Influence of a history of smoking on short term (six month) clinical and angiographic outcome after successful coronary angioplasty

A G Violaris, A Thury, E Regar, R Melkert, P W Serruys

Abstract

Objectives—To assess the influence of smoking on restenosis after coronary angioplasty.

Design and patients—The incidence of smoking on restenosis was investigated in 2948 patients. They were prospectively enrolled in four major restenosis trials in which quantitative angiography was used before and immediately after successful angioplasty and again at six months.

Results—Within the study population there were 530 current smokers, 1690 ex-smokers, and 728 non-smokers. Smokers were more likely to be men (85.9% v 87.5% v 65.3%, current v ex-v non-, p < 0.001), to be younger (54.0 (9.0) v 57.0 (9.1) v 59.9 (9.4) years, p < 0.001), to have peripheral vascular disease (7.2% v 5.5% v 2.3%, p < 0.001), and have sustained a previous myocardial infarction (42.9% v 43.9% v 37.9%, p = 0.022), but were less likely to be diabetic (9.1% v 9.5% v 12.6%, p = 0.043) or hypertensive (24.9% v 29.3% v 37.2, p < 0.001). There was no significant difference in the categorical restenosis rate (> 50% diameter stenosis) at six months (35.28% v 35.33% v 37.09%, current v ex-v non-), or the absolute loss (0.29 (0.54) v 0.33 (0.52) v 0.35 (0.55) mm, respectively; p = 0.172).

Conclusions—Although smokers have a lower incidence of known predisposing risk factors for atherosclerosis, they require coronary intervention almost six years earlier than non-smokers and three years earlier than ex-smokers. Once they undergo successful coronary angioplasty, there appears to be no evidence that smoking influences their short term (six month) outcome, but because of the known long term effects of smoking, patients should still be encouraged to discontinue the habit.

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Keywords: coronary angioplasty; smoking; restenosis; quantitative angiography

Restenosis after successful coronary angioplasty remains a major limitation of the technique.1 2 Necropsy examination and recent intracoronary ultrasound studies suggest that it involves a combination of slow elastic recoil, vessel remodelling, thrombus incorporation, and late myointimal hyperplasia.2–4 Cigarette smoking can theoretically be involved in any of these mechanisms. Studies have shown that cigarette smoke can inhibit prostacyclin production by the vascular endothelial cells,5 impair endothelial function,6 activate platelets,7 reduce the baseline fibrinolytic activity in blood,8 thus enhancing platelet aggregation and thrombosis,9 all of which may be involved in the restenosis process. Cigarette smoke and its constituents can also cause acute coronary vasoconstriction,10 substantially altering local flow dynamics at the angioplasty site and causing increased platelet deposition and local thrombus formation,11 which further increases the possibilities of acute occlusion and long term restenosis. These theoretical considerations, and the large body of experimental and clinical evidence linking smoking habits with atherosclerosis, myocardial infarction, unstable angina, and sudden death,12 13 have led to several studies on the role of smoking on restenosis after successful coronary angioplasty.14–19 The results have been conflicting, however, with two studies suggesting a positive relation14 15 and others suggesting no relation16–19 between the two.

Discrepancies between studies have arisen for various reasons. First, most have been retrospective analyses using small numbers of patients and thus subject to type B error.12 Second, they have almost invariably used visual assessment of the angiogram which has been shown to have wide interobserver and intraobserver variability.20 Third, the angiographic follow up rate has been generally poor and follow up has usually been performed for recurrence of symptoms,14 16 thus introducing an important selection bias.

We attempted to overcome these limitations by using a validated automated edge detection technique in a large series of patients undergoing successful balloon angioplasty and routine follow up angiographic assessment at a pre-determined time interval. The aim of our study was to analyse the association between the information on smoking status available at the time of the procedure and the six month outcome.

