LMCA is an immediately life-threatening condition. With catheter intervention an occluded LMCA may be reperfused within minutes, thus resulting in saving lives.

Methods. Between January 1990 and July 2001, 17683 PCI procedures were performed at our site. In 35 cases this concerned an emergency PCI of the unprotected left main, representing 0.2% of the total PCI population. Twenty-six of the study patients (74.3%) were treated in the setting of acute myocardial infarction. In nine other cases (25.7%) this procedure concerned an emergency treatment for dissection that occurred during coronary angiography.

Results. The in-hospital mortality was 41%. Those who survived 1 year had an excellent prognosis: none of these patients died during the follow-up. Additional revascularizations occurred in 2 of these 20 patients (10%).

Conclusion. Emergency PCI of an occluded LM coronary artery, either due to acute myocardial infarction or catheter-induced dissection, is associated with a high peri-procedural mortality, but long term follow-up of the survivors is excellent.

Introduction

Ever since its introduction in 1979 (1) percutaneous coronary intervention (PCI) has been applied increasingly and today basically all manifestations of artherosclerotic coronary artery disease can be treated by PCI. In the setting of stable coronary artery disease however, stenosis of the left main coronary artery (LMCA) is still considered as a relative contraindication for PCI. It is considered too dangerous, unless the left main (LM) is protected by means of a bypass graft. Therefore, left main stenosis has been excluded in most trials and should be avoided according to the ACC guidelines (2).

However, PCI of the LMCA is practiced under emergency conditions such as acute myocardial infarction and in case of acute closure due to catheter manipulation during diagnostic or interventional catheterization. Acute occlusion of the LMCA is an immediately life-threatening condition. Although no controlled data are available, it generally results in death within hours or minutes in the majority of patients. In case of catheter induced dissection of the LM, bypass surgery is an option and the time to instalment of extra corporal circulation can be bridged by IABP. In case of LM occlusion due to acute myocardial infarction, even if emergency CABG is performed, the mortality is extremely high. In contrast, by means of catheter intervention the occluded LMCA may be reperfused within minutes, and several studies showed benefit for emergency PCI of the left LM in small subgroups of patients. The present study describes our experience from 10 year emergency PCI of LM occlusion.

Methods

Patient selection

Between January 1990 and July 2001, 17683 PCI procedures were performed in our hospital and stored into a database of relevant patient characteristics and procedural data. PCI of the left main was performed in a total of 218 cases (1.2 %) of the total population. In 35 cases, this concerned an emergency PCI of the unprotected left main, representing 0.2% of the total PCI population. This is the study population in the present study. In 26 of those patients the cause of the LM occlusion was acute MI

and in 9 of them iatrogenic dissection and closure due to catheter manipulation was the cause of the occlusion.

Procedural data

A stent was used in 25 patients (71.4%). In one case a cutting balloon was used. In one other case a rotablator was applied.

Endpoints

The main endpoint in this study was mortality. Furthermore acute myocardial infarction was defined as clinical documentation including new Q waves on the electrocardiogram and/or elevated cardiac enzymes (more than 3 times the upper limit). Repeated PCI was defined as any catheter based intervention occurring more than one hour after the index procedure. LV function was classified semi-quantitatively based on pre-treatment LV-angiography. Cardiogenic shock was defined as 1) systolic blood pressure (BP) persistently < 90 mmHg or inotropic drugs required to maintain BP > 90 mmHg, or 2) evidence of end organ hypoperfusion (e.g. urine output < 30 ml/hr or cold diaphoretic extremities or altered mental status, or 3) evidence of elevated filling pressure, for example, pulmonary congestion on examination or chest radiography.

Statistics

Data are presented as percent incidence, mean ± SD, or median and interquartile range if appropriate. Total and event-free survival were determined using Kaplan-Meier statistics.

Results

Patients

Patient characteristics are given in table 1. The average age of the patients was 67.1 years at the time of procedure. Twenty-six of the study patients (74.3%) were treated in the setting of acute myocardial infarction. In nine other cases (25.7%) this procedure concerned an emergency treatment for dissection that occurred during coronary angiography. Ten patients (29%) were female, and 30 patients (85.7%) had a

history of CAD. The vast majority of the patients had hypercholesterolemia, hypertension or smoked or combination of these risk factors.

Table 1. Characteristics & Angiographic data of 35 patients undergoing PCI of the LMCA.

Total PCI population 1990-2000	17683
PCI of the unprotected left main	
Rescue PCI for AMI	26 (0.15 %)
Complicated CAG/ catheter induced	9 (0.05 %)
Elective PCI of LMCA	71 (0.4%)
Age	67.1 +/- 12.3
Female gender	10 (29 %)
History of CAD	30 (85.7%)
Risk factors	
Smoking	26 (74.3%)
Diabetes	10 (2.6%)
Known hypercholesterolemia	28 (80%)
Hypertension	20 (57.1%)
Family history of CAD	13 (37.1%)
STT elevation in aVR	
+ 0,5 mV	8 (22.9 %)
+ 1,0 mV	7 (20.0 %)
+ 1,5 mV	1 (2.9 %)
+ 2,0 mV	8 (22.9 %)
acute ECG not available	9 (25.7 %)
no STT elevation	2 (5.7 %)
Duration of ischemia	104 min +/- 126, median 52, interquartile 20.75, 75%:165
Dominance of RCA	
Light	10 (28.6%)
Moderate	15 (14.3%)
None	4 (11.4%)
RCA occluded	6 (17.1%)
Occlusion of left main	20 (57.1 %)
Calcification	17 (48.6%)

PCI= percutaneous coronary intervention; AMI= acute myocardial infarction; CAD= coronary artery disease; ECG= electrocardiogram; RCA: right coronary artery.

Before the intervention 24 patients (68.6%) had ST segment elevation in lead aVR (Table 1). For the nine patients with a complicated coronary angiography pretreatment ECGs were not available.

Angiographic data are presented in table 1. Twenty patients (57.1%) had an occlusion of the LMCA, the remaining patients had a subtotal lesion. Most patients had a right dominancy of the RCA.

A total occlusion of the LMCA without any anterograde flow was observed in 20 patients. Cardiopulmonary resuscitation was needed in 7 patients, 4 patients were in cardiogenic shock. In these patients we succeeded in restoration of hemodynamics, whereafter we could perform PCI. Six patients were transferred to the operating room for emergency coronary bypass surgery immediately after anterograde flow in the LMCA was restored. In 20 patients an Intra Aortic Balloon Pump (IABP) was introduced immediately after the procedure. All these six patients survived and were finally dismissed from the hospital.

Table 2. Complications.

Dissection of LMCA	8 (22.6%)
Resuscitation	7 (20 %)
Urgent CABG	6 (17.1 %)
Elective CABG within 3 months	3 (8.6 %)
Peri-procedural death	15 (42.9 %)

CABG: Coronary Artery Bypass Grafting; LMCA: Left Main Coronary Artery.

Clinical outcome

Complications are mentioned in table 2. Median follow-up was 722 days. The in-hospital mortality was 43%, those 15 patients who died in-hospital, deceased under the following circumstances: seven patients died within 10 minutes after arrival in the catherisation laboratory due to deteriorating hemodynamics and despite cardiopulmonary resuscitation. In four of these patients attempts to open the occluded LMCA had not been successful. Three other patients died in cardiogenic shock despite restoration of blood flow. Two patients survived the PCI procedure but died within 24 hours due to cardiac failure, despite maximal inotropic stimulation and intra aortic balloon pump. The remaining three patients who died, deceased due to an aspiration

pneumonia on day three, an repeated arrest on day eight, and one patient had a groin bleeding for which he had to be operated on. After the surgical procedure this patient had a cerebrovascular accident. The 20/35 (57%) survivors had an excellent prognosis: none of these patients died during the long term follow-up. Additional revascularizations occurred in 2 of these 20 patients (10%), 1 patient underwent CABG after 31 months, the other CABG and MVP after 59 months. Survival depicted as Kaplan-Meier curves is given in figure 1.

