CLINICAL INVESTIGATIONS

Short-, medium-, and long-term follow-up after percutaneous transluminal coronary angioplasty for stable and unstable angina pectoris

The first 840 consecutive patients who underwent percutaneous transluminal coronary angioplasty (PTCA) performed in the same institution were retrospectively assessed at an average follow-up period of 25 months after the initial procedure. The study population consisted of 506 patients with stable angina pectoris (group 1) and 334 patients with unstable angina pectoris (group 2). Clinical end points were death, nonfatal myocardial infarction, recurrent angina pectoris necessitating bypass surgery or repeat PTCA, and event-free survival. The two groups were comparable with respect to age, sex, previous myocardial infarction, ejection fraction, and number of diseased vessels. PTCA was successful in 83.0% of group 1 and 87.1% of group 2. Follow-up rates were expressed as events per attempted PTCA in a patient group. No difference in survival was observed between the two groups, the mortality rate being approximately 2.8% at 25 months. In the group with stable angina pectoris there was a lower incidence of nonfatal myocardial infarction within the first 24 hours after angioplasty; 4.3% vs 9.0% ($p < 0.01$). During long-term follow-up the increase in the incidence of nonfatal myocardial infarction was similar, resulting in an overall long-term follow-up infarction rate of 8.3% and 14.2%, respectively ($p < 0.01$). A higher event-free survival was observed in group 1 within 24 hours after PTCA: 93.7% vs 84.2% ($p < 0.01$). During subsequent follow-up the difference in event-free survival between the two groups was no longer significant: 68.5% vs 61.2%. These results suggest that PTCA is an effective long-term treatment for both patients with stable and unstable angina pectoris but with an initially higher major complication rate in the latter patient group. (AM HEART J 1989;117:991.)

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The effectiveness of percutaneous transluminal coronary angioplasty (PTCA) for the treatment of coronary artery disease has been documented in stable and unstable angina pectoris.[1-13] The long-term efficacy of PTCA in patients with coronary artery disease has also been documented,[3, 14-16] with follow-up periods extending as far as 8 years.[13] It has been shown that PTCA combined with pharmacologic therapy can be performed relatively safely and

successfully in patients with refractory unstable angina pectoris.[1, 4, 6-11] Available data[2, 3, 13] suggest that significant numbers of all patients treated with PTCA are at risk for recurrent coronary events (16% to 50%). A higher early unfavorable outcome with regard to major complications has been demonstrated in patients with unstable angina pectoris after PTCA,[1, 6-11] but the longer-term outlook of these patients remains unclear.

Results of follow-up studies in both medically and surgically treated patients with unstable angina pectoris have reported an increased risk of myocardial infarction and death within the first year.[17-19] After treatment with PTCA this group of patients maintains a higher risk of myocardial infarction when compared to patients with stable angina pectoris.[6-11] The purpose of this study was to evaluate

Table I. Clinical characteristics of patients with stable and unstable angina pectoris

Clinical characteristics	Group 1 (stable AP)	Group 2 (unstable AP)	
No. of patients	506	334	
Age (yr)			
Median	55	54	(NS)
Range	22-79	22-80	(NS)
Sex (% male)	80.9	80.2	(NS)
Previous MI (%)	35.4	39.1	(NS)
Ejection fraction	0.60	0.59	(NS)
Success rate (%)	83.0	87.1	(NS)

AP = angina pectoris; MI = myocardial infarction; NS = not significant.