Methods

Patients

The study population comprised 2948 patients with significant primary stenoses in native coronary arteries who were prospectively enrolled into four major restenosis trials: CARPORT (coronary artery restenosis prevention on
repeated thromboxane-antagonism study), PARK (post-angioplasty restenosis ketanserin trial), MERCATOR (multicentre European research trial with cilazapril after angioplasty to prevent transluminal coronary obstruction and restenosis), and MARCATOR (multicenter American research trial with cilazapril after angioplasty to prevent transmural coronary obstruction and restenosis). These showed that active treatment had no effect on restenosis or clinical outcome in the first six months after balloon angioplasty, so for the purposes of this study the data for the active and placebo groups were pooled. Patients were eligible for study entry if they were symptomatic or asymptomatic men, or women without child bearing potential, with stable or unstable angina pectoris, and proven angiographically significant narrowing in one or more major coronary arteries. Informed consent was obtained in all cases before the coronary angioplasty procedure. Patients with developing myocardial infarction and significant left main coronary artery disease were excluded from the study.

SMOKING HISTORY
A history of smoking was requested as part of the routine workup. Patients were asked if they had ever smoked and whether they were continuing to smoke, and their answers were recorded on the data sheet. Ex-smokers were defined as patients who had ever smoked regardless of the time when they stopped.

ANGIOPLASTY PROCEDURE AND FOLLOW UP
ANGIOGRAPHY
Coronary angioplasty was performed with a steerable, moveable guide wire system by the femoral route. Standard balloon catheters were used. The choice of balloon type and brand, as well as inflation pressure and duration, were left to the discretion of the operator. Patients were followed up for six months, at which time a follow up study was performed. If symptoms recurred within six months, coronary angiography was carried out earlier. If no definite restenosis was present and the follow up time was below four months, the patient was asked to undergo further coronary arteriography at six months.

Quantitative angiography
Three coronary angiograms in all were obtained for each patient: before percutaneous transluminal coronary angioplasty (PTCA), after PTCA, and at angiographic follow up. The angiograms were recorded in such a manner that they were suitable for quantitative analysis by the computer assisted coronary angiography analysis system (CAAS) which has been described and validated earlier.25 To standardise the method of data acquisition and to ensure exact reproducibility of the angiographic studies, measures were taken as previously described and all angiograms were processed in a central angiographic core laboratory.21–24 Because the computer algorithm is unable to measure total occlusions, a value of 0 mm was substituted for the minimum lumen diameter and a value of 100% for the per cent diameter stenosis before PTCA. In these cases the post-angioplasty reference diameter was substituted for vessel size.

Angiographic definitions used
- Vessel size refers to the reference diameter of the relevant coronary segment and is represented by the interpolated reference diameter pre-PTCA.
- Minimum luminal diameter (MLD) is the point of maximum luminal narrowing in the analysed segment.
- Restenosis was assessed using both a categorical and a continuous approach.26 27 For the categorical approach we used a cut off point of > 50% diameter stenosis at follow up. For the continuous approach we examined the absolute and relative loss, which may be a better reflection of the behaviour of the lesion during and after angioplasty, and therefore provide a better representation of the pathological process involved during follow up.26
- Acute gain and late loss represent the improvement in minimum luminal diameter achieved at intervention and the absolute change during follow up, respectively, measured in mm:
  
  \[
  \text{Acute gain} = \text{MLD post-PTCA} - \text{MLD pre-PTCA}
  \]
  
  \[
  \text{Late loss} = \text{MLD post-PTCA} - \text{MLD at follow up}
  \]
- Relative gain and relative loss depict the improvement in minimum luminal diameter achieved at intervention and the change during follow up respectively, normalised for vessel size:
  
  \[
  \text{Relative gain} = \frac{\text{MLD post-PTCA} - \text{MLD pre-PTCA}}{\text{vessel size}}
  \]
  
  \[
  \text{Relative loss} = \frac{\text{MLD post-PTCA} - \text{MLD at follow up}}{\text{vessel size}}
  \]
- The absolute net gain is the MLD at follow up − MLD pre-PTCA.
- The net gain index is the net gain normalised for the vessel size:
  
  \[
  \text{Net gain index} = \frac{\text{MLD at follow up} - \text{MLD pre-PTCA}}{\text{vessel size}}
  \]
- The loss index is the late loss expressed as a fraction of the acute gain (loss/gain).

