European Heart Journal (1992) **13,** (*Supplement H*), 76–88

Coronary angioplasty — long-term follow-up results and detection of restenosis: guidelines for aviation cardiology

A European view

P. W. SERRUYS AND A. BREEMAN

Thoraxcenter, University Hospital Dijkzigt, Erasmus University, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands

KEY WORDS: Aircrew licensing, aviation, unstable, stable, multi/single vessel, complete/incomplete revascularization, detection of restenosis, long-term follow-up, multicentre trials, new interventional techniques.

Introduction

Interventional procedures carried out in the U.S.A. and Western Europe are growing exponentially. Fascinating techniques are blossoming: some are still at an investigational stage, others have already proven their value.

The clinical indications for these interventions are rapidly evolving but still unclear and in many cases an overlap exists with cardiac surgery. It is still unknown what is the best modality of treatment (surgery or angioplasty) for multivessel coronary artery disease; there are a variety of techniques and indications for cardiac interventions. This paper discusses the long-term results of percutaneous transluminal coronary angioplasty (PTCA) procedures for stable and unstable angina, multivessel/single vessel disease, complete and incomplete revascularization and some special interventions such as saphenous vein bypass graft angioplasty and stenting. It is therefore of major importance to try to establish the relative merits of these techniques and their indications to determine their respective niche in the therapeutic arsenal. Long-term follow-up analysis of non-randomized studies is essential to understand the progress made in the field of interventional cardiology. This paper will also address the future as regards cardiac complications for different subgroups of patients who have had a PTCA. Restenosis detection methods are discussed to facilitate a relative risk appropriation. Finally, guidelines for aviation cardiology will be proposed.

Part I: POBA, The plain old balloon angioplasty

PTCA PROCEDURE GROWTH IN EUROPE

In 1991 about 92 000 PTCA procedures were carried out in Europe. Over the last 4 years there has been a yearly increase in absolute numbers of 9000 PTCAs per year. In relative percentages we seem to have reached a plateau and are expecting a relative increase this year of 10% (Fig. 1).

Correspondence P. W. Serruys, MD, University Hospital Dijkzigt, Department of Cardiology, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

0195-668X/92/0H0076 + 13 $08.00/0

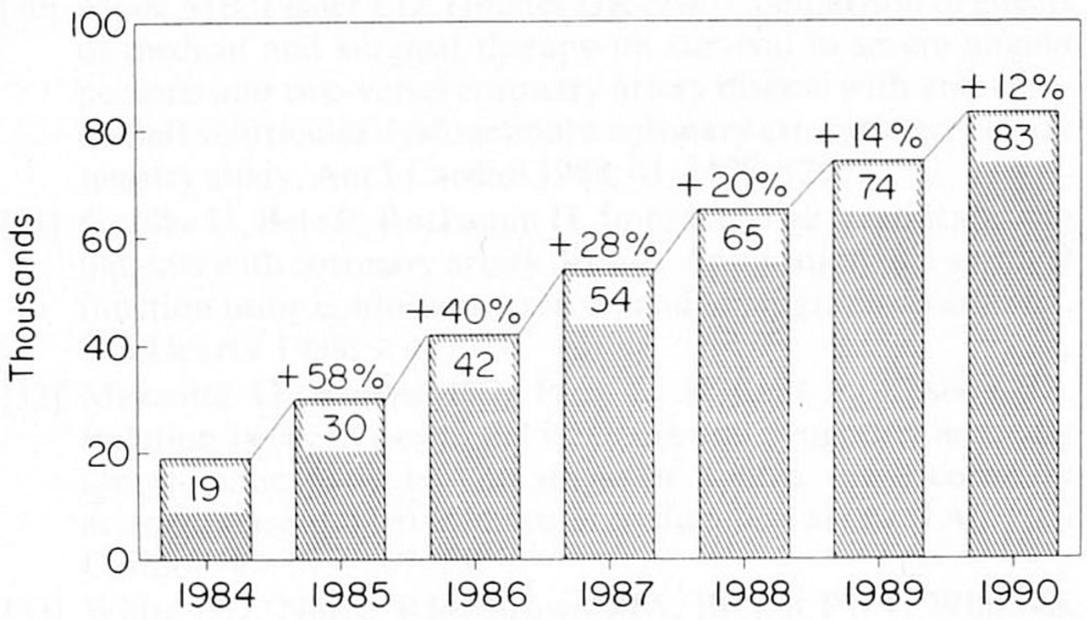

Figure 1 PTCA growth Europe

Table 1 PTCA centres in western Europe

Country	No. centres
France	136
Germany	93
U.K.	52
Italy	38
Spain	36
Eastern Bloc	32
Belgium	19
Scandinavia	17
The Netherlands	13
Switzerland	13
Austria	11
Ireland	7
Poland	6
Others	6
Total	450

NUMBER OF CENTRES PERFORMING ANGIOPLASTY IN EUROPE

The total number of European centres is about 450, which is more than half the number currently active in the United States. According to industry estimates, the Eastern Bloc has 32 centres performing PTCA. In absolute numbers, France has the largest number of centres performing PTCA followed by Germany, U.K., Italy and Spain (Table 1).

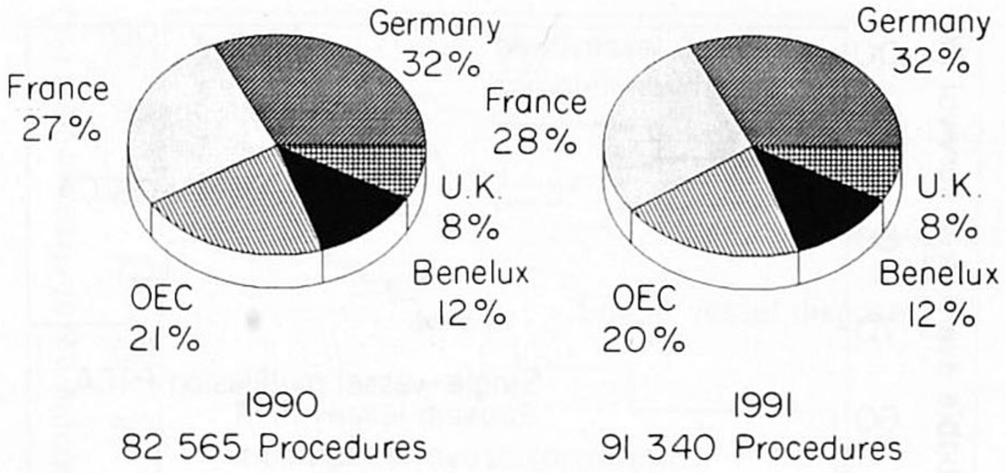

Figure 2 European PTCA procedure breakdown; procedures by country. (OEC = Other European countries)

Table 2 Worldwide PTCA centres

Country	No. centres
U.S.A.	850
Europe	450
Japan	325
Latin America	89
Canada	39
Eastern Bloc	32
Middle East	26
Australia	21
South Africa	20
New Zealand	4

PROCEDURES PERFORMED IN EACH COUNTRY IN EUROPE

In 1990, Germany carried out 32% of all the PTCAs performed in Europe, followed by France (27%) and Benelux, that is, Belgium, The Netherlands and Luxembourg, with 12% of the total number. The U.K. came in the fourth place with 8% of the total number of PTCAs performed. The remaining share, 21%, was performed by the other European countries. The Netherlands has the largest number of PTCAs performed per centre (Fig. 2)[1]. It is estimated that there will be a uniform growth in Europe this year for PTCA procedures, with approximately the same procedure ratio by country as in 1990.

WORLDWIDE ESTIMATION OF THE NUMBER OF PTCA CENTRES

In the United States there are 850 centres listed as performing PTCA procedures. In 1990, these centres accounted for about 280 000 to 290 000 procedures and the 1000 or so centres outside the U.S.A. accounted for about 130 000 to 140 000 procedures. Japan has 450 centres, which have initiated an angioplasty programme. There appears to be a fairly large number of low volume institutions, however, because there were only 25 000 procedures performed in Japan in 1990 (Table 2).

PTCAS AND CABGS PER MILLION CAPITA IN 1990

In 1990, the U.S.A. reached the point where the number of PTCA and coronary artery bypass graft (CABG) procedures per million capita were almost equal (Fig. 3).