Table II. Angiographic characteristics of patients with stable and unstable angina pectoris

Angiographic characteristics	Group 1 (Stable AP) (N = 506) N	%	Group 2 (Unstable AP) (N = 334) N	%	
Diagnostic catheterization					
1-Vessel disease	320	63.2%	214	64.1%	(NS)
2-Vessel disease	112	22.1%	75	22.4%	(NS)
3-Vessel disease	61	12.1%	40	12.0%	(NS)
Mainstem disease	13	2.6%	5	1.5%	(NS)
PTCA					
1-Vessel dilatation	453	89.5%	310	92.8%	(NS)
Multivessel dilatation	53	10.5%	24	7.2%	(NS)
Multidilatation of 1 vessel	106	20.9%	56	16.8%	(NS)

Abbreviations as in Table I.

the results of short-, medium-, and long-term follow-up of patients undergoing PTCA for stable and unstable angina pectoris in the same institution. Three follow-up time periods were analyzed: (1) short-term follow-up during which acute events occurred within the first 24 hours of the procedure; (2) medium-term follow-up; when events occurred within 6 months after PTCA, the period in which restenosis is most likely to occur, and (3) long-term follow-up, when events occurred from 6 months to the last follow-up. Patients with stable angina pectoris treated with PTCA were compared with patients with unstable angina pectoris with regard to death, nonfatal myocardial infarction, and recurrent angina pectoris necessitating coronary bypass surgery or repeat PTCA, and event-free survival.

METHODS

Between September 1980 and November 1985, PTCA was performed in 840 consecutive patients at the Thoraxcenter in Rotterdam. The study population consisted of 506 patients (60.2%) with stable angina pectoris and 334 patients (39.8%) with unstable angina pectoris. Unstable angina pectoris was defined as chest pain at rest lasting for at least 15 minutes, associated with documented ST or T wave changes and no signs of myocardial necrosis (cardiac enzyme rise less than twice normal and no pathological Q waves ($\geq$0.03 second). All patients were treated with a combination of intensive pharmacologic therapy, including beta-blockers, calcium antagonists, nitrates, and heparin intravenously. Before PTCA 250 mg acetylsalicylic acid and 100 mg heparin were given intravenously. The patients continued to receive treatment with nifedipine, 40 to 60 mg/day, and acetylsalicylic acid, 500 mg/day, for a period of 6 months. The method of PTCA changed during the enrollment period of this study: before February 1983 (25.6% of the procedures) a nonsteerable catheter system was used, as originally described by Gruentzig et al.,[20] in

129 patients (58.9%) with stable angina pectoris and 90 patients (41.1%) with unstable angina pectoris; after this date steerable balloon systems were used.

Primary success was defined as a reduction in the diameter of the dilated vessel to less than 50% diameter stenosis with no major complications, namely, death, myocardial infarction, or coronary artery bypass grafting, within 24 hours of the procedure. Procedural details including complications were recorded at the time of the procedure in the data base designed for this purpose. Primary end points considered at follow-up were death, nonfatal myocardial infarction, recurrent angina pectoris necessitating coronary artery bypass grafting or repeat PTCA, and event-free survival. These data were retrospectively obtained by interview during outpatient visit(s) and by questionnaires in 96% of the patients. The mean follow-up was 25 months, ranging from 6 to 66 months.