STATISTICAL ANALYSIS
Data were analysed using the SAS statistical software package. All values are expressed as mean (SD). Differences in categorical variables were assessed using the \( \chi^2 \) test. Analysis of variance was used to assess differences in continuous variables between the three groups. Whenever the difference between two of the three subgroups was tested, Bonferroni correction was applied. Comparisons of ranked variables (clinical end points) were tested using the Kruskal–Wallis test. The difference in event-free survival time between the three groups was evaluated using the Kaplan–Meier method with the log rank and Wilcoxon tests. As multiple lesions within a given patient are not independent with respect to smoking, a patient based analysis was performed, using a single randomly selected lesion in patients with mul-

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Smoking and coronary restenosis

Table 1 Baseline clinical characteristics of current smokers, ex-smokers, and non-smokers

<table>
<thead>
<tr>
<th>Non-smokers</th>
<th>Ex-smokers</th>
<th>Current smokers</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>728</td>
<td>1690</td>
<td>530</td>
</tr>
<tr>
<td>Men</td>
<td>65.3%</td>
<td>87.5%*</td>
<td>85.9%*</td>
</tr>
<tr>
<td>Age (years) (mean (SD))</td>
<td>59.9 (9.4)</td>
<td>57.0 (9.1)*</td>
<td>54.0 (9.0)</td>
</tr>
<tr>
<td>Previous myocardial infarct</td>
<td>37.9%</td>
<td>43.9%*</td>
<td>42.9%*</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>3.6%</td>
<td>4.6%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>4.1%</td>
<td>5.1%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12.6%</td>
<td>9.5%*</td>
<td>9.1%*</td>
</tr>
<tr>
<td>IDDM</td>
<td>1.8%</td>
<td>0.7%*</td>
<td>0.4%*</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>37.2%</td>
<td>29.3%*</td>
<td>24.9%*</td>
</tr>
<tr>
<td>History of hypercholesterolaemia</td>
<td>32.0%</td>
<td>31.5%</td>
<td>31.9%</td>
</tr>
<tr>
<td>History of PVD</td>
<td>2.3%</td>
<td>5.5%*</td>
<td>7.2%*</td>
</tr>
<tr>
<td>Anginal class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6.3%</td>
<td>5.8%</td>
<td>4.3%</td>
</tr>
<tr>
<td>CCS class I</td>
<td>9.8%</td>
<td>11.7%</td>
<td>11.3%</td>
</tr>
<tr>
<td>CCS class II</td>
<td>34.6%</td>
<td>32.6%</td>
<td>29.4%</td>
</tr>
<tr>
<td>CCS class III</td>
<td>31.5%</td>
<td>29.9%</td>
<td>29.1%</td>
</tr>
<tr>
<td>CCS class IV</td>
<td>17.9%</td>
<td>20.2%</td>
<td>25.9%*</td>
</tr>
<tr>
<td>Duration of angina (weeks) (mean (SD))</td>
<td>120 (208)</td>
<td>111 (209)</td>
<td>94 (202)</td>
</tr>
<tr>
<td>Days since deterioration of angina (mean (SD))</td>
<td>80 (198)</td>
<td>79 (181)</td>
<td>65 (127)</td>
</tr>
<tr>
<td>Drug treatment at screening</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β Blockers</td>
<td>52.3%</td>
<td>49.2%</td>
<td>51.5%</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>65.4%</td>
<td>70.4%*</td>
<td>72.5%*</td>
</tr>
<tr>
<td>Nitrates</td>
<td>62.1%</td>
<td>66.7%</td>
<td>66.3%</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>0.8%</td>
<td>1.5%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Platelet inhibitor</td>
<td>64.3%</td>
<td>63.5%</td>
<td>67.7%</td>
</tr>
<tr>
<td>Aspirin</td>
<td>77.9%</td>
<td>83.4%*</td>
<td>83.1%*</td>
</tr>
<tr>
<td>Persantin</td>
<td>10.6%</td>
<td>11.6%</td>
<td>15.2%</td>
</tr>
<tr>
<td>Laboratory investigations (mean (SD))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>8.72 (0.86)</td>
<td>8.89 (0.80)</td>
<td>8.99 (0.86)*</td>
</tr>
<tr>
<td>Packed cell volume (%)</td>
<td>41 (4)</td>
<td>42 (4)</td>
<td>43 (4)</td>
</tr>
<tr>
<td>White cell count (G/l)</td>
<td>7.05 (2.94)</td>
<td>7.34 (2.09)</td>
<td>8.26 (2.24)*</td>
</tr>
<tr>
<td>Platelet count (G/l)</td>
<td>260 (80)</td>
<td>255 (66)</td>
<td>258 (70)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.88 (1.31)</td>
<td>5.80 (1.21)</td>
<td>5.88 (1.20)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.20 (0.34)</td>
<td>1.13 (0.56)</td>
<td>1.11 (0.69)</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>4.15 (1.18)</td>
<td>4.16 (1.33)</td>
<td>3.94 (1.20)</td>
</tr>
</tbody>
</table>