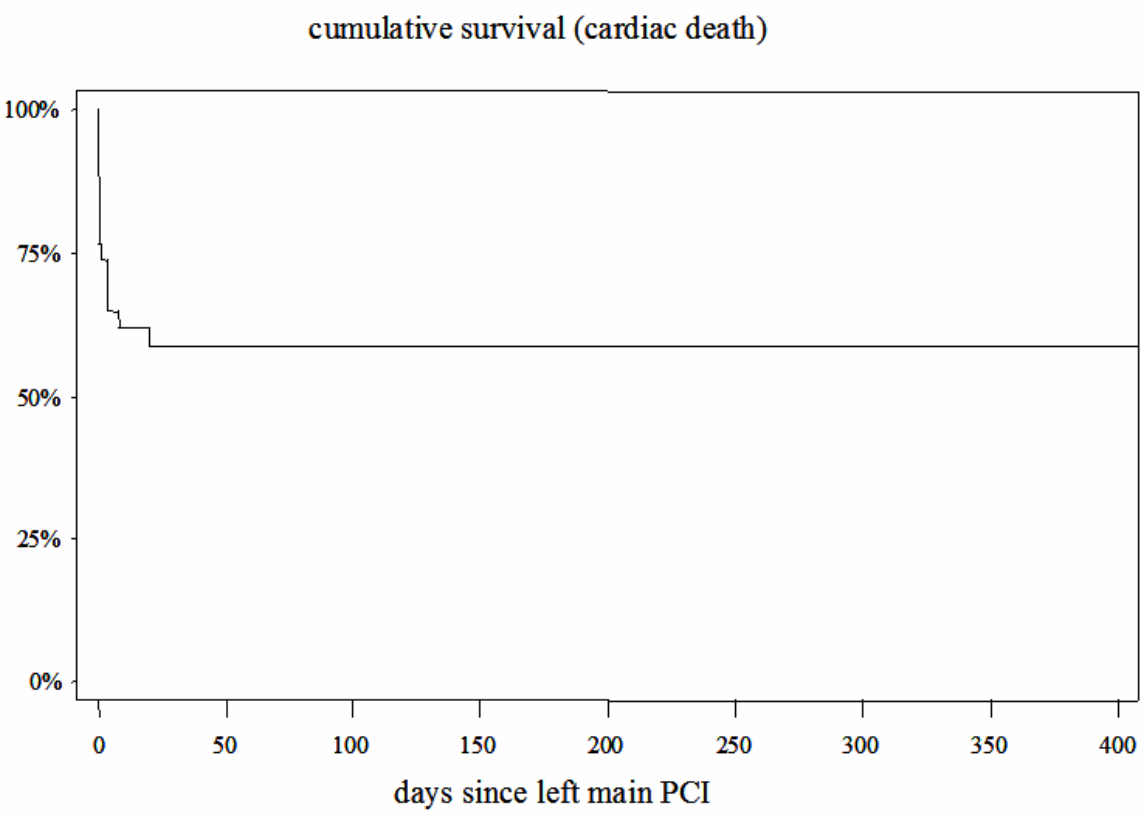


Figure 1. Cumulative survival following emergency PCI of the LMCA

Discussion

PCI in general is a safe and effective therapy for many patients with coronary artery disease. An exception is PCI of the LMCA, which is not practiced routinely, as it is considered too dangerous, because balloon-induced dissection of the LMCA may result in an immediately life-threatening condition. In contrast, for elective patients

with LM disease CABG is a safe alternative. However, emergency CABG is logistically not always feasible. Even when the operation theatre and the surgical team are available, the preparations for cardiac surgery may last longer than the hemodynamic situation of the patient allows. In contrast, catheter interventions do not require significant preparations and can be performed immediately. Once the patient has arrived in the catherisation laboratory, the procedure may be carried out within minutes. Emergency catheter interventions may result in an immediate restoration of blood flow and reverse hemodynamic abnormalities, thus potentially resulting in saving lives.

Ever since the introduction of PCI as a standard therapy for AMI, experience with emergency PCI for occlusion of the unprotected LMCA is increasing (1-12). Most publications on this issue concern subgroups from larger cohorts of patients undergoing PCI. Therefore, literature data are scarce and the patient groups are small. In 6 of the 13 relevant publications the patient group with the relevant condition was smaller than 10 patients. The largest group in literature so far was described by De Luca et al, and consisted of 24 patients undergoing PCI for LMCA obstruction in the setting of AMI. Fourteen of these patients (58%) died either in the catherisation laboratory or during the initial hospitalization. Predictors of death were absence of or poor collateral's, suboptimal postprocedural flow (TIMI<3), and cardiogenic shock at presentation.

Recently, Yip et al described 18 patients with a peri-procedural mortality rate of 33.3%. Those who survived had more collaterals, dominant RCA, and incompletely occluded LMCA (10). The multi center registry published by Tan (9) described 279 patients undergoing PCI of LMCA. In 41 of these patients the treatment occurred in the setting of AMI. Unfortunately separated data on this subset are lacking.

In some cases emergency PCI may be a bridge to later revascularization of other coronary segments affected by atherosclerosis. In our study the time delay between onset of symptoms and time of restoration of coronary blood flow appeared to be the only strong predictor of mortality in univariate analysis. Each quarter of delay results in a 30% increase of the risk of death.

From several studies it is well known that presence of cardiogenic shock is one of the strongest predictors of mortality during PCI. An occlusion of the LM is often accompanied with cardiogenic shock and as this condition is more frequent and severe the longer the time delay to restore blood flow, these observations are not surprising.

Our study concerns a group of 35 patients with LMCA stenosis or occlusion presenting at our high volume intervention center during a 10 year time period.

Fifteen patients died either during the procedure or during the hospital stay. Those who survived had an excellent prognosis: none of them died during the additional follow-up. Only two of them needed another revascularization procedure. This remarkable finding is consistent with the only larger study published so far by De Luca, mentioned above. Although 58% of the patients in that study died either in the catherisation laboratory or during the initial hospitalization, only one patient of the ten hospital survivors died during the follow up of 37 ± 23 months.

Conclusion

Although periprocedural mortality of PCI for acute occlusion of the LMCA is high, long term survival of the successful cases is excellent and justifies such treatment of this imminent condition, almost always lethal without treatment.

References

(1) O'Keefe J.H. jr, Hartzler G.O., Rutherford B.D., et al. Left main coronary angioplasty: early and late results of 127 acute and elective procedures. Am J Cardiol 1989;64:144-147.
(2) Hibbard M.D., Holmes Jr D.R., Bailey K.R., et al. Percutaneous transluminal coronary angioplasty in patients with cardiogenic shock. J Am Coll Cardiol 1992;19:639-46.
(3) Spiecker M., Erbel R., Rupprecht H-J., Meyer J. Emergency angioplasty of totally occluded left main coronary artery in acute myocardial infarction and unstable angina pectoris- Institutional experience and literature review. Eur Heart J 1994;15:602-607.
(4) Lopez J.J., Ho K.K.L., Stoler R.C., et al. Percutaneous treatment of protected and unprotected left main coronary stenoses with new devices: immediate angiographic results and intermediate-term follow-up. J Am Coll Cardiol 1997;29:345-52.
(5) Chauhan A., Zubaid M., Ricci D.R., et al. Left main intervention revisited: early and late outcome of PTCA and stenting. Cathet Cardiovasc DiaGN 1997;41:21-29.
(6) Ellis S.G., Tamai H., Nobuyoshi M., et al. Contemporary percutaneous treatment of unprotected left main coronary stenoses. Initial results from a mullticenter registry analysis 1994-1996. Circulation 1997;96:3867-3872.
(7) Laruelle C.J.J., Brueren G.B.R., Ernst S.M.P.G., et al. Stenting of 'unprotected' left main coronary artery stenoses: early and late results. Heart 1998;79:148-152.
(8) Bär F., Vainer J., Stevenhagen J., et al. Ten-year ectxperience with early angioplasty in 759 patients with acute myocardial infarction. J Am Coll Cardiol 2000;36:51-8.

(9) Tan W.A., Tamai H., Park S-J., et al. Long-term clinical outcomes after unprotected left main trunk percutaneous revascularization in 279 patients. Circulation 2001;104:1609-1614.
(10) Yip H-K., Wu C-J., Chen M-C., Chang H-W., et al. Effect of primary angioplasty on total or subtotal left main occlusion. Chest 2001;120:1212-1217.
(11) De Luca G., Suryapranata H., Thomas K., et al. Outcome in patients treated with primary angioplasty for acute myocardial infarction due to left main coronary artery occlusion. Am J Cardiol 2003;91:235-237.

Chapter 9

Present management of patients with acute myocardial infarction in the referral area of the Catharina Hospital in Eindhoven: Synthesis of what we learned.

Based upon literature and upon the lessons learned from this initial study, the care for patients with extensive myocardial infarction in the referral area of the Catharina-Ziekenhuis is organized as follows.

The area consists of the mid and eastern part of the province of Noord-Brabant and the north and middle part of Limburg. The intervention center in this region is the Catharina Ziekenhuis. In the direct vicinity of Eindhoven there are 4 hospitals, the St. Anna Ziekenhuis Geldrop, Elkerliek Ziekenhuis Helmond, and Maxima Medisch Centrum location Veldhoven and location Eindhoven, respectively. This area is called the inner area and has a radius of approximately 20 kilometers around Eindhoven.

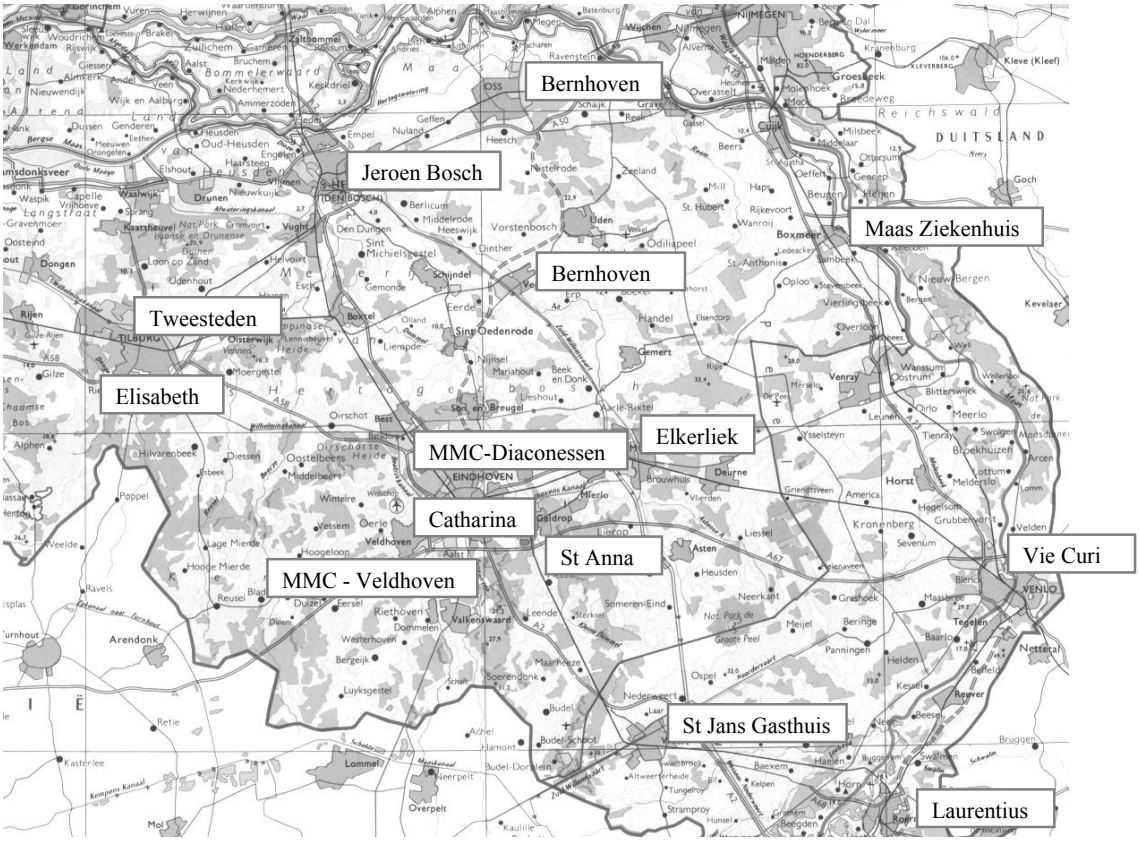


Figure 1. Map of inner and outer referral area.