Follow-up data included all patients after attempted PTCA. All patients' names were checked at the civil registry to confirm survival at follow-up or death. This part of the assessment was completed in The Netherlands and is a reliable and complete source of information concerning survival. Evidence of myocardial infarction immediately after the procedure was defined by a new Q wave, elevation of myocardial enzymes (oxaloacetic transaminase) lactate dehydrogenase, and/or creatine phosphokinase to more than twice the normal level), or both. Assessment of late myocardial infarction in the follow-up period included a history of prolonged chest pain necessitating hospitalization and documented records and/or ECG criteria for myocardial infarction (new Q waves). Information on coronary bypass surgery and repeat PTCA were obtained from hospital data bases, outpatient visit(s), or questionnaires. The 4% of patients from whom detailed follow-up data were not obtained were all residing abroad at the time of attempted contact. Procedural complications were included in all follow-up analyses.
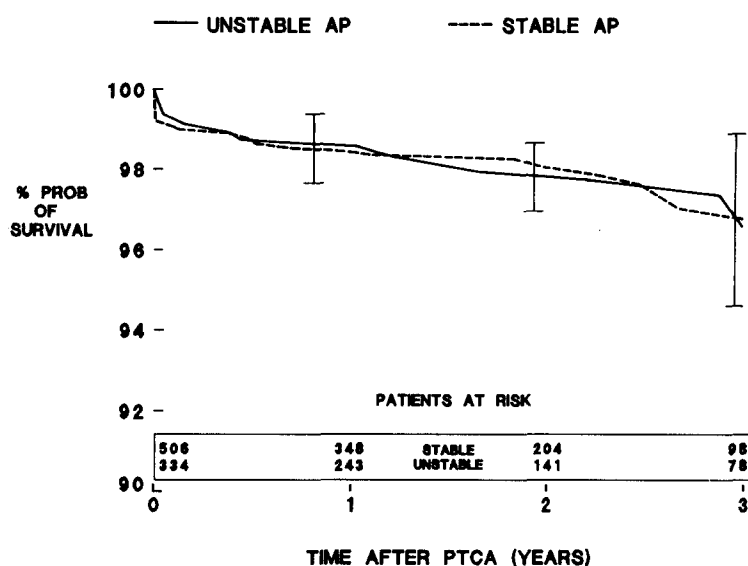
Fig. 1. Effect of PTCA on long-term cumulative survival, analyzed by Kaplan-Meier method, up to 3 years for patients with stable and unstable angina pectoris. Number of patients at risk is placed along horizontal axis.

Patient selection. In 506 patients PTCA was performed for stable angina pectoris (group 1) and in 334 patients for unstable angina pectoris (group 2). Baseline clinical characteristics (age, sex, previous myocardial infarction, and ejection fraction) were similar in both groups (Table I). No difference in vessel disease was observed between the two groups (Table II). Single-vessel disease was present in 63.2% of the patients in group 1 versus 64.1% of the patients in group 2. In the group with stable angina pectoris a trend toward more multivessel dilatations (10.5% vs 7.3%) and more multidilatations of one vessel (20.9% vs 16.9%) was noticed.

Statistical analaysis. The differences between the two groups for categoric variables were assessed with the chi-square test. Survival data were analyzed by the Kaplan-Meier method of actuarial survival probability (Fig. 1).

RESULTS

The overall primary success rate was 83.0% in group 1 versus 87.1% in group 2.

Short-term follow-up. In the group with unstable angina pectoris the incidence of acute nonfatal myocardial infarction within 24 hours was significantly higher (9.0% vs 4.3%) (Fig. 2). No significant difference in acute mortality, acute bypass surgery, or repeat PTCA was observed. The event-free survival rate was therefore significantly higher in the group with stable angina pectoris, 93.7% versus 84.2% within the first 24 hours (Fig. 3).

Medium-term follow-up. At the end of 6 months, the period in which restenosis is most likely to occur, an increased rate of coronary artery bypass grafting was present in the group with unstable angina pectoris:

17.5% versus 13.2% within 6 months. This was also true for the incidence of nonfatal myocardial infarction within the first 6 months (Fig. 2): 11.2% versus 6.0%. The difference in nonfatal myocardial infarction within 6 months was mainly due to the higher incidence of myocardial infarction within the first 24 hours after PTCA. There was no difference in the mortality, repeat PTCA, or event-free survival in this period.

Long-term follow-up. The actuarial survival curves between the two groups were not significantly different (Fig. 1). One-year survival in group 1 was 98 ± 1% versus 97 ± 1%; 3-year survival was 96 ± 3% (group 1) versus 95 ± 4% (group 2). Forty of the 44 deaths were cardiac, and four were noncardiac. The difference in the incidence of nonfatal myocardial infarction between the two groups persisted at long-term follow-up; 14.2% in the group with unstable angina pectoris and 8.3% in the group with stable angina pectoris. This was also true for the difference in the incidence of coronary artery bypass grafting at long-term follow-up: 20.8% versus 14.7%. During subsequent follow-up no difference in repeat PTCA between the two groups was noticed. The event-free survival in the two groups at long-term follow-up was no longer significant.