*p < 0.05 v non-smokers; †p < 0.05 v ex-smokers.
CABG, coronary artery bypass graft; HDL, high density lipoprotein; IDDM, insulin dependent diabetes mellitus; LDL, low density lipoproteins; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease.
urements were available, either before or after PTCA or at follow up, and who were therefore excluded from the study population. Of these patients 22.5% of the current smokers, 22.6% of the previous smokers, and 23.2% of the non-smokers had a clinical end point during follow up (redo PTCA, CABG, acute myocardial infarction, or death). The di

The individual components of worse clinical end point such as death, myocardial infarction, coronary artery bypass grafting, and re-PTCA were 7.14%, 2.04%, 6.12%, and 7.14%, respectively, for current smokers; 3.17%, 4.37%, 4.76%, and 10.32% for ex-smokers; and 0.89%, 3.57%, 7.14%, and 11.61% for non-smokers. The differences in the individual clinical end points between the three groups were not significant (p = 0.340).

QUANTITATIVE ANGIOGRAPHIC ANALYSIS AND CORONARY ANGIOPLASTY PROCEDURE
A mean of 2.12 matched angiographic projections per lesion had satisfactory quantitative analysis performed at the central angiographic core laboratory before and after PTCA and at follow up. The distribution of lesions was significantly different in the three groups, with non-smokers having more lesions in the left anterior descending coronary artery and less in the right coronary artery than smokers and ex-smokers. Non-smokers were also more likely to have visible collaterals on baseline angiography (table 2).

There were no significant differences in the baseline quantitative angiographic measurements between the three groups apart from a slightly higher minimum lumen diameter before PTCA in current smokers (borderline significance, table 3). Smokers, however, required a longer duration of inflation (current) and inflation pressure (both current and ex-smokers) for a successful angioplasty procedure (table 2). After PTCA all quantitative angiographic measurements and derived variables were similar for the three groups (table 3, fig 2), again confirming the similarity in acute angiographic outcome.

At the six month angiographic follow up there was no significant difference in angio-

Table 2 Baseline angiographic and procedural data on current smokers, ex-smokers, and non-smokers