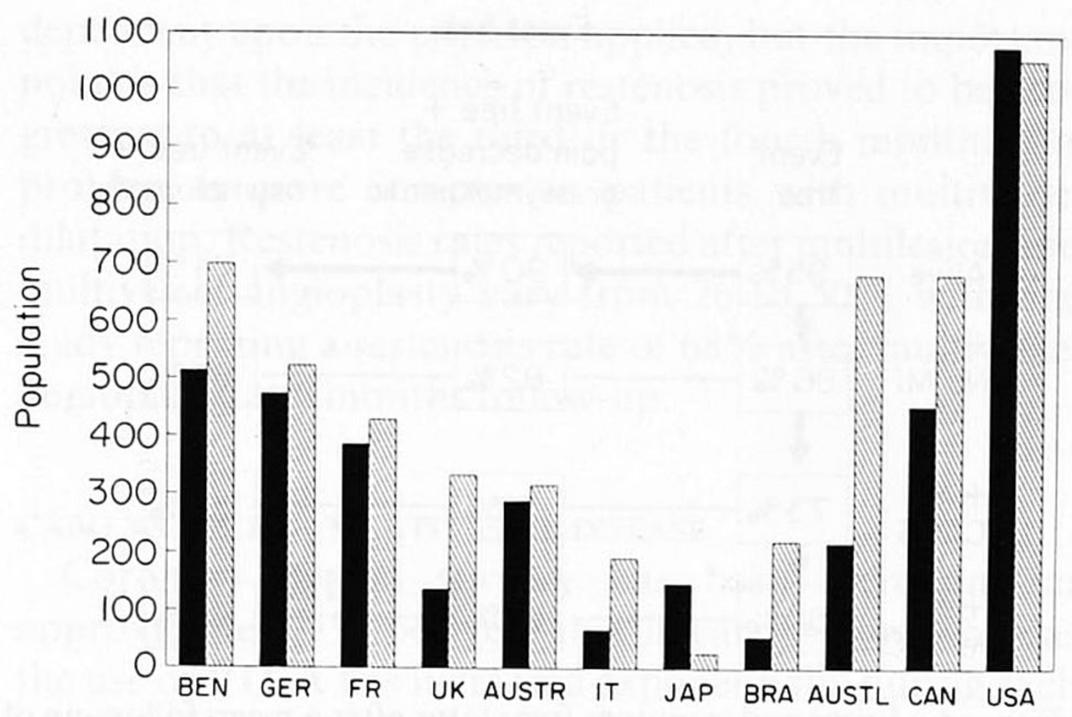

Figure 3 PTCA (■) and CABG (▨) per million population (capita), 1990.

Table 3 Longest reported follow-up, treated by Andreas Gruentzig

Primary success	n 133	% 100
Death (cardiac)	5	4
Early recurrence (6 months)	38	31
Late recurrence (2–7 years)	5	5
Progression (other vessel)	10	7
Re-PTCA	27	20
CABG	19	14
Long-term success (with re-PTCA)	98	74
Asymptomatic	89	67

Remarkably, in Japan PTCA is performed almost five times more frequently than CABG.

In Europe, the Benelux countries perform the most PTCA and CABG procedures per capita with 700 CABGs million^{-1} capita and 500 PTCAs million^{-1} capita. In decreasing rank order is Germany, France, U.K., Austria and Italy. Currently, the gap between the number of CABGs and PTCAs is still quite large in Australia and Canada.

Long-term follow-up studies

PTCA FOR STABLE ANGINA

To date, the longest reported follow-up is for the first 133 patients successfully treated by Andreas Gruentzig between September 1977 and October 1980[2]. These patients have now been followed for 5 to 8 years. In the follow-up period, five of the 133 patients died of cardiac disease, that is to say 4% of the population (Table 3). Early recurrence within 6 months was demonstrated in 31%, late recurrence was in 5%. Progression of coronary artery disease occurred in 10 patients, that is to say 7%. Over the mean follow-up period of 6 years, 20% of the patients had a second angioplasty and 14% had bypass

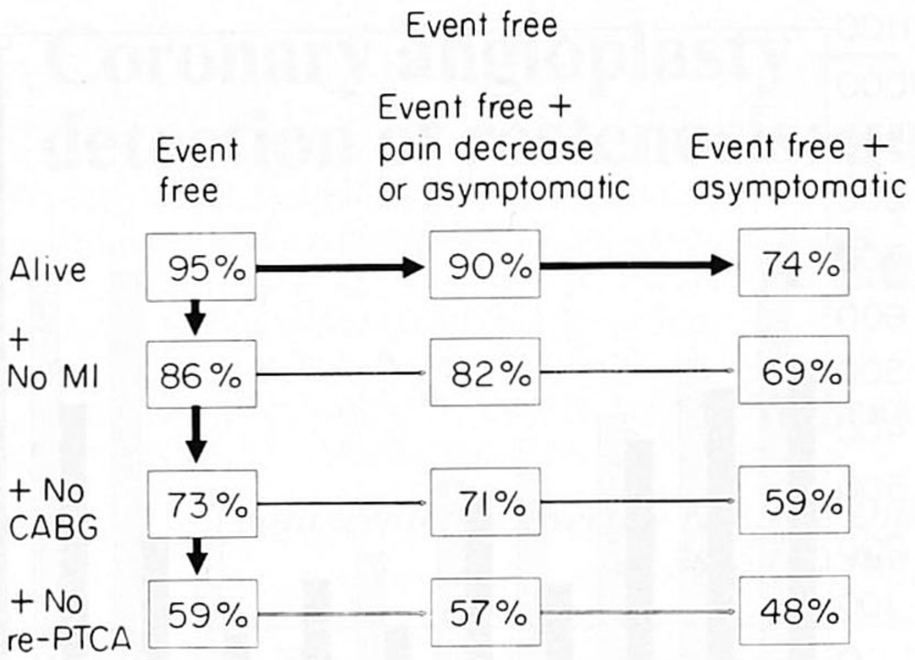

Figure 4 Event and symptom free status after a mean follow-up of 4·9 years of 1000 patients, Pittsburg Registry data.

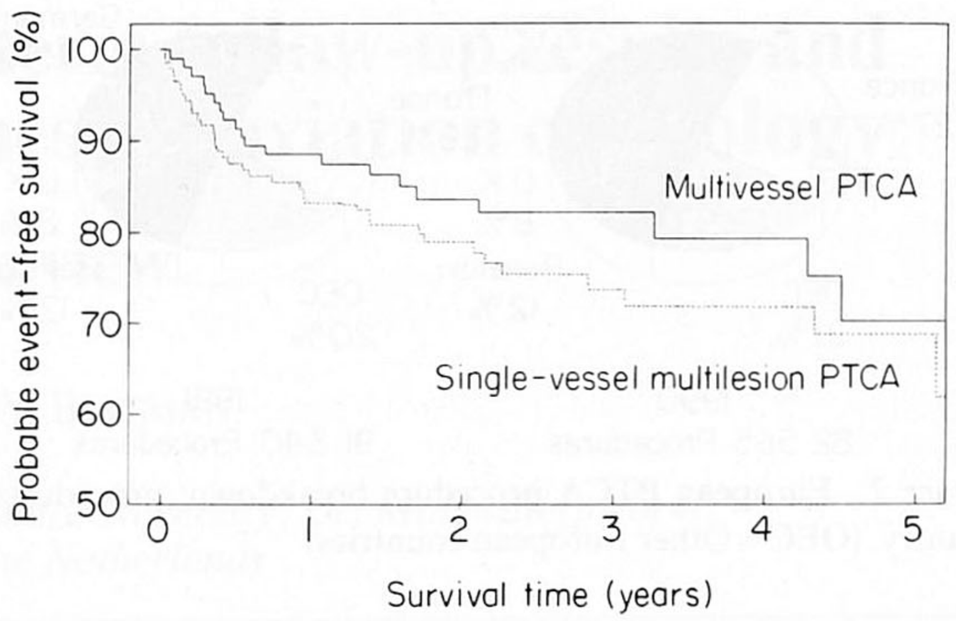

Figure 5 Event-free survival for multilesion and multivessel dilatations: P = non significant.

grafting for the original lesions. However, the important fact is that 74% of these patients, originally candidates for surgery have been successfully treated without surgery and 67% were asymptomatic at the last follow-up study. It would be difficult to match these patients with a control group in whom medical therapy or coronary bypass surgery was the primary treatment. However, the fact that there were five deaths from cardiac disease among the 169 original patients followed for 6 years makes the series at least comparable to other surgically or medically treated series of symptomatic patient with coronary artery disease.

The Registry data centre in Pittsburg has continued to follow-up the first 1000 patients in whom PTCA was classified as initially successful[3]. We believe that this original cohort of patients with successful PTCA will remain a good predictor of long-term results in patients who are currently successfully dilated. Figure 4 shows the event and symptom status after a mean follow-up of 4·9 years in the first 1000 patients who underwent an initially successful PTCA. Looking at the freedom of events, we see that 95% of the patients were alive, 86% were alive and had no myocardial infarction (MI) at follow-up, 73% were alive and had neither myocardial infarction (MI) nor bypass surgery at follow-up. Finally, at 5 years, 59% of the patients were free of all events: death, MI, CABG and repeat PTCA. Fifty-seven percent among this 1000 patients were event free, asymptomatic or had improved symptoms; 40% were event free and asymptomatic. With the adjunction of a second PTCA, 59% were asymptomatic at 5 years. Almost two thirds remain pain free, without having undergone a MI or coronary artery bypass surgery.

PTCA FOR UNSTABLE ANGINA AND MULTIVESSEL DISEASE: TWO UNSETTLED ISSUES

At the Thoraxcenter (Rotterdam), we have compared the long-term follow-up of patients undergoing PTCA for stable and unstable angina[4]. The median follow-up of these patients was 3·1 years, ranging from 18 months to 7 years. The indication for PTCA was stable angina in 530 patients and unstable angina in 366 patients. In terms of mortality, there was no significant difference between the two groups, 3·4% vs 5·2%. In the unstable group, the incidence of acute non-fatal myocardial infarction was significantly higher: 8·3 vs 14·2% and the difference in non-fatal myocardial infarction at follow-up was entirely explained by a higher incidence of infarction in the first 24 h after PTCA. (The influence of PTCA on the increased risk of non-fatal myocardial infarction in unstable angina pectoris is difficult to determine, but these figures seem comparable for medical or surgical outcome). At follow-up, an increased rate of CABG was noticed in the unstable group, 20·8% vs 14·7%. There was no difference in the need for repeat PTCA in the two groups and 68% of the stable and 61% of the unstable were event-free at follow-up.