DISCUSSION

The purpose of this study was to evaluate the short-, medium-, and long-term follow-up of patients undergoing PTCA for both stable and unstable angina pectoris in the same institution. To determine whether patients with stable angina pec-
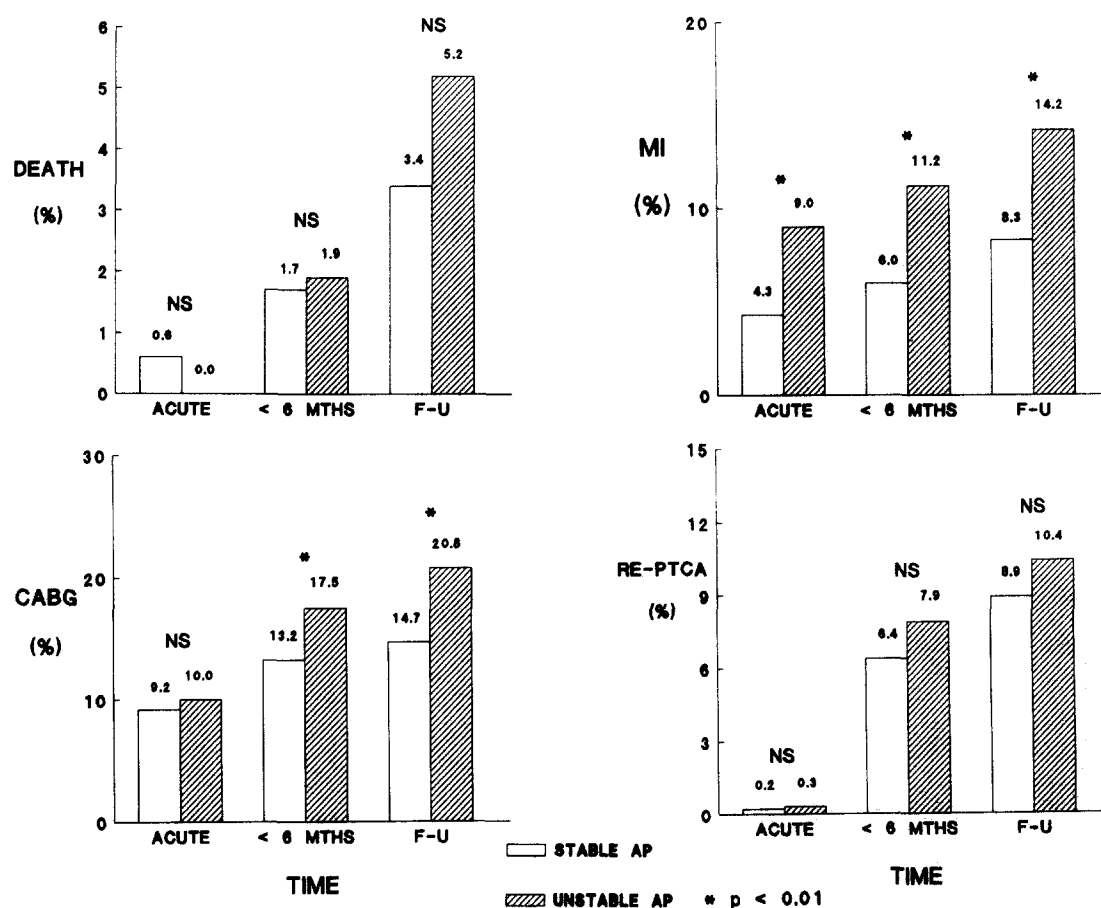
Fig. 2. Comparison of cumulative death *(upper left)*, nonfatal myocardial infarction *(upper right)*, coronary artery bypass grafting *(lower left)*, and repeat PTCA *(lower right)* in patients with stable and unstable angina pectoris, within 24 hours *(acute)*, within 6 months *(<6 mths)*, and at follow-up *(F-U)*.

toris differ from those with unstable angina pectoris in terms of major complications, the clinical outcome of each group after coronary angioplasty was evaluated at a mean follow-up period of 25 months, with a follow-up rate of 96% for major events. No statistical significance in success rate was observed between the two groups.