The larger area has a radius of about 50 kilometers around Eindhoven, in which several more hospitals are located: St. Jans Gasthuis Weert, Vie Curi Medisch Centrum Venlo, Maas Ziekenhuis Boxmeer, Elisatbeth Ziekenhuis Tilburg, TweeSteden Ziekenhuis Tilburg, Jeroen Bosch Ziekenhuis ‘s-Hertogenbosch and

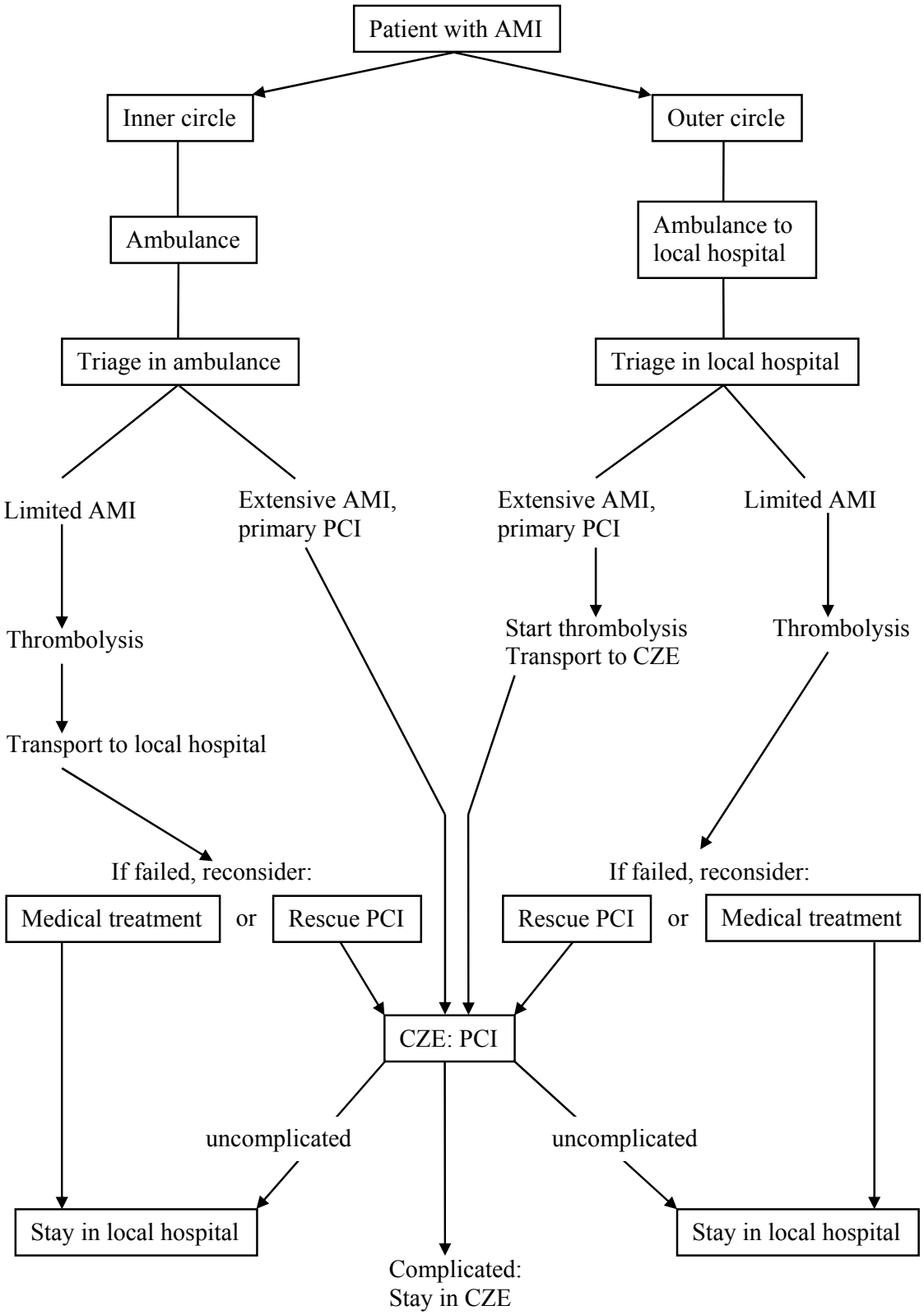


Figure 2. Flow chart of peri-infarction care in the Eindhoven region. AMI=Acute Myocardial Infarction; CZE=Catharina Ziekenhuis; PCI=Percutaneous Coronary Interbvention.

Bernhoven Ziekenhuis location Veghel-Uden and location Oss. This area is referred to as the larger referral area (Figure 1).

The care for acute infarct patients is performed in close coorperation with the ambulance services (CPA Noord/midden Limburg, CPA Den Bosch, CPA Tilburg, CPA Eindhoven, CPA Maastricht, CPA Nijmegen and CPA Tilburg) and the cardiologists in the referring hospital.

Within the inner area, the ambulance nurses decides based upon the electrocardiographic criteria if a patient is considered as high risk acute myocardial infarction (Figure 2) and in that case, the patient is transferred directly to the Catharina-hospital for primary PCI. If the patient is diagnosed as having a moderately sized myocardial infarction, the patient is transferred to a local hospital and treated with thrombolysis. In case of failed thrombolysis or hemodynamic deterioration, the patient is transferred as yet for rescue PCI to the Catharina Hospital. In those patients undergoing primary or rescue PCI, the ambulance waits upon the result and if PCI is successful, transfers the patient thereafter to the local hospital closest to his place of habitation or the referring hospital. For the larger area, most often the patients are transferred to the local hospital directly and it is to decide by the cardiologist on duty if thrombolysis is started, or the patient is transferred directly to the Catharina-hospital. In the inner area, in those patients transferred to the Catharina-hospital for primary PCI, thrombolysis has sometimes already been started in the ambulance by the ambulance-nurses, based again upon certain predefined criteria.

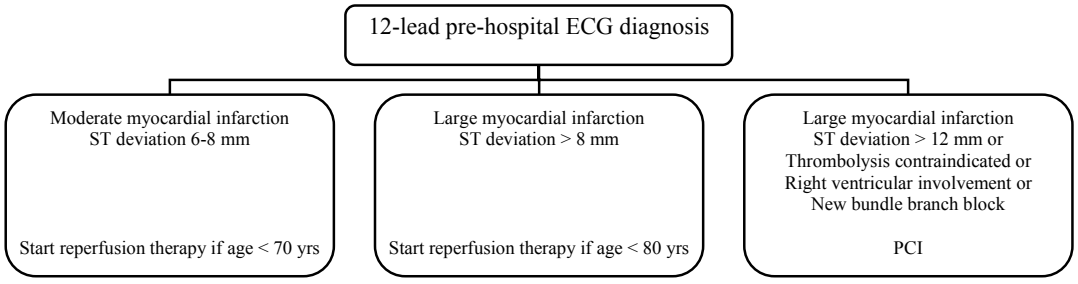


Figure 2. Pre-hospital triage: decision tree for treatment of acute myocardial infarction (onset < 6 hours) patients based on 12-lead ECG.

In this way, optimum care can be provided around the clock and it is secured that sufficient beds are available for all patients at every time. The logistics

implications are large, in that sense that around the clock, an interventional cardiologist, two catheterization laboratory-nurses, and one radiological technician need to be standby in the hospital. The Catharina-hospital and its referral centers were the first area in The Netherlands where care was provided in this way and presently it is the area where the largest number of infarction patients is treated according to this optimum strategy. In 2003 we performed in the Catharina Hospital 394 emergency procedures. Of the 321 patients in our area with an acute myocardial infarction, 321 patients underwent a primary PCI, and for 73 patients it concerned a rescue PCI.

An issue not yet solved is the optimum medical treatment while the patient is transferred to the interventional center. All patients start with aspirin and plavix as soon as possible, i.e. in the local hospital or in the ambulance. Within the inner area, thrombolysis is started by the ambulance nurse if particular criteria are fulfilled (Figure 2). In many cases, either thrombolysis or GP IIb/IIIa inhibitors are started in a local hospital if a patient is transferred for primary PCI from the larger area. Insufficient data are available yet to decide if thrombolysis or GP IIb/IIIa inhibition should be started prior to every primary PCI.

Chapter 10

Lessons from the nineties.

Despite angiographical differences between diabetics and non-diabetics six months after PCI of one or two arteries, both short-term and long-term clinical follow-up appeared to be similar. (Chapter 2).

Management strategies after myocardial infarction should not be based on the absence or presence of Q waves on the electrocardiogram. Most likely, residual left ventricular function and the presence of inducible ischaemia are of more importance. (Chapter 3).