<table>
<thead>
<tr>
<th></th>
<th>Non-smokers</th>
<th>Ex-smokers</th>
<th>Current smokers</th>
<th>Significance value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of diseased vessels</td>
<td></td>
<td></td>
<td></td>
<td>0.347</td>
</tr>
<tr>
<td>1-VD</td>
<td>65.0%</td>
<td>62.9%</td>
<td>66.0%</td>
<td></td>
</tr>
<tr>
<td>2-VD</td>
<td>26.4%</td>
<td>29.5%</td>
<td>26.7%</td>
<td></td>
</tr>
<tr>
<td>3-VD</td>
<td>7.8%</td>
<td>7.2%</td>
<td>7.6%</td>
<td></td>
</tr>
<tr>
<td>Lesion location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>50.6%*†</td>
<td>42.0%</td>
<td>41.1%</td>
<td>0.002</td>
</tr>
<tr>
<td>LCx</td>
<td>22.8%</td>
<td>24.7%</td>
<td>23.8%</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>26.5%*†</td>
<td>33.3%</td>
<td>34.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Lesion characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total occlusion pre-PTCA</td>
<td>7.8%</td>
<td>7.5%</td>
<td>7.0%*</td>
<td>0.852</td>
</tr>
<tr>
<td>Concentric</td>
<td>46.2%</td>
<td>43.8%</td>
<td>44.6%</td>
<td>0.606</td>
</tr>
<tr>
<td>Tandem lesion</td>
<td>3.8%</td>
<td>4.2%</td>
<td>3.1%</td>
<td>0.871</td>
</tr>
<tr>
<td>Multiple irregularities</td>
<td>8.3%</td>
<td>7.5%</td>
<td>8.4%</td>
<td>0.742</td>
</tr>
<tr>
<td>Branch point in stenosis</td>
<td>37.3%</td>
<td>32.2%</td>
<td>26.8%</td>
<td>0.054</td>
</tr>
<tr>
<td>Branch point in dilation site</td>
<td>65.4%</td>
<td>65.5%</td>
<td>61.8%</td>
<td>0.635</td>
</tr>
<tr>
<td>Coronary artery bend</td>
<td>19.9%</td>
<td>19.7%</td>
<td>18.3%</td>
<td>0.772</td>
</tr>
<tr>
<td>Calcified lesion</td>
<td>12.5%</td>
<td>12.8%</td>
<td>10.2%</td>
<td>0.275</td>
</tr>
<tr>
<td>Thrombus visible (pre-or post-PTCA)</td>
<td>5.4%</td>
<td>4.3%</td>
<td>6.0%</td>
<td>0.316</td>
</tr>
<tr>
<td>Degree of collateral supply</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No collaterals</td>
<td>78.5%*†</td>
<td>85.1%</td>
<td>87.7%</td>
<td>0.005</td>
</tr>
<tr>
<td>Slight (minimal perfusion)</td>
<td>5.9%*†</td>
<td>4.2%</td>
<td>3.1%</td>
<td>0.005</td>
</tr>
<tr>
<td>Medium (partial perfusion)</td>
<td>6.8%*†</td>
<td>4.4%</td>
<td>4.6%</td>
<td>0.005</td>
</tr>
<tr>
<td>Major (complete perfusion)</td>
<td>4.0%*†</td>
<td>3.7%</td>
<td>1.6%</td>
<td>0.005</td>
</tr>
<tr>
<td>Not assessed</td>
<td>4.8%*†</td>
<td>2.7%</td>
<td>2.9%</td>
<td>0.005</td>
</tr>
<tr>
<td>PTCA procedure data (mean (SD))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nominal size of largest balloon (mm)</td>
<td>2.87 (0.42)</td>
<td>2.89 (0.43)</td>
<td>2.87 (0.42)</td>
<td>0.342</td>
</tr>
<tr>
<td>Balloon to artery ratio</td>
<td>1.13 (0.18)</td>
<td>1.12 (0.18)</td>
<td>1.12 (0.19)</td>
<td>0.402</td>
</tr>
<tr>
<td>Total number of inflations</td>
<td>3.6 (2.0)</td>
<td>3.6 (2.2)</td>
<td>3.8 (2.4)</td>
<td>0.412</td>
</tr>
<tr>
<td>Total duration of inflation (s)</td>
<td>301 (267)</td>
<td>323 (264)</td>
<td>344 (288)*</td>
<td>0.021</td>
</tr>
<tr>
<td>Maximum inflation pressure (atm)</td>
<td>8.2 (2.5)</td>
<td>8.6 (2.5)*</td>
<td>8.7 (2.5)*</td>
<td>0.001</td>
</tr>
<tr>
<td>Pre-PTCA result</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissection at the dilated site</td>
<td>37.5%</td>
<td>34.2%</td>
<td>31.3%</td>
<td>0.069</td>
</tr>
<tr>
<td>Dissection type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type A</td>
<td>16.0%</td>
<td>14.9%</td>
<td>15.7%</td>
<td>0.255</td>
</tr>
<tr>
<td>Type B</td>
<td>16.7%</td>
<td>15.1%</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td>Type C</td>
<td>4.1%</td>
<td>3.7%</td>
<td>4.0%</td>
<td></td>
</tr>
<tr>
<td>Type D</td>
<td>0.2%</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Type E</td>
<td>0.2%</td>
<td>0.2%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Type F</td>
<td>0.2%</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Days to follow up (mean (SD))</td>
<td>161 (45)</td>
<td>162 (44)</td>
<td>163 (44)</td>
<td>0.553</td>
</tr>
</tbody>
</table>

*p < 0.05 v non-smokers; †p < 0.05 v current smokers.

1, 2, 3-VD, one vessel, two vessel, three vessel disease; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; PTCA, percutaneous transluminal coronary angioplasty; RCA, right coronary artery.
graphic outcome between the three groups (table 3, fig 2). The overall restenosis rate for the study population was 35.8% using the categorical approach (> 50% stenosis at follow up): current smokers 35.28%, ex-smokers 35.33%, non-smokers 37.09% (p = 0.687).