After the introduction of the steerable balloon system in February 1983, there was an improvement in the success rate for both groups from approximately 70% to 90% with an overall success rate of 83.0% in the group with stable angina pectoris and 87.1% in the group with unstable angina pectoris. Results of recent studies have reported success rates of 93%, which represents a significant improvement from the success rates of earlier studies[1-12,14-21] as a result of increased experience of the operators and improvement in procedures, balloon catheters, wires, and x-ray equipment.[23] In this study the fact that all patients were included, starting from the first PTCA procedure and extending over 5 years, was responsible for the lower success rates.

Short-term follow-up. The incidence of acute mortality related to the PTCA procedure was 0.6% in patients with stable angina pectoris, and no acute deaths occurred among patients with unstable angina pectoris in this series. This compares favorably with data from the National Heart, Lung, and Blood Institute PTCA registry,[3] which reported a 1.1% in-hospital mortality rate.

Within the first 24 hours after angioplasty there were significantly more events among the patients with unstable angina pectoris, mainly because of the difference in incidence of acute nonfatal myocardial infarction. This higher incidence of post-PTCA nonfatal myocardial infarction in patients first seen with unstable angina pectoris was observed particularly during or immediately after coronary angioplasty.

This is probably related to the more complicated coronary lesions containing thrombus and thrombogenic material,[24-27] which may more readily induce total occlusion during the procedure resulting in myocardial infarction. Our investigators[28] has previ-

ously identified a subgroup of patients with unstable angina pectoris with marked ST elevation or persistent negative T waves who have an increased risk of a major procedural-related complication after PTCA.

Medium-term follow-up. The event-free survival rate within a half year remained high in both groups—75.7% in group 1 versus 71.6% in group 2—suggesting clinically important events in 24.3% (group 1) and 28.4% (group 2) in the period when restenosis is most likely to occur, with no significant difference between the groups.

It was our policy to treat restenosis with a second PTCA rather than coronary bypass surgery. The occurrence of restenosis was the same in patients with stable angina pectoris and unstable angina pectoris, as expressed by the event rates.

This was also shown in a recent study that used quantitative angiographic data. In a subgroup of this patient cohort the cumulative incidence of restenosis was similar in patients with stable angina pectoris (n = 206) and unstable angina pectoris (n = 133), irrespective of the type of definition. If a loss of at least 50% of the gain in luminal diameter achieved at the time of PTCA is used as a definition of restenosis, the rates are 26.7% for stable angina pectoris and 24.8% for unstable angina pectoris, which is not statistically significant.[29]

Long-term follow-up. The 1-year survival rate among patients after PTCA with stable angina pectoris was 98% versus 97% in those with unstable angina pectoris; the 3-year survival rates were 96% and 95%, respectively. The difference was not statistically significant. The mortality rate of 2.8% at 25 months in our patients was similar to the outcome of both the medical and surgical treatment of stable and unstable angina pectoris.[18, 30, 31] The National Heart, Lung, and Blood Institute PTCA registry[3] has reported an annual mortality rate after PTCA in all patients with one-vessel disease of less than 1% a year and 3% a year in patients with multivessel disease. During subsequent follow-up there was an increased rate of coronary bypass surgery in the group with unstable angina pectoris, which again can be partially explained by our policy or initially dilating only the culprit lesion. There was a trend toward a higher incidence of multivessel dilatation and multidilatation of one vessel in the group with stable angina, because in unstable angina pectoris and multivessel disease only the culprit lesion was dilated in the majority of the patients, that is, the lesion judged by ECG and anatomic location to be the lesion responsible for the ischemia.[7, 21] It is inevitable, if the policy of treating only
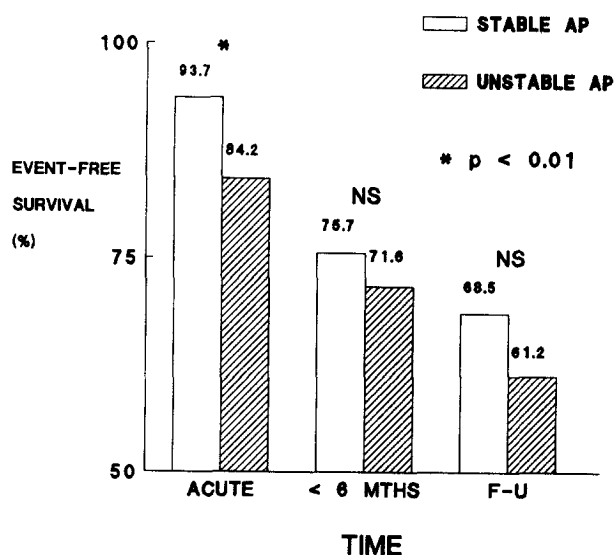