In 1990 another investigation was being carried out at the Thoraxcenter to evaluate the long-term value of performing multiple dilatation according to procedural type (single-vessel multilesion or multivessel dilatations) and anatomical type (single-vessel disease with multiple dilatations or multivessel disease dilatations; complete and incomplete revascularization)[5]. Between 1980 and 1988, 248 patients met the following criteria: (1) at least two lesions dilated (range: 2–4) and (2) all attempted lesions successfully dilated. The mean length of follow-up was 33 months.

The end-points analysed were death, myocardial infarction, redilatation and bypass surgery. No differences were found for these events between the single-vessel multilesion group (144 patients) and the multivessel group (104 patients). The 4·5 years probability of event-free survival was 68% and 70%, respectively (Fig. 5). In the event-free patients, 57% vs 59% were asymptomatic and 45% vs 46% were not taking anti-anginal drugs.

In the anatomical sub-groups, there were less event-free patients in the incompletely revascularized multivessel disease group (55% of 55 patients) when compared with those who were completely revascularized (84% of 79 patients) and with those in the single-vessel disease multiple dilatation group (74% of 107 patients) (Fig. 6). The 4·5 years event-free survival probability for each group was 44%, 78% and 74% respectively. This difference was caused by more infarctions (9% vs 2% vs 4%, respectively) and more bypass operations in the multivessel disease and incomplete revascularization groups (20% vs

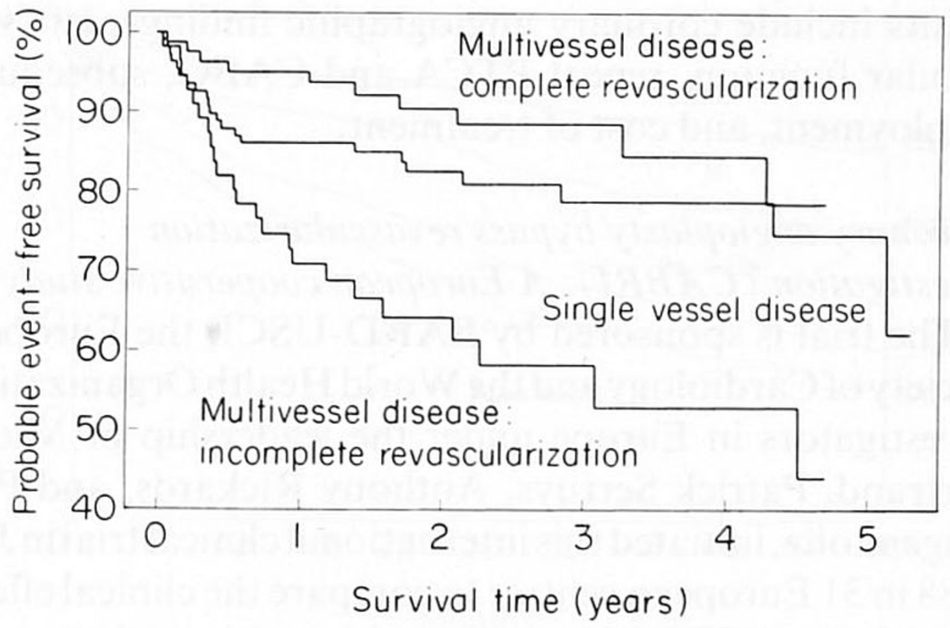

Figure 6 Event-free survival. The multivessel disease incomplete revascularization group is significantly different from (1) complete revascularization ($P<0{\cdot}001$) and (2) single vessel disease ($P<0{\cdot}01$).

5% vs 10%, respectively). In event-free patients, improvement of angina was similar and documented in over 85% of patients in each group. Furthermore, the number of asymptomatic patients at follow-up was similar in all groups except that within the incomplete revascularization group, fewer patients were free of antianginal drugs (21% vs 51% vs 48%).

Finally, 48% of the entire cohort performed an exercise test 4·6 months (mean) after dilatation and no difference was found in any of the variables in any group. About 10% of the patients experienced angina and approximately 30% had a positive exercise test for ischaemia by ST segment criteria. The functional performance in every group was over 90% of predicted workload.

Between 1980 and 1985, the French PTCA Registry collected more than 5000 patients[6]. Just before discharge, 2373 patients underwent an exercise test: a maximal negative exercise test was obtained in 63% of patients with single vessel disease and 47% of patients with multiple vessel disease. In both groups 22% and 26% respectively were unable to reach the maximal age predicted heart rate. Before discharge, 15% of patients with single vessel disease and 27% of patients with multiple vessel disease still had a positive exercise test. Six months after the procedure, 1881 patients had a complete clinical and angiographic examination, and 71% of patients with single vessel disease remained symptom free vs 65% of patients with multiple vessel disease. One thousand three hundred and eleven patients underwent exercise electrocardiography. Among the patients with single vessel disease, 71% had a negative test as opposed to 60% of patients with multivessel disease. This left 40% in the multivessel group and 29% in the single vessel with a positive exercise test. Restenosis, defined as a 50% loss of the initial gain achieved at PTCA was observed in 31% of patients with single vessel disease vs 34% of patients with multiple vessel disease.

We have prospectively studied the incidence of restenosis using the four NHLBI criteria, the 50% diameter stenosis at follow-up criterion, as well as criterion based upon a decrease of more than 0·72 mm in luminal lumen diameter at follow-up. Patients were recatheterized at either 30, 60, 90 and 120 days following successful PTCA. A wide variation in the incidence of restenosis was found dependent upon the criterion applied, but the important point is that the incidence of restenosis proved to be progressive to at least the third or the fourth month. The problem is more complex in patients with multivessel dilatation. Restenosis rates reported after multilesion and multivessel angioplasty vary from 26 to 50% with one study reporting a restenosis rate of 68% after multivessel angioplasty at 6 months follow-up.

CABG VS PTCA IN MULTIVESSEL DISEASE

Coronary bypass surgery has been increasing at approximately 7% per year in a linear fashion, whereas the use of PTCA has increased exponentially during each of the last 5 years. Balloon angioplasty is unequivocally here to stay, but as the late Dr Andreas Gruentzig stated in 1979, randomized trials are 'clearly needed if we are to evaluate the efficiency of this new technique as compared with current medical and surgical treatment'. Yet the first randomized trial of PTCA compared to coronary bypass surgery began in 1987, approximately 10 years after the initial performance of PTCA.

Currently, there are three European randomized trials of PTCA vs CABG[7].

Randomized interventional treatment of Angina (RITA)

This trial is jointly sponsored by the British Cardiac Society, the British Heart Foundation, and the Department of Health. It was initiated in April 1988 at medical centres in the United Kingdom under the leadership of Edgar Sowton.

In January 1992 the study completed the intake of 1000 patients. Patients with single-, double-, or triple-vessel coronary artery disease were eligible if they had clinical and angiographic characteristics that were judged to be appropriate for either PTCA or for CABG, and if a cardiologist and a surgeon agreed that equivalent revascularization is feasible by both PTCA and by CABG.

An absence of symptoms and presence of heart failure did not exclude patients who are judged appropriate for revascularization. The angiographic eligibility for intervention included coronary artery diameter stenoses $>50\%$ in an artery supplying at least 20% of viable myocardial mass. Patients not randomized were entered into a registry. Follow-up was planned for 3 to 5 years, and endpoints were death, myocardial infarction, repeat PTCA or CABG, severity of angina pectoris, exercise test performance, subsequent employment and left ventricular function. Almost 50% of the patients enrolled in this trial had single vessel disease and only 13% had three vessel disease.

The preliminary results of 870 patients have been analysed. More than 90% of the patients were initially symptomatic with almost 60% in classes III and IV. After either surgery or angioplasty less than 20% of the patients were still symptomatic and the early follow-up tends to demonstrate that these effects persist over a period of 2 years. At 2 years, less than 5% of the patients were in class III or IV of the Canadian functional class (Fig. 7).