Additionally, the absolute and relative loss were also similar between current smokers, ex-smokers, and non-smokers: absolute loss, 0.29 (0.54) vs 0.33 (0.52) vs 0.35 (0.55) mm (p = 0.172); relative loss, 0.12 (0.22) vs 0.13 (0.21) vs 0.14 (0.22) (p = 0.083) (table 3, fig 3).

MULTIPLE LINEAR REGRESSION ANALYSIS
We have previously shown that vessel size, minimum lumen diameter before PTCA, absolute gain, and location of the left anterior descending coronary artery make a significant contribution to late angiographic outcome.28 Adding smoking to this model did not improve its predictive value. Least squares means for absolute loss were 0.348, 0.311, and 0.307 for non-smokers, ex-smokers, and current smokers, respectively. The p value of adding the variable “smoking” to the model was 0.15, which is not significant.

To determine whether the tendency towards improved clinical outcome in patients who

Table 3 Quantitative angiographic analyses of current smokers, ex-smokers, and non-smokers

<table>
<thead>
<tr>
<th></th>
<th>Non-smokers</th>
<th>Ex-smokers</th>
<th>Current smokers</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference diameter (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before angioplasty</td>
<td>2.60 (0.54)</td>
<td>2.65 (0.52)</td>
<td>2.64 (0.54)</td>
<td>0.116</td>
</tr>
<tr>
<td>After angioplasty</td>
<td>2.65 (0.52)</td>
<td>2.69 (0.50)</td>
<td>2.67 (0.51)</td>
<td>0.129</td>
</tr>
<tr>
<td>At follow up</td>
<td>2.67 (0.56)</td>
<td>2.71 (0.56)</td>
<td>2.71 (0.54)</td>
<td>0.200</td>
</tr>
<tr>
<td>Minimum lumen diameter (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before angioplasty</td>
<td>0.96 (0.40)</td>
<td>1.00 (0.40)</td>
<td>1.02 (0.38)*</td>
<td>0.046</td>
</tr>
<tr>
<td>After angioplasty</td>
<td>1.75 (0.37)</td>
<td>1.78 (0.36)</td>
<td>1.76 (0.34)</td>
<td>0.144</td>
</tr>
<tr>
<td>At follow up</td>
<td>1.40 (0.62)</td>
<td>1.44 (0.57)</td>
<td>1.46 (0.59)</td>
<td>0.096</td>
</tr>
<tr>
<td>Differences in minimum lumen diameter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute gain (mm)</td>
<td>0.78 (0.43)</td>
<td>0.78 (0.41)</td>
<td>0.74 (0.40)</td>
<td>0.128</td>
</tr>
<tr>
<td>Relative gain</td>
<td>0.31 (0.16)</td>
<td>0.30 (0.16)</td>
<td>0.29 (0.15)</td>
<td>0.074</td>
</tr>
<tr>
<td>Absolute loss (mm)</td>
<td>0.35 (0.55)</td>
<td>0.33 (0.52)</td>
<td>0.29 (0.54)</td>
<td>0.172</td>
</tr>
<tr>
<td>Relative loss</td>
<td>0.14 (0.22)</td>
<td>0.13 (0.21)</td>
<td>0.12 (0.22)</td>
<td>0.085</td>
</tr>
<tr>
<td>Absolute net gain</td>
<td>0.43 (0.61)</td>
<td>0.45 (0.56)</td>
<td>0.45 (0.61)</td>
<td>0.870</td>
</tr>
<tr>
<td>Net gain index</td>
<td>0.16 (0.25)</td>
<td>0.17 (0.22)</td>
<td>0.16 (0.24)</td>
<td>0.282</td>
</tr>
<tr>
<td>Loss index</td>
<td>0.41 (2.37)</td>
<td>0.60 (5.01)</td>
<td>0.49 (1.34)</td>
<td>0.545</td>
</tr>
<tr>
<td>Percentage stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before angioplasty</td>
<td>62.4 (14.4)</td>
<td>61.8 (14.3)</td>
<td>60.7 (14.0)</td>
<td>0.142</td>
</tr>
<tr>
<td>After angioplasty</td>
<td>33.6 (8.4)</td>
<td>33.6 (8.3)</td>
<td>33.7 (7.8)</td>
<td>0.919</td>
</tr>
<tr>
<td>At follow up</td>
<td>47.3 (20.3)</td>
<td>46.2 (18.9)</td>
<td>45.7 (19.1)</td>
<td>0.278</td>
</tr>
<tr>
<td>Diameter stenosis at follow up &gt; 50%</td>
<td>37.1%</td>
<td>35.3%</td>
<td>35.3%</td>
<td>0.687</td>
</tr>
</tbody>
</table>

Values are mean (SD) unless stated.
*p < 0.05 vs non-smokers.