Fig. 3. Comparison of cumulative figures of time-related, event-free survival in patients with stable and unstable angina pectoris, within 24 hours *(acute)*, within 6 months *(<6 mths)*, and at follow-up *(F-U)*.

the culprit lesion is adopted, that some patients will not undergo complete revascularization and therefore further intervention in the future might be expected. The higher incidence of surgery in the patients with unstable angina reflects this incomplete revascularization. No difference in repeat PTCA was observed during follow-up between the two groups.

From 6 months until follow-up the event-free survival rates were reduced to 68.5% (group 1) and 61.2% (group 2). The majority of the events were related to progression of the atherosclerotic disease in nondilated coronary artery segments. In conclusion, PTCA is an effective long-term treatment for both stable and unstable angina pectoris but with an initially higher major complication rate for patients with unstable angina pectoris.

REFERENCES

1. Meyer J, Schmitz HJ, Kiesslich T, et al. Percutaneous transluminal coronary angioplasty in patients with stable and unstable angina pectoris: analysis of early and late results. Am Heart J 1983;106:973-80.
2. Dorros G, Cowley MJ, Simpson J, et al. Percutaneous transluminal coronary angioplasty: report of complications from the National Heart, Lung, and Blood Institute PTCA registry. Circulation 1983;67:723-30.
3. Kent KM, Bentivoglio LG, Block PC, et al. Long-term efficacy of percutaneous transluminal coronary angioplasty (PTCA): report from the National Heart, Lung, and Blood Institute PTCA registry. Am J Cardiol 1984;53: 27c-31c.

4. Williams DO, Riley RS, Singh AK, Gewirtz H, Most AS. Evaluation of the role of coronary angioplasty in patients with unstable angina pectoris. AM HEART J 1981;102:1-9.

5. Faxon DP, Detre KM, McGabe CH, et al. Role of percutaneous coronary angioplasty in the treatment of unstable angina. Am J Cardiol 1983;5:131c-135c.

6. de Feyter PJ, Serruys PW, Wijns W, et al. Emergency PTCA in refractory unstable angina. N Engl J Med 1985;313:342-6.

7. de Feyter PJ, Serruys PW, Arnold A, et al. Coronary angioplasty of the unstable angina related vessel in patients with multivessel disease. Eur Heart J 1986;7:460.

8. de Feyter PJ, Serruys PW, Suryapranata H, Beatt K, van den Brand M. Coronary angioplasty early after diagnosis of unstable angina. AM HEART J 1987;114:48-54.

9. Quigley PJ, Erwin J, Maurer BJ, Walsh MJ, Gearty GF. Percutaneous transluminal coronary angioplasty in unstable angina: comparison with stable angina. Br Heart J 1986; 55:227-30.

10. Timmis AD, Griffin B, Crick JCP, Sowton E. Early percutaneous transluminal coronary angioplasty in the management of unstable angina. Int J Cardiol 1987;14:25-31.

11. Steffenino G, Meier B, Finci L, Rutishauser W. Follow-up results of treatment of unstable angina by coronary angioplasty. Br Heart J 1987;57:416-19.

12. Rosing DR, Cannon RO, Watson RM, et al. Three year anatomic, functional and clinical follow-up after successful percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1987;9:1-7.