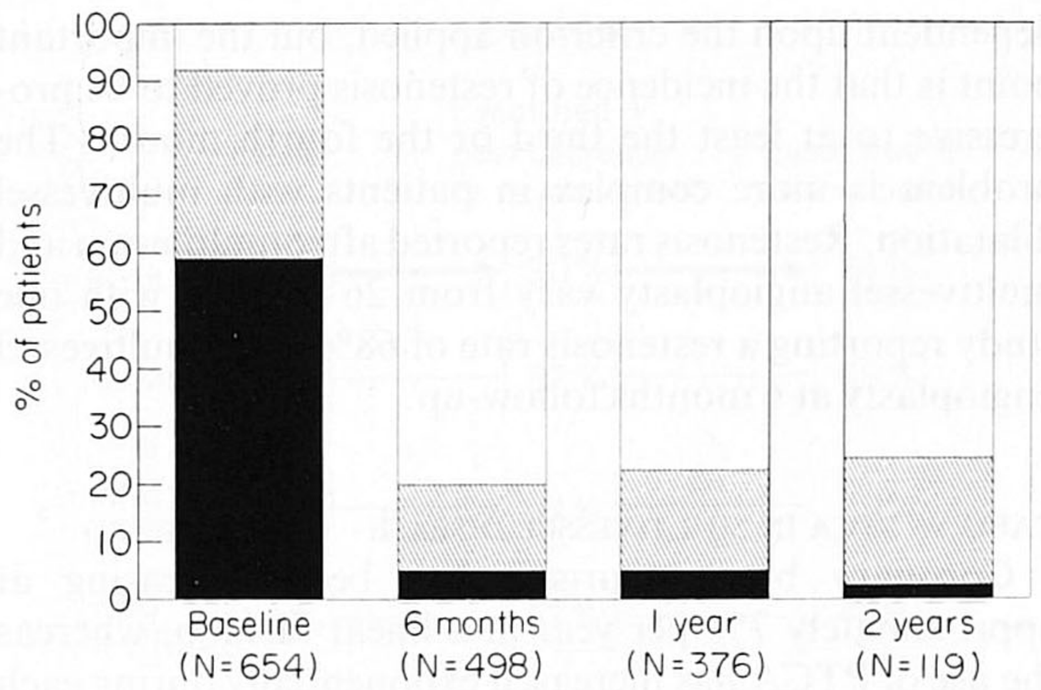

Figure 7 RITA angina pectoris follow-up data. □ = no angina; ▨ = grade I–II; ■ = III–IV.

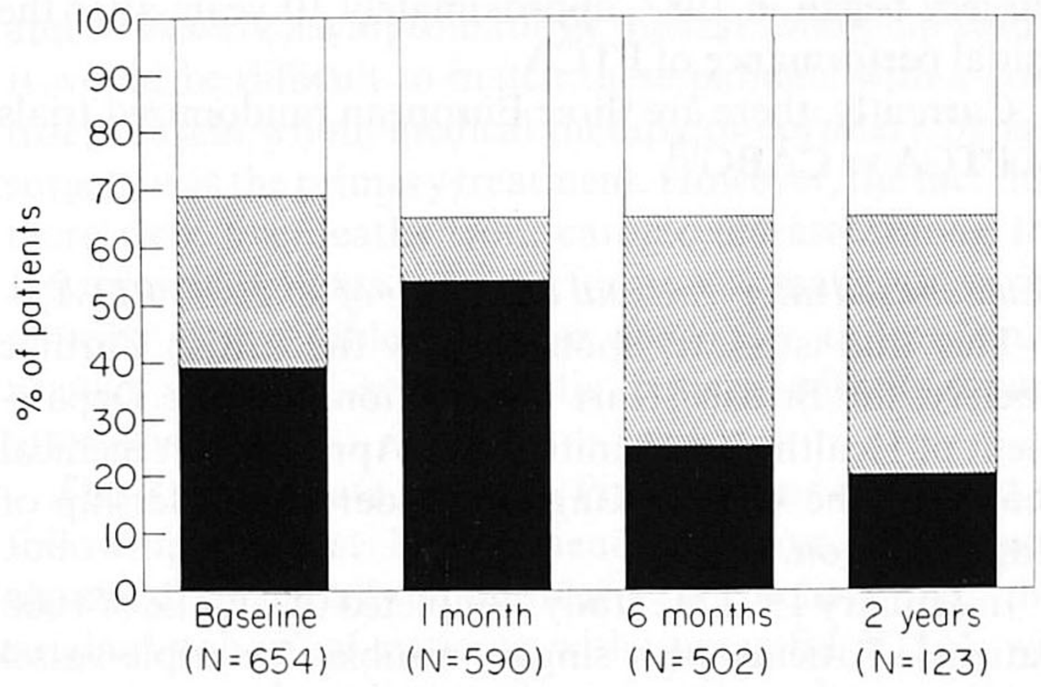

Figure 8 RITA employment status follow-up data. □ = others (retired, HW); ▨ = working; ■ = not working, CAD.

The employment status at follow-up was very encouraging, showing that at 2 years less than 20% of the patients were not actively working while 50% of the total population has kept working or resumed their job (Fig. 8)

German angioplasty-bypass intervention trial (GABI)

This randomized clinical trial is sponsored by the German government (Department of Research and Technology), and was initiated in December 1986 at eight university medical centres in West Germany under the leadership of the late Walter Bleifeld.

In December 1991, the study had completed the intake of 400 patients. Patients are eligible for randomization if they have severe angina pectoris (Canadian Cardiovascular Society class III) and clinical and angiographic indications considered amenable to intervention by both PTCA and by CABG in at least two coronary arteries with 70% or greater stenosis.

Follow-up is to be obtained at 3, 6, and 12 months; the primary end-points are severity of angina pectoris and dyspnœa, exercise performance with thallium 201 imaging, myocardial infarction, and death. Secondary end-points include coronary angiographic findings, left ventricular function, repeat PTCA and CABG, subsequent employment, and cost of treatment.

Coronary angioplasty bypass revascularization investigation (CABRI): A European cooperative study

The trial is sponsored by BARD-USCI, the European Society of Cardiology and the World Health Organization. Investigators in Europe under the leadership of Michel Bertrand, Patrick Serruys, Anthony Rickards, and Paul Hugenholtz, initiated this international clinical trial in July 1988 in 31 European centres to compare the clinical effects of CABG and PTCA in patients with multivessel coronary disease for whom both PTCA and CABG are considered clinically appropriate.

Patients may be randomized if they have 2 or 3 vessel disease and at least one lesion suitable for PTCA from the standpoint of the cardiologist. Clinical entry criteria include patients with stable and unstable angina pectoris, prior myocardial infarction and atypical chest pain or no symptoms if myocardial ischaemia is found on objective testing. Twelve hundred patients have been randomized (September 1992). In the Netherlands three centres participate in this study. The contribution of The Netherlands and Belgium in recruiting patients is 30% of the total intake of patients in Europe.

Follow-up is to be obtained at 6, 12, and 24 months. The primary end-points are relief of angina and objective assessment of functional capacity by treadmill exercise stress testing and thallium scintigraphy. Other end-points include mortality, new cardiovascular events, repeat revascularization and the angiographic assessment of coronary artery changes and left ventricular function.

Hopefully, these European trials, together with the two major American trials, EAST and BARI will shed some light on the respective merits of balloon angioplasty and bypass surgery as regards revascularization strategy. It is interesting to note that the CABRI protocol does not exclude new technologies if these new interventions are routinely used by some of the participating investigators.

SAPHENOUS VEIN BYPASS GRAFT ANGIOPLASTY: LONGTERM FOLLOW-UP IN THE NETHERLANDS

The Inter-university Cardiology Institute of the Netherlands (ICIN), has recently evaluated the long-term clinical effects of balloon angioplasty in venous bypass grafts in 454 patients who underwent angioplasty of a saphenous vein bypass graft. Between April 1980 and January 1989, of a total of 19 994 PTCA procedures were performed in the Netherlands[8].

In 46% of patients, single graft angioplasty was attempted, and in 54% of patients sequential graft angioplasty was attempted. The clinical primary success rate was 90%. In-hospital mortality was 0·7%; 2·8% of patients sustained a procedural myocardial infarction, and 1·3% of patients underwent emergency bypass surgery.

After a follow-up period of 5 years, 74% of patients were alive, and 26% were alive and event-free (no myocardial infarction, no repeat bypass surgery or repeat

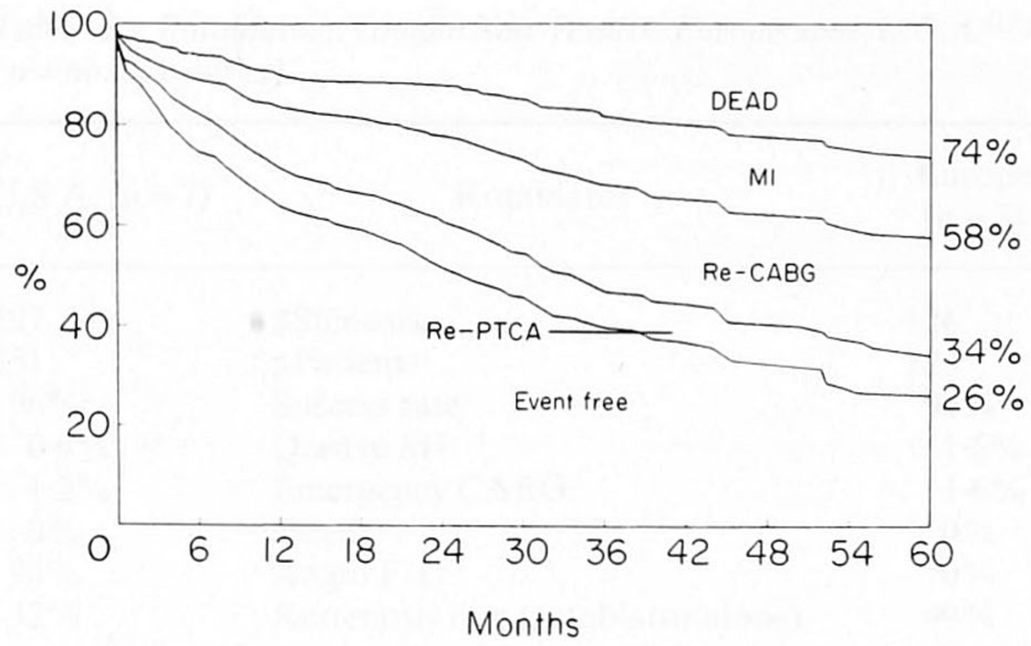

Figure 9 Event-free survival, 5 years after PTCA of saphenous vein grafts[3].

angioplasty) (Fig. 9). In patients in whom the initial angioplasty attempt was unsuccessful, only 3% were event-free at 5 years, vs 27% in successfully dilated patients.