It is feasible within The Netherlands to cluster care for patients with acute myocardial infarction in a heart center, similar to the situation for elective PCI and bypass surgery. The logistic consequences should not be underestimated because this means a 24-hours availability of a team of 4-5 specialists/technicians, adequate training and organization of emergency and coronary care departments in the referring hospitals and ambulance services.Patients can be admitted to the nearest hospital and receive thrombolytic therapy or transported directly to the regional heart center in case of high risk (large anterior wall infarctions or RCA occlusions with right ventricular involvement and/or hemodynamic instability).Even in these patients with high risk, 48 hours mortality can be reduced to approximately 5% with another 5% during the first year. (Chapter 4).

Hemodynamic stenosis severity can often be predicted from the angiogram, even not by experienced interventional cardiologists. In case of any ambiguity, measuring of fractional flow reserve should be performed. The population selected for PCI will extend to patients with more complex disease. A more refined and individualized understanding of disease, and a more appropriate selection of the epicardial lesions to be treated in patients with complex disease, will be paramount not only for patient care but also to keep health care affordable.(Chapter 5)

Predicting periprocedural risk of a PTCA remains difficult. A small subgroup of patients can be discriminated beforehand with a high risk. However, the majority of

major complications occur in patients assessed beforehand as only having small or moderate risk. Therefore, in-house surgical stand/by remains mandatory. Abandoning this principle, although attractive from non-medical points of view will result in unnecessary loss of lives in a country like the Netherlands. (Chapter 6).

In experienced hands, PCI of a non/bifurcational unprotected left main stenosis is an alternative for bypass surgery, especially if relative contra/indications for CABG are present. (Chapter 7).

Emergency PCI of an occluded LM coronary artery, either due to acute myocardial infarction or catheter induced has high peri/procedural mortality, but long term follow-up of the survivors is excellent. (Chapter 8).

We learned that it is possible to achieve care around the clock 365 days per year for patients suffering from an acute myocardial infarction in close cooperation with the ambulance services, referring hospitals and a PCI centre. (Chapter 9).

Chapter 11

Summary

The use of percutaneous coronary interventions has been expanded tremendously since its introduction in 1977. After the initial experience in the late seventies, the eighties were characterized by mastering elementary techniques in coronary interventions. Still, a common feature of that period was that mostly only single vessel disease could be treated and that a number of complex anatomic situations were not accessible for PCI. Also, the high restenosis rate was one of the features of the eighties. During the nineties, more sophisticated equipment became available (like coronary stents and the possibility for refined physiologic assessment of coronary artery disease). Also, more complex situations and multivessel disease became the area of the interventional cardiologist.

Although the state-of-the-art in interventional cardiology is based on large randomized trials and evidence-based medicine, many individual patients do not fit within the frame work of such trials. For this large majority of patients, also the personal experience of the operator is important in the choice of treatment and in providing the best possible care in the every day world. Therefore, in order to have a continuous feed-back and feed-forward upon our way of treating patients, it is necessary to learn from our experience in a systematic way.

For that reason, a database was developed which contained all procedure related data concerning patients undergoing percutaneous coronary interventions during the nineties. By analyzing these data, we tried to develop a universally valid view upon complications, mortality, influence of new techniques, and so on. More importantly, such a database also can serve as a quality control instrument.

In this thesis, the important issues that were extracted from this database, are described and these lessons from the nineties are summarized. Based upon those lessons, the approach of patients with acute myocardial infarction in the referral area of the Catharina-hospital, was developed.

From that database we studied in **chapter 2** all patients with diabetes mellitus. In prospectively randomised trials coronary angioplasty is considered an inferior method of revascularization compared with coronary artery bypass grafting. However, this is based on patients with diabetes mellitus and multivessel disease. We studied 97 diabetic patients (9.2%) in the BAAS trial (a prospective randomised trial with 1058 angioplasty patients compared the effects of aspirin alone versus aspirin plus coumarins), of whom 50 patients were randomised to follow-up angiography. Diabetics were identified by treatment with insulin or oral hypoglycaemic medication. Primary end point comprised all cause mortality, myocardial infarction or target-vessel revascularization. The baseline characteristics of the diabetics and nondiabetics were the same except for significant more males and smokers among nondiabetics. At 6 months the minimal luminal diameter was significantly smaller in the diabetics (1.55 ± 0.76 mm versus 1.78 ± 0.66 mm; p=0,01). Diabetics had also more restenosis (41% versus 23%; p=0.003). However, with respect to clinical follow-up, diabetics fared as good as nondiabetics. At 30 days, the primary end point occurred in 5 diabetic patients (5.2%) and 47 nondiabetics (4.9%), (p=0.8), and at 1 year in 17 (17.5%) and in 165 (17.1%), respectively. Univariate hazard ratio for the primary composite endpoint was not statistically significant (p=0.9; 95% CI 0.6-1.7). Multivariate analysis showed that only the presence of a LAD lesion was a significant predictor of the endpoint with a hazard ratio of 1.486 (p=0.01; 95% CI 1.1-2.0). Although diabetics have more restenosis, the short-term follow-up turned out to be as good as in nondiabetics.

In **Chapter 3** we retrospectively studied if one could prevent recurrent ischaemia or myocardial infarction after non-Q wave myocardial infarction by target vessel revascularization. Some studies have suggested that patients suffering a non-Q wave myocardial infarction have a better prognosis due to less necrosis, which has been disproved in some other studies. Currently, however, there are few data on the immediate and long-term results of PTCA after non-Q wave myocardial infarction. Retrospectively we studied two consecutive groups of patients who underwent PTCA for ischaemia after either a Q wave myocardial infarction (n=175) or a non-Q wave myocardial infarction (n=175). Baseline characteristics and angiographic data were comparable, except that fifteen of the 175 non-Q wave myocardial infarction patients

had moderately diminished left ventricular function as opposed to 30 in the Q wave myocardial infarction patients, (p=0.016). There were more total occlusions in the Q wave patients (51% vs 29%; p=0.02). Success rates of the PTCA were similar in both groups (94% vs 97%; p=0.21). At a mean follow-up of 44 months 114 patients (65.1%) of the patients in the Q-wave group remained free from any event compared to 101 in the non-Q wave group (57.8%). Repeat revascularization (surgical or PTCA) was performed in 26 patients (14%) in the Q-wave myocardial infarction group compared to 31 patients (18%) in the non-Q wave myocardial infarction group (p=ns). So, we concluded that the outcome (initial and long-term) after PTCA was similar for patients who suffer from a non-Q wave myocardial infarction group or a Q-wave myocardial infarction group. Therefore: the management strategies after myocardial infarction should not be based on the absence or presence of Q waves at the ECG but rather on the presence of inducible ischaemia.

In **Chapter 4** we studied the question whether a regional myocardial infarction centre would be an option. Early reperfusion of the occluded coronary artery for patients with an acute myocardial infarction is mandatory for saving myocardial tissue, reduction of complication and mortality. PTCA is more and more often performed in case of an acute myocardial infarction, primary or as a rescue procedure; but coronary angiography is difficult to organise, because of logistic problems, mainly. Only few hospitals have possibilities to perform coronary angiography 24 hours per day We studied the results of all 173 patients who underwent an acute PTCA in our hospital in 1997 (146 primary procedures (84.3%), 27 rescue procedures (15.6%)). It concerned patients with an acute myocardial infarction who where admitted at our hospital or who were referred from hospitals in the region within 6 hours after the start of the symptoms. Admission from these hospitals could be accomplished within 45 minutes in all cases. Most patients underwent this procedure within 6 hours (88.4%). No patient died during the transportation to our hospital. The procedure was successful in 169 out of those 173 patients (98%), and a myocardial infarction was completely prevented (aborted) in 32 of these patients (19%). One hundred and fifteen patients had a Q-wave myocardial infarction (66%). Urgent coronary artery bypass grafting was necessary in 1 patient. Nine patients died in the acute phase, and nine (5%) in the

one year follow-up. Within 6 months 3 patients had a repeat myocardial infarction (1.7%), 5 patients underwent re-PTCA, because of restenoses and 7 (4%) underwent elective CABG. Which patients have to be send to a so called myocardial infarction centre? We concluded that patients can be safely transported to a regional myocardial infarction centre in case of primary or rescue PTCA. The in hospital results are satisfactory with an in hospital mortality of 5%. We have to keep in mind that there was a strong selection bias toward patients with a large myocardial infarction, an anterior myocardial infarction or with hemodynamic instability.

In **Chapter 5** we studied whether eyeball assessment of intermediate coronary stenosis is as good as measuring the fractional flow reserve (FFR). The physiological significance of angiographically severe stenosis (>80% diameter stenosis) or minimal disease (<30% diameter stenosis) is obvious. However, the angiographic interpretation of an intermediate stenosis has a poor correlation with the actual measurements of coronary blood flow reserve. Decisions on revascularization on patients with intermediate lesions based on angiographic appearance are potentially fraught with a high degree of inaccuracy. Decisions regarding coronary interventions should be based on objective evidence of ischemia. Such evidence may be obtained from non-invasive testing, such as exercise tests, myocardial scintigraphy and stress-echocardiography. In daily clinical practice the indication for PTCA is often based mainly on angiography, especially for so-called secondary lesions. In patients with intermediate coronary stenosis where no mutual agreement was obtained by experienced interventional cardiologists, we used FFR as the gold standard. We studied fifty-two patients, performed FFR, and compared the relation between the eyeball assessment and FFR. The procedure consisted of a repeat control angiogram, FFR measurement and PCI only in case of an FFR<0.75. Agreement between both assessments was obtained in 36 patients (69.2%), overestimation of hemodynamic severe stenosis occurred in 6 patients (11.5%) and under estimation in 10 cases (19.2%). The positive predictive value of eyeball assessment was 63%, the negative predictive value was 76%. The sensitivity was 74%, the specificity 66%. Our study shows that patients with intermediate stenosis an unnecessary PTCA would have been performed in 11.5% of the cases, if FFR would not have been measured, and a potentially therapeutic PTCA

would have been withheld in 19.2% of the cases. We concluded that assessment of hemodynamic severity of intermediate coronary stenosis should not rely on eyeball estimation, as this would have resulted in a wrong decision in 30.7% of the cases.