13. Gruentzig RA, King SB, Schlumpf M, Siegenthaler W. Long-term follow-up after percutaneous transluminal coronary angioplasty. N Engl J Med 1987;316:1127-32.

14. Mabin TA, Holmes DR, Smith HC, et al. Follow-up clinical results in patients undergoing percutaneous transluminal coronary angioplasty. Circulation 1985;71:754-60.

15. Holmes DR, Vlietstra RE. Percutaneous transluminal coronary angioplasty: current status and future trends. Mayo Clin Proc 1986;61:865-76.

16. Ernst SMPG, van den Feltz TA, Bal ET, van Bogerijen L, van den Berg E, Ascoop CAPL, Plokker HWT. Long-term angiographic follow-up, cardiac events, and survival in patients undergoing percutaneous transluminal coronary angioplasty. Br Heart J 1987;57:220-5.

17. Gazes PC, Mobley Jr EM, Faris Jr HM, Duncan RC, Humphries GB. Preinfarctional (unstable) angina pectoris a prospective study: Ten-year follow-up. Circulation 1973;48: 331-6.

18. Russell Jr RO, Morashi RE, Kouchoukos N, et al. Unstable angina pectoris: national cooperative study group to compare surgical and medical therapy. Am J Cardiol 78;42:839-48.

19. Cairns JA, Fantus IG, Klassen GA. Unstable angina pectoris. AM HEART J 1976;92:373.

20. Gruentzig AR, Senning A, Siegenthaler WE. Non-operative dilatation of coronary artery stenosis. N Engl J Med 1979;301:61-7.

21. Wohlgelernter D, Cleman M, Highman HA, Zaret BL. Percutaneous transluminal coronary angioplasty of the "culprit" lesion for management of unstable angina pectoris patients with multivessel coronary artery disease. Am J Cardiol 1986;58:460-4.

22. Giuliani ER. Percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1985;6:992-4.

23. Meier B, Gruentzig A. Learning curve for percutaneous transluminal coronary angioplasty: skill, technology or patient selection. Am J Cardiol 1984;53:65c-6c.

24. Ambrose JA, Winters SL, Stern A, Eng A, Teichholtz LE, Gorlin R, Fuster A. Angiographic morphology and the pathogenesis of unstable angina pectoris. J Am Coll Cardiol 1983;5:609.

25. Mabin TA, Holmes DR, Smith HC, et al. Intracoronary thrombus: role in coronary occlusion complicating percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1985;5:198-202.

26. Ischinger T, Gruentzig AR, Meier B, Galan K. Coronary dissection and total coronary occlusion associated with percutaneous transluminal coronary angioplasty: significance of initial angiographic morphology of coronary stenosis. Circulation 1986;72:1371-8.

27. de Feyter PJ, Suryapranata H, Serruys PW, Beatt KJ, van Domburg R, van den Brand M, Hugenholtz PG. Coronary angioplasty for unstable angina—immediate and late results in 200 consecutive patients with identification of risk factors for unfavorable early and late outcome. J Am Coll Cardiol 1988;12:324-33.

28. Serruys PW, Luijten HE, Beatt KJ, et al. Incidence of restenosis after successful coronary angioplasty: a time-related phenomenon. Circulation 1988;77:361-71.

29. Luijten HE, Beatt KJ, de Feyter PJ, van den Brand M, Reiber JHC, Serruys PW. Angioplasty for stable versus unstable angina: are unstable patients more likely to get restenosis. Int J Card Imaging 1988;3:87-97.

30. Kennedy JW, Kaiser GC, Fisher LD, et al. Clinical and angiographic predictors of operative mortality from the Collaborative Study in Coronary Artery Surgery (CASS). Circulation 1981;63:783-802.

31. Luchi RJ, Scott SM, Deupress RH. Comparison of medical and surgical treatment for unstable angina pectoris. Results of a veterans administration cooperative study. N Engl J Med 1987;316:977-84.