The time interval between the angioplasty attempt and previous surgery was a significant predictor for 5-year event-free survival. The event-free survival rates for patients who had bypass surgery 1 year before angioplasty, between 1 and 5 years, and 5 years before angioplasty, were 45%, 25%, and 19%, respectively (Fig. 10). Less than one-third of patients with previous bypass surgery who had angioplasty of the graft remained event-free after 5 years.

Part II: New technologies

STENTS

One of the most recent developments has been the use of the intravascular stent, although the original concept of intravscular stenting precedes the introduction of coronary artery interventional cardiology by many years. In 1969, Dotter developed a coil spring endovascular prothesis in an attempt to improve the long-term patency of peripheral atherosclerotic vessels submitted to recanalization and dilatation. Even at that time he envisaged that 'prompt fibroblastic development and a rapid formation of a new, firmly anchored autogenous lining surface' would be a critical factor in the long-term patency of the device.

Since the original description of Dotter's tubular coil spring, there have been many variants of the original concept deployed experimentally including: thermal shaped memory alloy stents, self expanding steel spirals, balloon expandable stainless steel mesh stents, balloon expandable interdigitating coils, synthetic polymeric stents and biodegradable stents. These various devices differ greatly in their fundamental geometry, (mesh, single wire) composition (metal, plastic) and mechanical behaviour (active or passive expansion).

Besides these fundamental differences there are a variety of subtle differences which may be important in themselves, such as thickness of filaments, alloy composition, electrostatic behaviour, biocompatible or therapeutic coatings. The prolonged presence of these materials residing in the arterial wall may generate late unknown and unexpected conseqeunces.

There is a consensus among investigators in the field that stent implantation improves the immediate post-dilatation result, producing a smooth, straight, dilated segment. This visual impression has been confirmed by quantitative analysis using both edge detection and video denisitometric techniques. Favourable results have also been reported in the 'bail out' situation, when the stent has been implanted following dilatation where presence of intimal dissection has led to a poor and even critical haemodynamic result.

The first intracoronary stent, the Wall-stent was implanted in France and Switzerland by Jack Puel and Ulrich Sigwart.

WALL-STENT

Over a period of 4 years between March 1986 and March 1990, wall-stents were implanted in 265 patients in Europe by six centres. In 265 patients, 308 coronary lesions were stented but unfortunately 41 of these lesions occluded in the early phase after stent implantation. This left 272 stented lesions in 225 patients at hospital discharge; among these we have late angiographic follow-up from 178.

Summarizing the wall-stent experience, between 1986 and 1990 it could be said that early occlusion in the first 2 weeks after implantation was observed in 19% of the implants in native coronary arteries and in 8% of implants in bypass grafts. In terms of restenosis (according to 50% diameter stenosis criteria), restenosis was observed in 19% of the remaining patients with an implantation in the native circulation and in 39% of the patients with a bypass graft, at $6{\cdot}6 \pm 4{\cdot}8$ months follow-up (Table 4)[9].

STENTING OF SAPHENOUS VEIN BYPASS GRAFTS: A NEW TREATMENT MODALITY FOR PATIENTS WHO ARE POOR CANDIDATES FOR REINTERVENTION. SINGLE CENTRE EXPERIENCE

In 1990 at the Thoraxcenter, during a 2-year period, 130 self-expanding wall-stents (Medinvent, Lausanne) were implanted in 65 patients during 77 procedures in 91 coronary artery bypass graft stenoses. All patients had severe symptoms and were considered to be a high risk group: in 42 patients, surgeons were reluctant or had refused to perform a new bypass operation because of unfavourable coronary vessel anatomy. PCTA was not an attractive option in 47 patients because of the age of the grafts (mean 83 months), the length of the stenosis (mean 16·5 mm) and the unfavourable angiographic picture (tandem lesions ($n = 21$), lesions containing ulcers, aneurysm, calcification or dissection ($n = 34$)). The mean unconstrained diameter of the stent was 4·3 (3·5–6·0 mm), implanted in grafts with a mean diameter of 3·3 (1·6–7·0 mm). The mean minimal luminal diameter of the stenosis was $1{\cdot}4 \pm 0{\cdot}8$ mm.

All procedures were technically successful and resulted in a significant increase of the mean minimal luminal diameter to $2{\cdot}7 \pm 0{\cdot}7$ mm. During hospital stay, an acute thrombotic occlusion occurred in seven patients (11%),

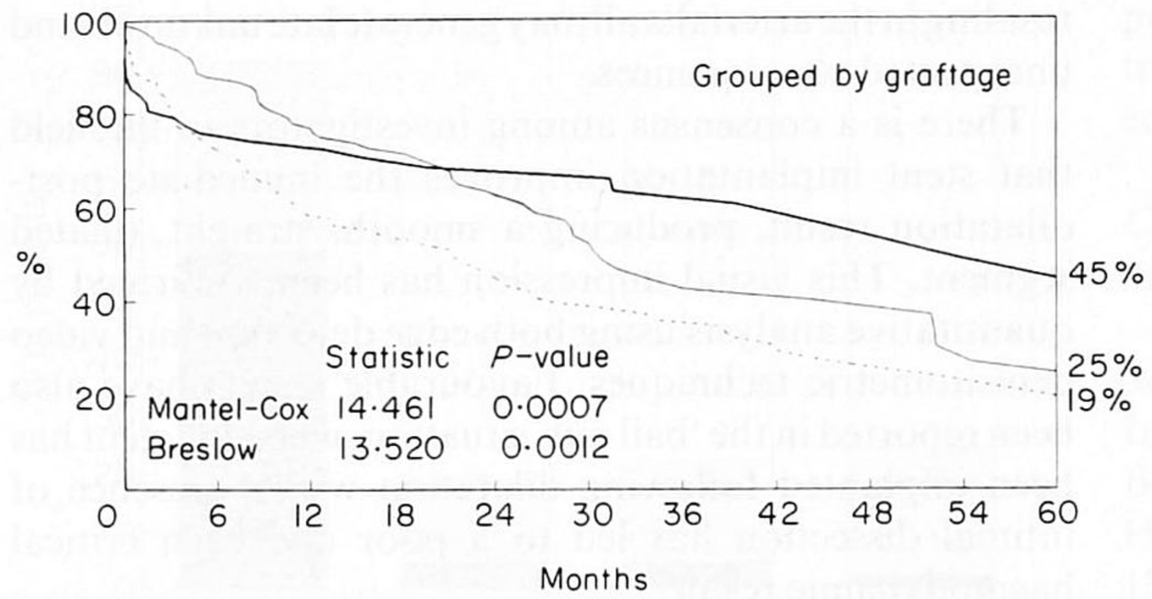

Figure 10 Event-free survival, 5 years after PTCA of saphenous vein grafts, related to date of previous CABG[3]. ——— = < 1 year; —— = 1–5 years; · · · · · · · = 5 years and over.

Table 4 Wall-stent experience (1986–1990). (DS = diameter stenosis)[4]

	Native	Graft
Patients	165	100
Early occlusion	19%	7·9%
Patients	101	74
50% DS	19%	39%

necessitating reintervention in four (re-CABG) and leading to an acute myocardial infarction in three. Two patients died due to an intracerebral bleeding, directly related to anticoagulation therapy.

At late follow-up (3–6 months, n = 46), 16 patients (35%) developed a restenosis (> 50% DS) within the stent, necessitating reintervention in 15 patients (PTCA: n = 11; re-CABG: n = 4). In the patient group without stent-related restenosis (n = 30), 15 patients developed progression of native or bypass disease leading to recurrence of major angina pectoris symptoms within 1 to 24 months. Ten of these patients underwent further intervention (stent: n = 6; PTCA: n = 3; re-CABG: n = 1).

Implantation of the wall-stent was interupted in March 1990 but will be resumed. In the meantime three other stents, the Palmaz-Schatz stent, the Strecker-stent, and the Wiktor-stent have been used in Europe.

PALMAZ-SCHATZ STENT

There is no formal registry of the implantation of the Palmaz-Schatz stent in Europe and most of the information on this stent has been collected by Jean Marco and Jean Fajadet from the Clinique Pasteur in Toulouse.

Between March 1989 and June 1990 the Palmaz-Schatz stent was successfully implanted in 207 patients and they obtained a repeat catheterization in 173 (84%) of their patients. Restenosis, defined as a diameter stenosis > 50% at follow-up, was observed in 24% of their patients; among the 154 patients who received a single stent, the restenose rate was 19%[10].