In **Chapter 6** the very actual issue was studied whether risk of the PCI can be estimated beforehand. Complications during PCI are hard to predict due to the complexity of clinical and angiographical factors. The guidelines defined by the American College of Cardiology/American Heart Association (ACC/AHA) do not provide hard data to predict clinical consequences, especially because the technical difficulty and the risk of procedural complications have been considered as one entity. We developed a combined clinical and angiographic risk assessment system based on the experience in our hospital and evaluated it prospectively. We wanted to investigate to what extent a strategy can be worked out to predict the risk and difficulty of a PCI procedure. Between 1991 and 1995 five experienced interventional cardiologists categorised all 7144 patients with 10081 stenoses (1.4 lesion/patient) for both the ***risk*** and the ***difficulty*** of the procedure. Risk categories are as follows: 1= low risk, 2= intermediate risk, 3= high risk. Difficulty categories are as follows: 1= low risk, 2= intermediate risk, 3= high risk. All possible clinical variables were taken into account. Success was achieved in difficulty category 1 in 98.4%, in category 2 in 96.5%, and in category 3 in 90.1% ($p<0.005$). Complications occurred in risk category 1 in 3.5%, in category 2 in 5.2%, and in category 3 in 12.4% ($p<0.05$). Death following the procedure occurred in risk category 1 in 0.3%, in category 2 in 0.2%, and in category 3 in 1.9%. Although cardiologists were very well capable to predict the risk and difficulty in high risk groups of patients, the magnitude of serious events occurred in patients, classified beforehand as low or intermediate risk. Therefore we conclude that there always remains the need for surgical back-up as even in the lowest risk groups the need for emergent surgery was 0.3%.

In **Chapter 7** we described the patients who underwent elective PCI for a non-bifurcational left main stenosis between 1990 and 2001 in our hospital. Although PCI is a potential indication, it is considered too dangerous due to expected high mortality of acute closure, in contrast with coronary bypass surgery (CABG) that can be performed with a risk less than 5%. Due to the experience with PCI of the LMCA

under special circumstances, this technique is applied increasingly in broader categories of patients. We found 71 patients out of a total of 17683 (0.4%). In 49.3% of the patients, only the left main had a significant stenosis. In six patients (8.5%) excellent collaterals to the perfusion area of the LMCA were noted. Twelve patients (16.9%) had a severely impaired LV function, 43 patients (60.6%) had a normal LV function. A stent was used in 23 cases (32.4%). No patients had the support of an intra aortic balloon pump. Severe concomitant disease was an argument for choosing PCI instead of CAGB in 37 (51.1%) of the cases. Nineteen patients (26.8%) had severe peripheral arterial occlusive disease, 6 patients had severe pulmonary disease (8.5%), 4 patients (5.6%) had a cardiomyopathy or a recent myocardial infarction, 3 patients had severe renal insufficiency (4.2%) and 1 patient a malignancy (1.4%). Urgent CABG was required in 1 patient immediately upon PCI because of a dissection spreading out from the left main coronary artery into the LAD and LCX, the further clinical course was without sequelae. Urgent repeat PCI was needed in 2 patients. One patient had an acute closure within 30 minutes and a bail out stent was used, in the other patient myocardial ischemia occurred because of thrombus formation in the LCX, and angioplasty was performed successfully. One patient died within 24 hour because of massive thrombus formation in the LMCA, and all angioplasty attempt failed. The annual mortality was 2.5%, mostly because of non cardiac reasons. Throughout the follow up period 13 patients (18.3%) required CABG. We conclude that elective PCI of the non-bifurcational LMCA can safely be performed, in case of suitable anatomy.

In **Chapter 8** we described emergency PCI for unprotected LMCA. Acute occlusion of the LMCA is an immediately life-threatening condition, which will result in death within minutes or hours. Therefore, emergency CABG is not often a feasible alternative for PCI. Between 1990 and 2001 thirty-five patients underwent an emergency PCI for threatening LMCA occlusion (0.2% of the total PCI population). Twenty-six of the study patients (74.3%) were treated in the setting of acute myocardial infarction, in nine patients the PCI procedure was needed because of dissection of the LMCA during coronary angiography. Twenty patients (57.1%) had an occlusion of the LMCA, a stent was used in 25 patients (71.4%). Cardiopulmonary resuscitation was needed in 7 patients (20%), six patients needed urgent CABG after

anthegrade flow was achieved in the LMCA. One year mortality was 41%, all patients died due to cardiac failure, aspiration pneumonia or a cerebrovascular accident. Twenty patients (59%) survived. Additional revascularization occurred in 2 of these 20 patients (10%), one patient underwent CABG after 31 months, the other CABG and MVP. We conclude that the lives of those 20 patients (59%) were saved by to the procedure and that PCI is the method of choice in patients with acute LMCA occlusion.

In **chapter 9** we described the organisation of patients suffering a myocardial infarction in the referral area of the Catharina Hospital. In close cooperation with the ambulance services an around the clock service is guaranteed, which is demanding on the logistics; an interventional cardiologists, two catheterization laboratory nurses and one radiological technician need to be on-call. In 2003 we performed according to this strategy 321 primary PCI, and 73 rescue PCI's. If a patient is considered as high risk, he will be transferred directly to the Catharina Hospital for primary PCI. If a patient is considered as low risk the patient is transferred to the nearby hospital and treated with thrombolysis. In case of failed thrombolysis and deterioration, the patient is transferred for rescue PCI, accordingly to the judgement of the threatening cardiologist.

Chapter 12

Samenvatting

Het gebruik van percutane coronair interventie is enorm gegroeid sinds de introductie in 1977. Na de initiële ervaringen in de late jaren zeventig, werden de jaren tachtig gekenmerkt door verdere verfijningen in de te gebruiken technieken en materiaal.

Desondanks, het was in die periode gebruikelijk dat louter één-taks afwijkingen behandeld kon worden. Daarnaast overheerste de mening, dat complexe anatomische situaties niet toegankelijk waren voor PCI. Ook was restenosering na interventie een groot probleem. In de jaren negentig kwamen meer geavanceerde technieken beschikbaar, zoals coronair stents en de mogelijkheid om een fysiologische meting van de coronairen te verrichten. Zodoende werden complexere laesies en meertaks afwijkingen het terrein van de interventie cardiologen.

Ondanks dat ‘state-of-the-art’ interventie cardiologie wordt gebaseerd op grote gerandomiseerde trials en evidence-based geneeskunde, passen vele individuele patiënten niet in het ontwerp van dergelijke trials.

Voor de overgrote meerderheid van de patiënten is ook de persoonlijke ervaring van de interventie cardioloog belangrijk in de therapiekeuze, zodat de best mogelijke zorg in de alledaagse wereld gegeven kan worden.

Om een continue ‘feed-back en feed-forward’ te creëren bij het behandelen van patiënten, is het noodzakelijk om systematisch van onze ervaringen te leren. Met dit doel werd een database gemaakt waarin alle patiënten die een percutane coronaire interventie ondergingen werden geregistreerd. Door deze gegevens te analyseren kregen we een valide kijk op complicaties, mortaliteit, invloed van nieuwe technieken enzovoort. Een dergelijke database kan ook dienen als een kwaliteitsmeter.

In dit proefschrift worden een aantal belangrijke aspecten die we hebben geleerd door middel van deze database beschreven, om zodoende de ’lessen van de jaren negentig’ samen te vatten. Gebaseerd op deze lessen, werd een optimale strategie ontwikkeld om de patiënten met een acuut myocardinfarct in de regio van Eindhoven te behandelen.

Vanuit die database bestudeerden we in **hoofdstuk 2** alle patiënten met diabetes mellitus. In prospectief gerandomiseerde trials wordt angioplastiek als inferieure manier van revasculariseren gezien in vergelijking met bypass chirurgie. Echter dit is

gebaseerd op patiënten met diabetus mellitus en meertaks afwijkingen. Wij bestudeerden 97 diabetes patiënten (9.2%) in de BAAS trial (een prospectief gerandomiseerde trial met 1058 angioplastiek patiënten waarin de effecten van aspirine alleen versus aspirine plus coumarines), van wie 50 patiënten werden gerandomiseerd voor controle angiografie. Diabetes patiënten werden gedefinieerd als ze werden behandeld met insuline of orale antidiabetica. Als primair eindpunt werd overlijden, myocard infarct of reinterventie van het gedilateerde vat gedefinieerd. De basiskarakteristieken van de diabeten en niet-diabeten waren hetzelfde behoudens dat er meer mannen en rokers zich bevonden in de groep niet-diabeten. Na 6 maanden was het minimale lumen doorsnede significant kleiner in de patiënten met diabetes mellitus (1.55 ± 0.76 mm versus 1.78 0.66 mm; p=0.01). Diabeten hadden ook meer restenosering (41% versus 23%; p=0.003). Dit in tegenstelling tot klinische follow-up, hierbij was er geen verschil in beide groepen. Na 30 dagen, trad het primaire eindpunt op in 5 diiabeten (5.2%) en 47 niet diabeten (4.9%), en na 1 jaar bedroeg deze 17 (17.5%) en in 165 (17.1%),. Multivariate analyse toonde dat slechts het aanwezig zijn van een proximale LAD stenose een significante voorspeller was met een hazard ratio van 1.486 (p= 0.01; 95% CI 1.1-2.0). Hoewel diabeten meer restenose hadden, de korte termijn follow-up was even goed als in niet-diabeten.