Hopefully, these results will be confirmed by a prospective randomized trial in the future. The Belgium-Netherlands Stent interventional study (BENESTENT) was started in the Benelux in June 1991. The Stent Restenosis Study (STRESS) has already started in the U.S.A.

WIKTOR-STENT

Seven European, one Canadian and two American centres are currently evaluating this device. To date, 123 implantations have been performed[11].

On behalf of the Wiktor Working group, the Thoraxcenter evaluated the short and long-term results of a single Wiktor-stent implantation that was successfully carried out in 50 patients in Europe and Canada, between January 1990 and October 1990. Stent implantation was attempted because of recurrence of stenosis in a native coronary artery lesion following balloon angioplasty. Stent implantation, after balloon angioplasty, immediately resulted in an additional increase in minimal cross-sectional area and minimal luminal diameter with a concomitant decrease in percentage area and percentage diameter stenosis compared with the postangioplasty state. The initial increase in minimal luminal diameter after predilatation with the ballon in this study ($1{\cdot}09 \pm 0{\cdot}26$ mm to $1{\cdot}80 \pm 0{\cdot}32$ mm), has also been observed after conventional balloon angioplasty in other series. There is a five-fold increase in the minimal luminal cross-sectional area after stenting ($1{\cdot}00 \pm 0{\cdot}44$ mm^2 to $4{\cdot}83 \pm 1{\cdot}40$ mm^2). A normalization of the coronary flow reserve may be expected with such an increase in the luminal cross-sectional area.

The recurrent restenosis rate in the first 6 months after Wiktor stent implantation in this study amounts to 28% using the 50% diameter stenosis criterion.

It was concluded that changing the stenosis geometry by stent implantation does not eliminate the late neo-intimal hyperplasia. However, the further increase in minimal diameter and cross-sectional area after stent implantation compensates to some degree for the restenosis.

STRECKER-STENT

The Strecker-stent is a balloon-mounted flexible endoprosthesis of knitted tantalum wires successfully used in peripheral arteries. The first clinical experience with the Strecker-stent for acute coronary occlusions after PTCA was carried out at the University Hospital Hamburg. The

Table 5 Rotablator; comparison results Europe and U.S.A.[12–14] *(n = no. of centres)*

U.S.A. (n = 7)	Rotablator	Europe (n = 3)
297	♯Stenosis	126
251	♯Patients	123
96%	Success rate	90%
0·4%	Q wave MI	1·6%
1·2%	Emergency CABG	1·6%
0%	Death	0%
94%	Angio F/U	70%
32%	Restenosis rate (rotablator alone)	49%

Heart Technology M. Bertrand

safety and performance of 3·2 mm (n = 20) and 3·8 mm (n = 37) coronary stents in 51 patients undergoing elective (n = 49) or emergency (n = 2) PTCA complicated by abrupt occlusion was investigated. All except one stent could be correctly placed, even in curved segments (LAD n = 24, RCA n = 18, RCX n = 8, CABG n = 6) and were visible. For extensive dissections, one patient received three stents, four patients two stents. Five patients received thrombolytic agents early after the procedure for impending occlusions. According to angiography (n = 16 consecutive patients) all stents were patent after 24 h. Major bleedings at the puncture site were observed in six patients. During hospitalization 10 patients underwent bypass surgery (day 1–7) because of stent migration (n = 2) and thrombolytic occlusion. Three patients died due to acute thrombolytic occlusion (day 1), pericardial tamponade (day 2) and cerebral bleeding (day 2); another patient died postoperatively. Currently 12 patients had follow-up angiograms after 3–4 months all confirming patent stents without evidence of relevant restenosis.

Atherectomy

ROTABLATOR

All three atherectomy devices employed in Europe were developed in the U.S.A. From a historical point of view, however, the Rotablator was initially tested in France and Germany by two pioneers Michel Bertrand and Raymond Erbel. So far, 126 lesions have been treated in 123 patients in Lille, Mainz and Rotterdam[12–14].

Shortly after the initial experience in Europe, centres in the U.S.A. started actively to collect cases and so far 297 lesions have been treated in 251 patients in that country. The results from the European centres are somewhat less spectacular than the results observed in the U.S.A. The initial success rate in Europe was 90% with an incidence of 1·6% of Q-wave myocardial infarction and an incidence of 1·6% for emergency CABG, vs 0·4% and 1·2%, respectively in the U.S.A. In both the European and the U.S.A. series there were no deaths. The restenosis rate using the Rotablator alone was 49% in the European vs 32% in the American series. The angiographic follow-up in the European series was only 70%, however, vs an angiographic follow-up of 94% in the U.S.A. centres (Table 5).

ATHEROCATH

The second atherectomy device introduced from the U.S.A. into Europe was the Atherocath developed by John Simpson. To date, 533 patients have been treated in 57 centres primarily in Germany, the Netherlands, Belgium and France[15]. Devices for Vascular Intervention (DVI) has analysed the multicentre results to identify applications of atherectomy that may offer important insights for the interventionalist.

Table 6 shows a comparison of early and late results; excluded from this table are patients with acute myocardial infarction and distal and diffuse coronary disease. Treated lesions have been broken down into de novo lesions, restenotic lesions and saphenous vein graft-lesions. The analysis uncovered a consistent pattern of improvement during the time of the study. As far as de novo lesions are concerned, major complications decreased from 9·1% in the old cohort to 3·5% in the new cohort; the angiographic restenosis rate was reduced from 38% to 26% in the new series, compared with the earlier cases, at 6 months follow-up.

Low rates of major complications have been found in all native re-stenotic lesions with a percentage of 1·2% similar to old vein graft lesions with the same incidence of major complications of 1·2%. Primary success rates for the restenotic lesions and the saphenous vein graft lesions are 92% and 88%, respectively. Although atherectomy in a saphenous vein graft for a restenotic lesion is a safe procedure, the restenosis rate seems prohibitive — 81% at 6 months.

With proper patient selection, directional coronary atherectomy seems to offer good long-term benefit for the treatment of some de novo lesions. Angiographic restenosis following this technique appears lowest in focal lesions which fit in the 10 mm window. Such lesions show an overall restenosis rate of 14% and a restenosis rate of 11% for in the left anterior descending coronary artery (LAD). Eccentric lesions suited for an eccentric window have an overall restenosis rate of 17% and 13% in the LAD. Finally, proximal segments have an overall restenosis rate of 27% and 24% in the proximal LAD.

Comparative randomized studies need to be performed to assess the relative merits of directional atherectomy vs angioplasty. The Coronary Angioplasty vs Excisional Atherectomy Trial (CAVEAT) is an American randomized trial that started enrolling patients in September 1991.

TRANSLUMINAL EXTRACTION CATHETER

The Transluminal Extraction Catheter (TEC) designed by Interventional Technologies is yet another technique. In Europe, six countries are currently using the TEC device; a quick rundown reveals that in Spain 91 cases have been carried out, in Italy 29, in Germany 25, in Sweden 15, in Holland 25, Belgium 4 and Switzerland 22 cases were done[16].

An update in October 1990 indicated that worldwide 577 patients have been treated with this technique. If primary success is defined by reduction in diameter stenosis of more than 20% together with a residual diameter stenosis of less than 50% without the occurrence of

Table 6 Comparison of early (86–89) and later (89–90) results with directional coronary atherectomy in native vessels and saphenous vein graft-lesions (SVG) (excluding AMI patients, distal and diffuse coronary artery disease)[15]

	Primary success	Major complication	Angio-restenosis*
De novo (132)	—	9·1%	38%
De novo (397)	82%	3·5%	26%
Restenotic (196)	—	1·5%	42%
Restenotic (330)	92%	1·2%	48%
SVG (155)	88%	1·2%	—
De novo (84)	87%	2·3%	36%
Restenotic (71)	90%	0·0%	81%

Source: DVI *Angiographic Compliance (66–80%)

Table 7 Primary success rate of the Transluminal Extraction Catheter (TEC), in native and bypass-graft vessels[16]

	Native	Bypass
Overall	90% (331/367)	90% (187/207)
TEC + PTCA (after)	91% (214/235)	90% (128/142)
TEC + PTCA (before)	80% (4/5)	75% (3/4)
TEC only	89% (110/124)	91% (52/57)

577 patients
Interventional technologies Inc.

in-hospital death, Q-wave myocardial infarction or CABG, it appears that the overall success rate is about 90% for the native coronary arteries as well as for bypass grafts.

In a large proportion of patients, intervention with the coronary atherectomy catheter was followed by conventional balloon angioplasty. When the TEC device is used alone, it appears that the overall success rate is also 89% for native vessels and 91% for bypass grafts (Table 7). Major complications including non-fatal Q-wave myocardial infarction and complications leading to emergency CABG or in-hospital death were encountered in less than 4% of the patients.

Finally, early results regarding restenosis are about the same as balloon angioplasty in the native coronary tree where the restenosis rate ranged between 32 and 37%. However, the investigators found that the TEC catheter worked well in vein grafts and native arteries where there is thrombus present. The restenosis rate in this subset of patients would be less than the restenosis rate usually observed after using a balloon. It is too early to draw any conclusion but progress will be kept under review.

Laser

Two clinical varieties have been used in Europe; the laser balloon angioplasty and the excimer laser.

LASER BALLOON ANGIOPLASTY (LBA)

Three centres in Europe have been actively participating in the laser balloon angioplasty (LBA) study initiated by Richard Spears and USCI. These include the St. Antonius Hospital in Nieuwegein, the Centre Cardiologique du Nord à Paris and the National Heart Hospital in London. Thijs Plokker, Gijs Mast and Jeff Ernst of the Nieuwegein group in the Netherlands have summarized their experience by concluding that LBA is a safe device, user-friendly and with a reliable 'bail out' device. Restenosis is not reduced and restenosis seems proportionally related to the laser energy level. This is illustrated in Table 8.

Table 8 Laser Balloon Angioplasty: restenosis rate and level of energy (Nieuwegein group)

Restenosis > 50%	
PTCA only	43%
15 W protocol	50%
20 W protocol	62%
25 W protocol	78%

EXCIMER LASER

The last newcomer among the new interventional devices has been the Excimer laser (ELCA). In the U.S.A. an excimer laser coronary angioplasty registry (ELCA) had collected more than 1284 patients throughout the U.S.A. by the end of 1990. In Europe, Karl Karsch from the University of Tubingen has also launched a registry in collaboration with five other German centres which so far has collected 315 cases.

In both series, the procedural success is about 90%. Conventional balloon angioplasty is still playing a major adjunctive role in 56% of the U.S.A. cases and 43% of the European cases.

The incidence of emergency bypass surgery, Q-wave myocardial infarction and mortality are quite similar in both series and comparable to the complication rate observed with conventional balloon angioplasty (Table 9). However, both the U.S.A. and the European investigators concur in saying that the technique is efficacious as

Table 9 ELCA registry (F. Litvak, nov/90), anatomical complications (n = 1284)

Dissection	12·1%
Acute occlusion	6·5%
Perforation	1·6%
Spasm	1·6%
Embolism	0·8%
Aneurysm	0·5%

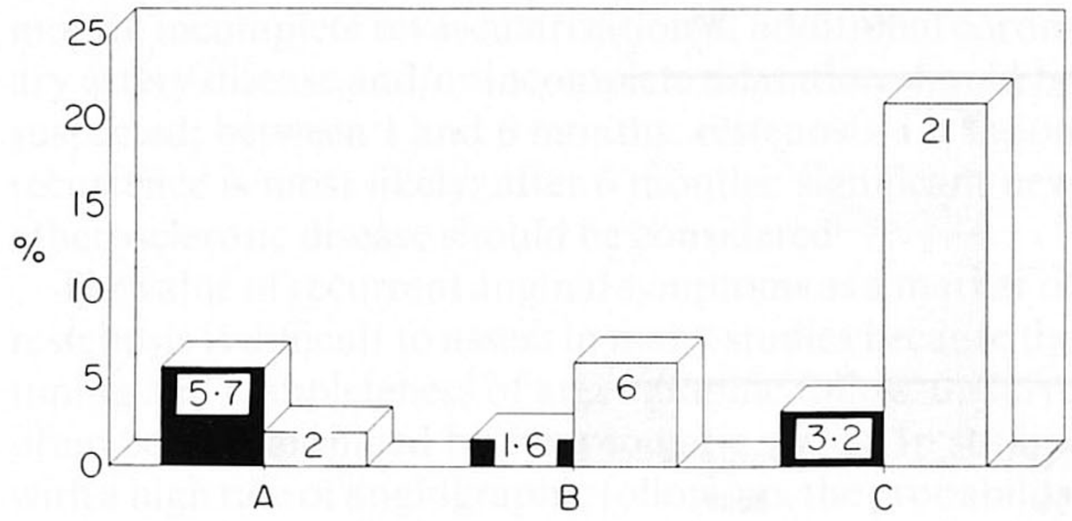

Figure 11 Relation between type of lesion and procedure (PTCA (□) vs excimer laser, ELCA (■)) and incidence of major ischaemic complications. A, B, C represents lesions in ascending order of severity. PTCA data from Ellis *et al.* Circulation 1990; 82. ELCA data from Cook *et al.* Circulation (in press).

an alternative or adjunct to PTCA especially in diffuse, long and aorta-ostial lesions.

The preliminary data on restenosis rate after ELCA, based on angiographic follow-up of a rather small cohort of patients, tend to demonstrate that ELCA at this stage is not the solution to the problem of restenosis. The overall restenosis rate is somewhat above the 30% level, but at this stage it is fair to conclude that the rate of restenosis appears comparable to restenosis after PTCA. However, data with respect to higher energy densities and greater initial debulking should be prospectively analysed.

Over the last 2 years, it has become fashionable to stratify the patients who are candidates for intracoronary intervention according to the classification proposed by the American College of Cardiology (ACC) and the American Heart Association (AHA). The complexity of the lesion to be dilated is based on severity, length, calcification, eccentricity, total occlusion, presence of thrombus, sidebranch involvement, tortuosity of the vessel, and take off vessels and has been stratified in three groups: A, B and C; lesion type B and C represent the most complex lesions. In observational studies it appears that the incidence of major ischaemic complications when dealing with lesions of type B and C are much larger for PTCA than for excimer laser therapy (Fig. 11). Up to 21% of major complications is observed in the PTCA group for the C lesion while the incidence of complications with the laser is only 3·2%. A similar although less impressive trend is observed for the lesion of type B.

Once again, this preliminary conclusion based on observational studies has to be confirmed by a properly conducted randomized trial which started in September 1991 in the Netherlands (AMRO-trial).

IS THERE A NICHE FOR ALL AVAILABLE CORONARY INTERVENTIONAL TECHNIQUES?

Eric Topol recently emphasized that all these new interventional devices have complementary therapeutic use[17]. Directional atherectomy is a good instrument with which to treat a proximal LAD stenosis, a de novo lesion and a complex ulcerated lesion not suitable for PTCA. On the other hand, the transluminal extraction catheter (TEC) works well in degenerated saphenous vein grafts. Rotablator might be the device of choice for calcified or tortuous vessels not amenable to angioplasty or other techniques and could be very useful in total coronary occlusion when the guidewire has crossed the lesion while the balloon cannot. The stent is an elegant solution for abrupt closure and refractory restenosis after conventional balloon dilation. The LBA technique is also useful though a more expensive technique for abrupt closure. Finally, excimer laser angioplasty might have found its field of action in diffuse diseased long lesions and aorta-ostial stenoses.

A review of preliminary data available for each of the new devices indicates that the overall restenosis rate is quite similar to that of balloon angioplasty and the relatively high rate of restenosis early on may reflect a common denominator in terms of intimal injury. None have so far been demonstrated to have a performance acceptable in the context of recertification to fly.

Recommendations for aviation cardiology

Since its introduction by Gruentzig, percutaneous transluminal coronary angioplasty has now been shown to be effective in a wide variety of coronary artery disease subjects and clinical situations. In particular, balloon angioplasty of multiple segments is becoming increasingly frequent. The success rate and acute complication rate of such procedures has been shown to be acceptable. However, its long-term effect is less well known, in part due to heterogenicity of the study populations that differ with respect to distinct anatomical and procedural characteristics. Its relative value compared with coronary bypass surgery has yet to be established.

Currently, there are three randomized European and two American studies which compare the clinical outcome of CABG and PTCA in patients with multivessel coronary disease for whom both PTCA and CABG are considered clinically appropriate. Their results will become available in the coming years. In the meantime, long-term follow-up analysis of non-randomized studies is essential for the understanding of the progress made in the field of interventional cardiology. The available information gives an estimation of short and long-term outcome for certain subgroups of patients.

Primary success and restenosis after PTCA may be defined by symptomatic criteria such as frequency and severity of anginal episodes, by functional criteria such as pressure flow characteristic of the dilated vessel, coronary flow reserve and various non-invasive diagnostic tests, or may be defined by anatomical criteria using postmortem histology, angiography or intervascular ultrasound.

Table 10 Detection of restenosis by symptoms[15]

Author	Year	Angiographic follow-up %	Restenosis %	Symtoms PPV %	Symtoms NPV %
Simonton	'88	90	35	48	75
Caldiff	'90	100	38	60	85
Zaidi	'85	100	49	66	70
Mabin	'85	55	32	71	86
Levine	'85	92	40	76	96
Jutzy	'82	88	47	92	83
Gruentzig	'87	93	31	92	98

Modified from Califf *et al.*
PPV: positive predictive value
NPV: negative predictive value

Table 11 Detection of restenosis by exercise treadmill testing

Author	Angiographic follow-up %	Restenosis %	PPV %	NPV %	Timing of test
O'Keefe	100	13	29	73	< 1 month
Scholl	83	12	40	27	1 month
Wijns*	74	35	50	65	3–7 weeks
Wijns*	89	40	60	52	3–8 weeks
Bengston	96	51	39	84	6 months
Rosing	100	34	47	76	8 months
Ernst	100	4	50	95	4–8 months
Honan	88	58	57	64	6 months
Scholl	83	12	64	50	6 months

Modified from Califf *et al.*
*Thoraxcenter
PPV: positive predictive value
NPV: negative predictive value

Table 12 Detection of restenosis by thallium 201 scintigraphy

Author	Angiographic follow-up %	restenosis %	PPV %	NPV %	Timing of test
Jain	55	14	79	88	0–6 days
Miller	76	39	76	94	2 weeks
Lam	100	9	89	96	2 weeks
Wijns*	74	35	74	83	3–7 weeks
Wijns*	89	40	82	72	3–8 weeks
Scholl	83	12	56	42	1 month
			100	75	6 months
Ernst	100	4	50	100	4–8 months
Rosing	100	21	37	83	8 months
Lefkowitz	planar thallium		62	80	6 months
	thomographic thallium		80	93	

Modified from Califf *et al.*
*Thoraxcenter
PPV: positive predictive value
NPV: negative predictive value

These three criteria may be considered separately or may be interrelated so that the definition of restenosis becomes a complex issue.