In **Hoofdstuk 3** bestudeerden we retrospectief of men recidief ischaemie of recidief infarcering kon voorkomen na een niet-Q-golf infarct door het aangedane vat te revasculariseren. Enkele studies hebben gesuggereerd dat patiënten met een niet-Q-golf myocard infarct een betere prognose hebben door minder necrose, welke in sommige andere studies wordt tegengesproken. Tegenwoordig zijn er slecht weinig gegevens beschikbaar over de korte en lange termijn resultaten van PTCA na een niet-Q-golf infarct. Wij bestudeerden retrospectief 2 consecutieve groepen patiënten die een PTCA ondergingen vanwege ischaemie na een Q-golf myocard infarct (beide groepen 175 patiënten). Basis karakteristieken en angiografische data waren vergelijkbaar, behalve dat 15 van de 175 niet-Q-golf een geringe verminderde linker kamer funcie hadden in tegenstelling tot 30 patiënten met een Q-golf infarct, (p=0.016). Er waren meer afgesloten vaten in de Q-golf groep (51% vs 29%, p=0.02). Het succes percentage van de PTCA was vergelijkbaar in beide groepen (94% vs 97%;

p=0.21). Na een gemiddelde follow-up van 44 maanden waren 114 patiënten (61.1%) van de Q-golf patiënten asymptomatisch vergeleken met 101 in de niet Q-golf groep (57.8%). Herhaaldelijke revascularisatie (chirurgie of PTCA) werd in 26 patiënten (14%) verricht in de Q-golf infarct groep vergeleken met 31 patiënten (18%) in de niet Q-golf infarct groep. Aldus concludeerden wij dat de korte en lange termijn prognose na PTCA gelijk was voor patiënten die een niet Q-golf myocard als patiënten die een Q-golf infarct doormaakten. Daarom dient de strategie na een myocard infarct niet gebaseerd te zijn op het al of niet aanwezig zijn van Q golven op het ECG maar wel op het al dan niet aanwezig zijn van induceerbare ischaemie.

In **hoofdstuk 4** bestudeerden we de vraag of een regionaal infarct centrum een optie zou kunnen zijn. Vroege reperfusie van het geoccludeerde bloedvat is voor patiënten met een acuut myocardinfarct van belang om moycardweefsel te redden, een vermindering van complicatie en mortaliteit te bewerkstelligen. PTCA wordt meer en meer verricht in geval van een acuut myocardinfarct, primair of als rescue procedure; maar coronair angiografie is omwille van logistieke problemen moeilijk realiseerbaar. Slechts weinig ziekenhuizen bieden de mogelijkheid om 24 uur per dag coronair agiografieën te verrichten. Wij bestudeerden de resultaten van alle 173 patiënten die in ons ziekenhuis in 1997 een acute PTCA ondergingen (146 primaire procedures 84.3%), 27 rescue procedures (15.6%)). Het betrof patiënten met een acuut myocardinfarct die in ons ziekenhuis of in een verwijzend ziekenhuis in onze regio werden gepresenteerd binnen 6 uur na start van de klachten. De aanrijtijd vanuit verwijzende ziekenhuizen bedroeg hooguit 45 minuten. Geen patiënt overleed tijdens transport. De procedure was succesvol in169 van de 173 patiënten (98%), een myocardinfarct werd zelfs voorkomen in 32 van deze patiënten (19%). Honderdenvijftien patiënten hadden een Q-golf infarct (66%). Spoed bypass chirurgie was nodig in 1 patiënt. Negen patiënten overleden in de acute fase, en 9 (5%) in het eerste jaar. Binnen 6 maanden hadden 3 patiënten een recidief myocardinfarct (1.7%), 5 patiënten ondergingen een re-PTCA vanwege restenosering en 7 patiënten ondergingen een electieve CABG. Welke patiënten dienden nu verwezen te worden naar het infarct centrum? Wij concludeerden dat het veilig was om patiënten met een acuut myocardinfarct te transporteren naar een regionaal myocardinfarct centrum om

een primaire of rescue PTCA te verrichten. De ziekenhuissterfte is acceptabel met een sterfte van 5%. We moeten ons wel realiseren dat er een selectiebias naar patiënten met een groot myocardinfarct, een voorwand myocardinfarct of met hemodynamische instabiliteit.

In **hoofdstuk 5** bestudeerden we of een globale schatting van middelmatige coronaire vernauwingen net zo goed is als het bepalen van de fractionele flowreserve (FFR). De fysiologische significantie van angiografische ernstige stenosis (>80% diameter stenosis) of minimale afwijkingen (<30% diameter stenosis) is overduidelijk. Echter, de angiografische interpretatie van een middelmatige stenose heeft een slechte correlatie met de daadwerkelijke meting middels FFR. Beslissingen om een revascularisatie te verrichten bij patiënten met een middelmatige stenose gebeuren met een potentiële inadequaatheid. Beslissingen om een coronaire interventie te verrichten dient te geschieden op basis van bewezen ischaemie. Zulks bewijs kan non-invasief verkregen worden, zoals een inspanningstest, een myocardscintigram of een stress-echocardiografie. In de dagelijkse praktijk wordt de indicatie voor PTCA vaak gesteld op het angiogram. Bij patiënten met een middelmatige stenose, waarbij ervaren interventiecardiologen het niet unaniem eens waren over de ernst van de stenose werd een FFR verricht, die diende als gouden standaard. We bestudeerden 52 patiënten, welke allen een FFR ondergingen, en vergeleken de relatie tussen globale schatting en FFR. De procedure bestond uit een controle angiogram, FFR meting en PCI slechts indien er sprake was van een FFR<0.75. Overeenstemming tussen beide methodieken was er in 36 patiënten (69.2%), overwaardering van hemodynamische ernstige stenosis kwam voor bij 6 patiënten (11.5%) en onderwaardering bij 10 patiënten (19.2%). De positief voorspellende waarde van globale schatting was 63%, de negatief voorspellende waarde was 76%. De sensitiviteit was 74%, de specificiteit 66%. Onze studie laat zien dat patiënten met een middelmatige stenose in 11.5% van de gevallen onnodig een PTCA hadden ondergaan, als een FFR meting niet was verricht, en een potentieel therapeutische PTCA was onthouden aan de patiënt in 19.2% van de gevallen. Wij concludeerden dat de hemodynamische ernst van middelmatige stenosis niet kan worden bepaald met globale schatting, omdat hierdoor in 30.7% van de gevallen een onjuiste beslissing zou zijn genomen.

In **hoofdstuk 6** werd bestudeerd of het risico van een PCI kan worden voorspeld. Door de complexiteit van klinische en angiografische factoren zijn complicaties tijdens een PCI procedure moeilijk voorspelbaar. De richtlijnen welke zijn gedefinieerd door de American College of Cardiology/American Heart Association (ACC/AHA) geven geen houvast om klinische consequenties te voorspellen, in het bijzonder omdat de technische moeilijkheid en het risico van de procedure zijn gekoppeld in deze richtlijnen. Wij hebben een gecombineerd klinisch en angiografisch risicostartificatie systeem ontworpen, gebaseerd op de ervaringen in ons ziekenhuis en prospectief geëvalueerd. Wij wilden onderzoeken in hoeverre het risico en de moeilijkheid van een PCI procedure kan worden voorspeld. Tussen 1991 en 1995 deelden 5 ervaren interventiecardiologen alle 7144 PCI patiënten met 10081 stenosis (1.4 laesies/patiënt) in voor zowel het **risico** als **moeilijkheid**. Risico categorieën waren: 1=laag risico, 2=middelmatig risico, 3=hoog risico. Moeilijkheids categorieën waren: 1=laag risico, 2=middelmatig risico, 3= hoog risico. Alle mogelijke klinische variabelen werden meegenomen. Succes werd bereikt in moeilijkheids categorie 1 in 98.4%, in categorie 2 in 96.5% en in categorie 3 in 90.1% ($p<0.005$). Complicaties gebeurden in risico categorie 1 in 3.5%, in categorie 2 in 5.2% en in categorie 3 in 12.4% ($p<0.05$). Overlijden na de interventie gebeurde in risico categorie 1 in 0.3%, in categorie 2 in 0.2% en in categorie 3 in 1.9%.

Ondanks dat cardiologen goed in staat zijn om het risico en de moeilijkheid van patiënten te voorspellen, waren er een niet onaanzienlijk aantal complicaties in de laag of gemiddelde risicogroepen. Wij concluderen dan ook dat er altijd behoefte is aan chirurgische back-up, mede omdat in de laagste risicogroep er in 0.3% van de patiënten spoedchirurgie nodig was.

In **hoofdstuk 7** beschreven we de patiënten die een electieve PCI ondergingen voor een non-bifurcational hoofdstam stenose in de jaren 1990 en 2001 in ons ziekenhuis. Ondanks dat PCI een potentiële indicatie is, wordt het als te gevaarlijk beschouwd, door de verwachte hoge mortaliteit ten gevolge van acute afsluiting, in tegenstelling tot coronaire bypass chirurgie, dat met een klein risico (<5%) kan worden verricht. Door de ervaringen onder speciale omstandigheden van PCI van de hoofdstam, wordt deze techniek meer en meer toegepast bij een steeds grotere groep

patiënten. Wij vonden 71 patiënten die een dergelijke PCI ondergingen van in totaal 17683 patiënten (0.4%). In 49.3% van deze patiënten, had alleen de hoofdstam een stenose. In 6 patiënten (8.5%) waren er goede collateralen naar het gebied van de hoofdstam. Twaalf patiënten (16.9%) hadden een ernstig verminderde linker kamerfunctie, 43 patiënten (60.6%) had een normale linker kamer functie. Een stent werd in 23 procedures gebruikt (32.4%). Geen patiënt had de ondersteuning van een intra aortale ballonpomp. Er werd in 37 patiënten (51.1%) afgezien van bypass chirurgie door ernstige comorbiditeit. Negentien patiënten (26.8%) hadden ernstig perifeer vaatlijden, 6 patiënten hadden ernstig longlijden (8.5%), 4 patiënten had een cardiomyopathie of een recent myocard infarct (5.6%), 3 patiënten hadden een ernstige nierinsufficientie (4.2%) en 1 patiënt had een maligniteit (1.4%). Spoed chirurgie was nodig bij 1 patient na de PCI procedure, omdat een dissectie zich uitspreidde vanuit de hoofdstam richting LAD en RCX, het verdere beloop was ongecompliceerd. Spoed re-PCI was nodig in 2 patienten. Een patiënt had een acute afsluiting binnen 30 minuten, waarbij een stent werd geplaatst, in de andere patient was er persisterende myocard ischaemie ten gevolge van trombusvorming in de RCX, PTCA was bij deze patiënt succesvol. Een patiënt overleed binnen 24 uur na de procedure ten gevolge van massale trombusformatie in de hoofdstam, en alle PCI pogingen mislukten. De jaarlijkse mortaliteit was 2.5%, meestal ten gevolge van niet cardiale oorzaken. Tijdens de follow-up periode ondergingen 13 patiënten (18.3%) bypass chirurgie. Wij concluderen dat electieve PCI van een non-bifurcational hoofdstam in geval van een geschikte anatomie, veilig kan worden uitgevoerd.