It is fair to emphasize the five following points. Firstly, although the subjective improvement of symptoms after PTCA is probably the most desirable end-point, it is also

the least objective evaluation[18]. Secondly, the frequency of symptomatic improvement appears to be lower than that of angiographic success: only 80–85% of the patients with a satisfactory angiography result immediately post-PTCA exhibit such an improvement[19]. Thirdly, the reappearance of angina as a sole criterion of restenosis underestimates the angiographic rate of restenosis. The reported incidence of silent restenosis may be as high as 33%. Fourthly, the elapsed time between PTCA and recurrence of symptoms has been shown to be clinically useful in identifying the most probable cause of recurrent angina i.e. within one month: incomplete revascularization of additional coronary artery disease and/or incomplete dilatation should be suspected; between 1 and 6 months: restenosis, i.e. lesion recurrence is most likely; after 6 months: significant new atherosclerotic disease should be considered[20].

The value of recurrent anginal symptoms as a marker of restenosis is difficult to assess in many studies because the timing and completeness of angiographic follow-up have often been determined by symptomatic status. In studies with a high rate of angiographic follow-up, the probability that patients with symptoms had restenosis (i.e. the positive predictive value of symptoms) ranged from 48% to 92%, whereas the probability that patients without symptoms were free of restenosis (i.e. the negative predictive value of symptoms) ranged from 70 to 98% (Table 10)[21]. The low positive predictive value found in many of these studies may be explained by the presence of other mechanisms for angina, such as incomplete revascularization or progression of disease in other vessels.

Several studies have examined the ability of the exercise electrocardiogram to detect restenosis after PTCA. These studies have generally found that the presence of exercise-induced angina or ST segment depression or both is not highly predictive of restenosis whether the test is performed early or late after angioplasty. The positive predictive values of early treadmill testing range from 29 to 60% whereas the corresponding values for late treadmill testing range from 39 to 64% (Table 11). The low positive predictive value is most likely a consequence of incomplete revascularization: that is either a totally occluded vessel, or a significant stenosis at a site other than that dilated by angioplasty. It is also possible that the non-invasive test is accurately demonstrating a functionally inadequate dilatation, despite the appearance of success on angiography.

Table 12 shows the accuracy of thallium scintigraphy for detection of restenosis in series which have a resonable angiographic follow-up ranging from 55 to 100%. Since cardiac catheterization remains 'the gold standard' for detection of restenosis, the reported value of a non-invasive test is determined not only by the actual accuracy of the test but also by the completeness of angiographic follow-up.

In these studies with a high rate of angiographic follow-up the positive predictive value of thallium scintigraphy ranges between 56 and 89%. Recently Lefkowitz *et al.* have shown that the positive and negative predictive values for tomographic imaging in detection of restenosis were superior to the predictive values observed with planar imaging. In addition, the specific vascular territory was correctly localized to the PTCA territory in 77% of the tomographic studies[22].

Conclusion

Coronary angiography is still the most reliable method of judging the late result following angioplasty. It is therefore advisable for candidates for recertification who have undergone angioplasty to have a further angiogram 6 months after a PTCA procedure. Whether or not event-free survival after 6 months will be comparable with CABG and enable identification of a group in whom a 99% per annum survival or better is to be expected, remains to be seen. Single native vessel lesion angioplasty with a good 6 month angiographic appearance may be the only subgroup which will bear consideration in the context of certification to fly and even this group may require regular (i.e. 2–3 year) angiographic follow-up in view of the relatively poor negative predictive value of the exercise electrocardiogram. Even so, the concordance of a good treadmill walking time with no electrocardiographic changes after angioplasty for single vessel disease is year on year likely to be associated with a favourable outcome.

References

[1] Bourassa MG, Alderman EL, Bertrand M *et al.* Report of the joint ISFC/WHO Task Force on coronary angioplasty. Circulation 1988; 78: 780–9.

[2] Gruentzig AR, King SB, Schulmpf M, Siegenthaler W. Long term follow-up after percutaneous transluminal coronary angioplasty. The early Zurich experience. N Engl J Med 1987; 316: 1127–32.

[3] Detre K, Holubkov R, Kelsey S, *et al.* Percutaneous transluminal coronary angioplasty in 1985–1986 and 1977–1981. The National Heart, Lung and Blood Institute Registry. N Engl J Med 1988; 318: 265–70.

[4] Kamp O, Beatt KJ, Feyter PJ de, *et al.* Short, medium and long term follow-up after percutaneous transluminal coronary angioplasty for stable and unstable angina pectoris. Am Heart J 1989; 117: 991–6.

[5] Samson M, Meester HJ, Feyter PJ de, Strauss B, Serruys PW. Successful multiple segment coronary angioplasty: Effect of completeness of revascularisation in single-vessel multilesions and multivessels. Am. Heart J 1990; 120: 1–12.

[6] Bertrand ME, Marco J, Cherrier F, *et al.* French percutaneous transluminal coronary angioplasty (PTCA) registry: Four years experience. J Am Coll Cardiol 1986; 7: 21A.

[7] Gersh BJ, Robertson. The efficacy of percutaneous transluminal coronary angioplasty (PTCA) in coronary artery disease—why we need randomized trials. In: Topol EJ, ed. Textbook of interventional Cardiology. Philadelphia, London, Toronto, Montreal, Sydney, Tokyo: W. B. Saunders 1990; 240–54.

[8] Dorros G, Lewin RF, Mathiak LM *et al.* Percutaneous transluminal coronary angioplasty in patients with two or more previous coronary artery bypassing grafting operations. Am J Cardiol 1988; 61: 1243–7.

[9] Serruys PW, Strauss BH, Beatt KJ *et al.* Angiographic follow-up after placement of a self-expanding coronary artery stent. N Engl J Med 1991; 324: 13–7.

[10] Cleman MW, Cabin HS, Leon M *et al.* Major complications associated with intracoronary delivery with the Palmaz-schatz stent. J Am Coll Cardiol 1991; 17: 280A (Abstr).

[11] Van der Giessen WJ, Serruys PW, van Loon H *et al.* Balloon-expandable tantalum Wiktor stents: Initial results of implantation in autologous saphenous vein graft in pigs. Eur Heart J 1990; 11(Suppl A): 370.
[12] Bertrand M, Fourrier J, Buchbinder M *et al.* Abrupt closure following rotational ablation with the rotablator—short term clinical follow-up. J Am Coll Cardiol 1991; 17: 22A.
[13] Buchbinder M, Warth D, O'Neill Wm *et al.* Multi-center registry of percutaneous coronary rotational ablation using the Rotablator. J Am Coll Cardiol 1991; 17: 31A.
[14] Warth D, Buchbinder M, O'Neill Wm *et al.* Rotational ablation using the Rotablator for angiographically unfavorable lesions. J Am Coll Cardiol 1991; 17: 125A.
[15] Robertson GC, Simpson JB, Selmon MR *et al.* Coronary occlusions associated with directional coronary atherectomy. J Am Coll Cardiol 1991; 17: 219A.
[16] Leon MB, Pichard AD, Kramer BL *et al.* Efficacious and safe transluminal extraction atherectomy in patients with unfavorable coronary lesions. J Am Coll Cardiol 1991; 17: 219A.
[17] Topol E. Promises and pitfalls of new devices for coronary artery disease. Circulation 1991; 83: 689–94.
[18] Block PC. Percutaneous transluminal coronary angioplasty: role in the treatment of coronary artery disease. Circulation 1985; 72(Suppl V): 161–5.
[19] Kent KM, Bonow RO, Rosing DR *et al.* Improved myocardial function during exercise after successful percutaneous transluminal coronary angioplasty. N Engl J Med 1982; 306: 441–6.
[20] Joelson J, Most AS, Williams DO. Angiographic findings when chest pain recurs after successful percutaneous transluminal coronary angioplasty. Am J Cardiol 1987; 60: 792–5.
[21] Califf RM, Ohram EM, Frid DJ *et al.* Restenosis: the clinical issues. In: Topol EJ ed. Textbook of interventional cardiology. Philadelphia, London, Toronto, Montreal, Sydney, Tokyo: W. B. Saunders 1990; 363–94.
[22] Lefkowitz CA, Ross BL, Schwartz L *et al.* Superiority of tomographic thallium imaging for the detection of restenosis after percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1988; 13: 161A.