In **hoofdstuk 8** beschreven we de resultaten van spoed PCI van de onbeschermde hoofdstam. Acute afsluiting van een onbeschermde hoofdstam is een levensbedreigende toestand, welke binnen enkele minuten tot uren tot de dood lijdt. Daarom is spoed chirurgie vaak geen goede alternatief voor PCI. Tussen 1990 en 2001 ondergingen 35 patiënten een spoed PCI omwille van een afgesloten hoofdstam (0.2% van de totale PCI populatie). Zesentwintig van de studiepatiënten (74.3%) ondergingen de procedure in verband met een acuut myocardinfarct, in 9 patiënten werd deze procedure verricht vanwege een dissectie die bij een electieve angiografie was ontstaan. Twintig patiënten (57.1%) hadden een occlusie van de hoofdstam, 25

patiënten kregen een stent (71.4%). Reanimatie was nodig in 7 patiënten (20%), 6 patiënten hadden een spoed bypass operatie nodig nadat antegrade bloeddoorstroming was bewerkstelligd. De eenjaars mortaliteit bedroeg 41%, alle patiënten overleden tgv hartfalen, aspiratiepneumonie of een CVA. Twintig patiënten (59%) overleefden de follow-up. Additionele revascularisatie was nodig bij 2 van deze patiënten (10%), een patiënt onderging een CABG na 31 maanden, de andere CABG en MVP. Wij concludeerden dat de levens van deze 20 patiënten (59%) door de procedure zijn gered en dat PCI is de voorkeursbehandeling is voor patiënten met acute occlusie van een onbeschermde hoofdstam.

In **hoofdstuk 9** beschreven we de organisatie van patienten met een acuut myocardinfarct in de regio van het Catharina Ziekenhuis, Eindhoven. In nauwe samenwerking met de GGD is een 24 uurs zorg gewaarborgd, welke zijn beslag legt op de logistiek; een interventiecardioloog, twee catheterisatieverpleegkundigen en een radiologietechnicus dienen oproepbaar te zijn. In 2003 werden volgens deze organisatie 321 primaire PCI's en 73 rescue PCI's verricht. In 2004 nam dit aantal verder toe tot 513 primaire PCI's en 125 rescue PCI's. Als een patiënt als hoog risico wordt geclassificeerd, wordt hij direct naar het Catharina Ziekenhuis vervoerd voor primaire PCI. Als een patiënt wordt geclassificeerd als laag risico, wordt hij naar het dichtstbijzijnde ziekenhuis vervoerd en behandeld met trombolyse. In geval van falen van deze therapie, of in geval van verslechtering van de toestand van de patiënt, wordt de patiënt alsnog vervoerd naar het Catharina Ziekenhuis, al naar gelang de beoordeling van de verwijzende cardioloog.

Dankwoord

De verschillende onderzoeken die in dit proefschrift worden beschreven zijn tot stand gekomen in twee grote perifere ziekenhuizen: het St. Antonius ziekenhuis te Nieuwegein en het Catharina ziekenhuis te Eindhoven.

Velen hebben bijgedragen aan de afronding van dit proefschrift. Gaarne zou ik een ieder die een steentje bijgedragen heeft willen bedanken. Ik realiseer me echter dat er meer personen geholpen hebben bij mijn promotie dan ik hier kan benoemen.

Desalniettemin: een poging!

Allereerst mijn twee promotoren:

Prof. dr. N.H.J. Pijls. Beste Nico, jouw ontembare enthousiasme en kritische blik maakten dit proefschrift compleet. Mijn dank dat je halverwege het proefschrift 'het roer'over wilde nemen en je wilde verdiepen in de al geschreven stukken. Mede dank zij jou ben ik gekomen tot dit eindresultaat.

Prof. dr. HW.M. Plokker. Beste Thijs, jouw engelengeduld was er voor nodig om mij vanaf mijn studententijd te begeleiden tot dit resultaat. De rode pen liep als een leidraad door mijn 'concepten'. Mijn eerste mondelinge voordracht in Berlijn, werd tot aan de vliegtuigtrap verfijnd!

Voorts: dr. J.M.P.G Ernst, co-promotor. Beste Sjef, voor mij de 'grote, kleine man'. Tomeloze energie! In mijn dagelijkse werk denk ik vaak bij moeilijke problemen en/of complicaties: Wat zou Sjef nou doen?

De leden van de beoordelingcommisie: prof. dr. P.J. de Feyter, prof. dr. F. Zijlstra en prof. mr dr. B.A.J.M. de Mol dank voor hun bereidwilligheid om naast hun drukke werkzaamheden tijd vrij te maken ten einde dit proefschrift kritisch te beoordelen.

En dan een compleet adresboek aan collega's:

Leden van de maatschap cardiologie van het St.Antonius ziekenhuis te Nieuwegein: drs. E.T. Bal, dr. J.M. ten Berg, dr. L.V.A.Boersma drs. E.G. Mast, dr. W. Jaarsma, dr. B.J.W.M. Rensing, dr. M.J. Suttorp, dr. E.F.D. Wever, prof. dr. H.W.M. Plokker. Met name Gijs Mast was een 'soort vader', Jur, een echte 'zoutwaterdrijver' $\geq$ 40°C!, Maarten-Jan, van jou mocht ik de kunst van het catheteriseren afkijken, Wybren, door jou kennen we Jacques nu allebei!, Benno, van Rome tot Aspen! Lucas, jij ging me enkele jaren voor, maar ook ik heb het nu gehaald.

De leden van de maatschap cardiologie van het Catharina ziekenhuis te Eindhoven:

Dr. J.J.R.M. Bonnier. Beste Hans, de bezielende vader achter het (dotter)glas; ik zal m'n handschoenen maar weer eens aandoen! Dr. J.J. Koolen. Beste Jacques, een mooie mix van kennis, kunde en een geweldig gevoel voor humor. Dr. H.R.M. Michels. Beste Rolf, rustig, doordacht, niet gek te krijgen hoe druk het ook is. Drs. K. Peels. Beste Kathinka, nooit direct uitgesproken, maar ik vind het een welkome aanvulling: een vrouw in de maatschap, hetgeen resulteert in een rustpunt. Dr. J.M. van Dantzig. Beste Jan-Melle, sportiviteit staat bij jou nóg hoger in het vaandel. Dr. F.L.A.E. Bracke. Beste Frank, kundigheid en humor zijn de eigenschappen waar ik bij jou aan denk. Dr. A. Meijer. Beste Albert, waar ik nu al jaloers op ben; jij woont nu al als een god in Frankrijk. Drs. C.J.B.M. Botman. Beste Kees-Joost, 'grote broer', met jou als gids in het Catharina Ziekenhuis werd voor mij de start gemakkelijk. Dr. J.C. Post. Beste Hans, gezellig dat ik de mooiste kamer van het Catharina samen met jou en Kees-Joost mag delen. Ik hoop dat er nog vele avondjes BBQ rond jullie zwembad zullen volgen.

Pascal van Dessel (thans werkzaam in het Universitair Medisch Centrum, Groningen). Beste Pascal de onmisbare afrondende schakel naar het eind resultaat; jij liet me meerdere malen zien dat 'Word' de slechtste basis was voor een serieus tekstverwerkingsprogramma! Bedankt voor alle hulp en steun tijdens mijn opleiding en de opmaak van het proefschrift.

Yolande Appelman. Beste Yolande, een tijd lang beide lopen Sjeffen; in Brabant zegt men terecht: alles komt goed!

Assistenten en collegae uit het St. Antonius ziekenhuis te Nieuwegein en het Catharina Ziekenhuis te Eindhoven voor de leuke tijd, met in het bijzonder: Rob van Tooren, een cynicus pur sang! Karim Hamaraoui, bescheidenheid kent geen grens! Braim Rahel, te weinig samen gefietst (wat wil je zonder fietsplan), Adriaan Voors (thans werkzaam in het Universitair Medisch Centrum, Groningen), op en top onderzoeker, ik begrijp af en toe niet hoe je 'dat' volhoudt! Hans Kelder, zonder jou geen statistiek! Dr. A.J. Six. Beste Jacob, volgens 'Heart': 'outstanding english', dat jij moeiteloos dicteerde.

De secretaresses uit het St. Antonius ziekenhuis: dank voor alle denkbare steun tijdens het typen! Carola Meerleveld, Nathalie Pardoel, Sandra Noter, Helga Visser, Antoinette Honcoop.

De secretaresses uit het Catharina Ziekenhuis: In het bijzonder Anne Hol, Monique van den Broek, Annie Keijzers, Lisette Aarts-vd Kam en Willeke Broers voor alle hulp bij de organisatie rondom de promotie zelf.

Personeel HCK uit het Catharina ziekenhuis te Eindhoven: Berry van Gelder, Lex Lakerveld, Eduard van Hagen, Ruud Boogers, Arjen Bazelmans, Kees de Bruin, Jan Fleerakkers, Tessa van Hulst, Henk Kusters, Boudewijn Steerneman, Marie-Jose van Sanders, Jan Elders, Gert Hendrix, Roy Nathoe, Bonnie Ter Burg, Hans Römers en Claudia Zimmerman. Ontspannen, behulpzaam, gezellig: de beste scheepslui stonden vaak naast me en gaven me een warm welkom.

De secretaresses van de HCK: Nicole Bartels-Sandler, Petrie van de Biggelaar en Wilma Oomen-van Rijswijk: een strakke planning, zonder jullie een schier oneindige chaos.

Hartfunctie laboranten, verpleegkundigen ICU, CCU en verpleegafdelingen cardiologie uit het St. Antonius ziekenhuis en Catharina ziekenhuis voor de prettige sfeer en samenwerking.

Paranimfen:

Jacques Koolen, en Michel Voragen, dank voor jullie ondersteuning tijdens het laatste deel van mijn promotieproces en jullie hulp bij het afhandelen van alle organisatorische kwesties. Opvallend dat beide paranimfen dezelfde hobby als ik hebben: skiën!

Mijn vrienden:

Peter de Jong. Beste Peter, jouw nuchterheid en rekenkunde hebben dromen helder en bereikbaar gemaakt. Bram Berden. Beste Bram, jarenlang al een vriend; plannen van vakanties kun je als de beste. Fieke de Beukelaer. Beste Fieke, door jou toedoen: verslaafd aan het skiën.

Mijn huischgenoten van de Skapstraat, zonder hen was de studententijd o.a. zonder huischweekends, pijnshows, mokjes, aspergediners, Dommelsch en reünies. Richard Donders (‘ga jij maar eens onderzoek doen, anders wordt het nix met jou!’), Bob van der Zwaan (de kantine van het ‘TAZU’, kende in het weekend in ieder geval twee klanten!), Has van Helvoirt (toonbeeld van brabantse gezelligheid), Toon Kuipers (Olédokter, drie keer is scheepsrecht!), Stephan Boeijen (‘Boeije’), Hut (‘de Hut 7’), Bob Luijkx (dierendokter BOB), Maarten van Thiel (Helmond=oke, onder het kanaal), Jaap Vreugdenhil (‘voor jou altijd de LOVE-dokter’), Joost Fledderus (gezellig aanwezig), Michel Voragen (behalve ceremoniemeester, paranimf, ook een goede vriend).

De familie Boerrighter, wil ik danken voor het ‘voorproeven’ van de locatie en met name Emmy voor het lenen van de Bosatlas.

Olaf Brueren en Thekla Winters - Brueren. Mijn broer en zus, wil ik danken voor hun begrip, het is ook af en toe niet makkelijk om gezellige dingen af te spreken met zo’n ‘streber’.

Mijn schoonouders: Bram en Rik Bloemendal wil ik danken voor de keren dat zij op de kinderen wilden passen. Jullie zijn werkelijk een tweede thuis voor Pim, Pol en Linde. Te allen tijde kon ik op jullie rekenen, zonder jullie zouden de vele uren ‘zinloos invoeren in de database’ niet mogelijk zijn geweest.

Mijn ouders wil ik danken: Ook dankzij jullie heb ik dit alles kunnen bereiken. Lieve pa: jij stond mij altijd bij met raad en daad, grote stappen in mijn leven hebben we samen gewogen. Lieve ma: de bagage die ik dagelijks tot mijn beschikking heb, is door jou aangegeven.

Mijn 3 kinderen; Pim, Pol en Linde: stelletje druktemakers. Het is jammer dat jullie nog niet zo door hebben wat opleiding, werken of promoveren betekent, laat staan om dit allemaal tegelijk te doen; hoe kan ik jullie het dan ook kwalijk nemen dat jullie al mijn tijd vergen als ik thuis ben.

Als laatste; lieve P, we komen hopelijk in een rustiger vaarwater, na al die jaren opleiding, onderzoek en kinderen tegelijkertijd. Vaak genoeg roem ik mondeling je doorzettingsvermogen, doortastendheid en geduld. Het werd tijd dat ik dit ook eens op deze manier aan je vertel. Zonder jou was er weinig van terechtgekomen.

Publications of the author

Publications

B.R.G. Brueren, G.J.E. Rinkel, A. Algra, M. Vermeulen, J. van Gijn. Registration of Risk Factors for Stroke in Hospital Records. Cerebrovascular Diseases 1995; 5: 366-368.

Brueren B.R.G., Rosseel M.P.P., Plokker H.W.M, Ernst J.M.P.G. Are there differences in late outcome after PTCA for angina pectoris after non-Q vs Q wave myocardial infarction. Eur Heart J 1997; 18: 1903-12.

C.J.J. Laruelle, G.B.R. Brueren, S.M.P.G. Ernst, E.T. Bal, G.E.Mast, M-J. Suttorp, Brutel de la Rivière, T.H.W. Plokker. Stenting of unprotected left main coronary artery stenoses: early and late results. Heart 1998; 79: 148-52.

B.R.G. Brueren, E.G. Mast, MJ. Suttorp, J.M.P.G. Ernst, E.T. Bal, H.W.M. Plokker. How good are experienced interventional cardiologists in predicting the risk and difficulty of a coronary angioplasty procedure? Catheterization and Cardiovascular Interventions 1999; 46: 257-62.

B.R.G. Brueren, MJ Suttorp, M.A.J. Landman, E.G. Weijers, A.C. Bredero, H.W.M. Plokker. Percutane transluminale coronaire angioplastiek bij patiënten met een acuut myocardinfarct: op weg naar een regionaal infarctcentrum? Cardiologie 2001; 8: 104-109.

Brueren B.R.G., Berg ten J.M., Suttorp MJ, Bal E.T., Ernst J.M.P.G., Mast E.G., Plokker H.W.M. How good are experienced cardiologists at predicting the hemodynamic severity of coronary stenoses when taking fractional flow reserve as the gold standard. The International Journal of Cardiovascular Imaging 2002; 18: 73-76.

B.R.G. Brueren, J.M.P.G. Ernst, M-J Suttorp, J.M. ten Berg, E.G. Mast, E.T. Bal, B.M. Rensing, A.J Six, H.W.M. Plokker. Long term follow-up after elective percutaneous coronary interventions for non-bifurcational unprotected left main, is it time to change the guidelines? Heart 2003; 89: 1336-1339.

Brueren BR, Ernst JM, Suttorp MJ, ten Berg JM, Rensing BJ, Mast EG, Bal ET, Six AJ, Plokker HW. Emergency percutaneous coronary interventions for unprotected left main stenoses: immediate and long term follow up. Heart 2004; 90: 1067-8.

Abstracts

B.R.G. Brueren, E.G. Mast, H.W.M. Plokker, J.M.P.G. Ernst, E.T. Bal, M.J. Suttorp, How good are experienced interventional cardiologists in predicting the risk of an angioplasty procedure? A prospective study to optimize surgical stand-by. Eur Heart J, 1994; 15, 122.

M.P.P. Rosseel, B.R.G. Brueren, H.W.M. Plokker, J.M.P.G Ernst, PTCA in Non-Q Myocardial Infarction (MI). Int Symposium on Cardiological Intensive Care 1995; p63.

R.J.C.M. Donders, L.J. Kappelle, A. Algra, B.R.G. Brueren, J. v Gijn, Diagnosis and management of transient monocular blindness (TMB) by general practitioners. J of Neurol 1995; 242: S25.

B.R.G. Brueren, J.M. ten Berg, E.T. Bal, E.G. Mast, M.J. Suttorp, J.M.P.G Ernst, H.W.M. Plokker. Urgent repeat PTCA for subacute stent occlusion.

B.R.G. Brueren, J.M. ten Berg, J.C. Kelder, T. Plokker. How good are experienced cardiologists in predicting the hemodynamic severity of coronary stenoses: comparison to fractional flow reserve.

B.R.G. Brueren, J.M.P.G. Ernst, M-J Suttorp, J.M. ten Berg, E.G. Mast, E.T. Bal, B.M. Rensing, A.J Six, H.W.M. Plokker. Long term follow-up after elective percutaneous coronary interventions for unprotected left main.

B.R.G Brueren, A.J. Six, J.M.P.G. Ernst, M-J Suttorp, J.M. ten Berg, E.G. Mast, E.T. Bal, B.M. Rensing, A.J Six, H.W.M. Plokker. Elective PCI of left main coronary stenosis.

Curriculum Vitae

Geboren	Tegelen, Nederland, 17 september 1968
Nationaliteit	Nederlandse
Burgelijke staat	Gehuwd met Petra Bloemendal Kinderen: Pim, Pol en Linde
1980 – 1981	St. Martinus MAVO, Tegelen
1981 – 1989	St. Thomas College, Atheneum B, Venlo
1989 – 1990	Farmacie, Universiteit Utrecht
1990 – 1996	Geneeskunde, Universiteit Utrecht
1997 – 2003	Cardiologie opleiding, St. Antonius ziekenhuis, Nieuwegein
1997 – 1999	Interne Geneeskunde vooropleiding, Bronovo ziekenhuis, Den Haag Opleider: Dr. R. Bieger
1999 – 2003	Cardiologie vervolgopleiding, St. Antonius ziekenhuis, Nieuwegein Opleider: Dr.W. Jaarsma
2003 – 2005	Opleiding tot interventiecardioloog, Catharina ziekenhuis , Eindhoven Chef de Clinique, afdeling cardiologie
2005	Lid maatschap Cardiologie, Catharina ziekenhuis, Eindhoven