Figure 2 (A) Cumulative distribution curve of minimum lumen diameter before and after PTCA and at follow up, for current smokers, ex-smokers, and non-smokers. (B) Cumulative distribution curve of percentage stenosis before and after PTCA and at follow up for current smokers, ex-smokers, and non-smokers.

Figure 3 (A) Cumulative distribution curve of absolute loss for current smokers, ex-smokers, and non-smokers. (B) Cumulative distribution curve of relative loss for current smokers, ex-smokers, and non-smokers.
smoke was related to differences in the under- 
lying baseline characteristics, we corrected for 
these variables to see whether smoking had any 
significant independent predictive value. We 
performed logistic regression with the above 
mentioned baseline characteristics as covari-
ates, resulting in a p value for the variable 
smoking of 0.122. This suggests that differ-
ences in clinical outcome were related to 
differences in baseline characteristics.

Discussion

Smoking is generally thought to have deleteri-
ous long term health effects, especially on the 
pulmonary and cardiovascular systems. How-
ever, the effect of smoking on the outcome of 
certain therapeutic procedures, such as coro-
ary angioplasty, is poorly understood. The aim 
of our study was to analyse whether the smok-
ing habit known at the time of the procedure 
affect the long term outcome.

Our results indicate that there are pro-
nounced differences in baseline clinical, angi-
ographic, and procedural characteristics be-
tween smokers and non-smokers undergoing 
coronary angioplasty. Smokers, despite having 
a lower incidence of known predisposing risk 
factors for atherosclerosis, require coronary 
intervention much earlier than non-smokers, 
but once they undergo successful coronary 
angioplasty their short term (six month) 
outcome is similar to non-smokers.

Two previous studies have suggested that 
smoking may be associated with an increased 
risk of restenosis.14 15 Both studies, however, 
were in small patient populations, with a low 
angiographic follow up rate, performed for 
recurrence of symptoms, and without quantita-
tive angiographic analysis. Using a large patient 
population with a high quantitative angiogra-
phic follow up rate at a predetermined six 
month time interval, our study has shown that 
smoking—a risk factor for atherosclerosis in 
general—is not a significant risk factor for res-
stenosis.

There are several possible reasons for this. 
First, although cigarette smoking has been 
shown to be a risk factor for atherosclerosis, 
this is over the course of years,12 13 whereas 
careful serial quantitative angiographic studies 
have shown that restenosis occurs in the first 
three to six months after intervention.1 Thus 
cigarette smoking may have little influence on 
the process over this short time frame. Second, 
the mechanisms of restenosis are still incom-
pletely understood and are likely to involve dif-
fering contributions of slow elastic recoil, 
thrombus incorporation, vessel remodelling, 
and myointimal hyperplasia in each individual 
patient.2–4 Cigarette smoking is unlikely to 
influence all of these mechanisms. Third, it is 
possible that the sudden withdrawal of ciga-
rettes during and immediately after the proce-
dure in the smokers may have had some 
favourable effect on vascular or haemato-
logical systems29 which discouraged local platelet 
deposition, mural thrombus formation, and 
consequent restenosis. Fourth, there may be 
substantive differences in plaque characteris-
tics between smokers and non-smokers, which 
could ameliorate any thrombogenicity associ-
ated with smoking. In support of this are the 
higher inflation pressures and duration of infla-
tion required for successful dilatation of the 
atherosclerotic plaque in the smoking group, 
and also the published reports suggest-
ing that lesions in smokers have a higher 
content of collagen30 and that the type of lesion 
that precipitates myocardial infarction in 
smokers is less severe and possibly generated 
by a different mechanism.29 31

DIFFERENCES IN BASELINE CHARACTERISTICS

There were significant differences in the 
baseline clinical, angiographic, and procedural 
characteristics between the smoking classes 
which could have been responsible for, or asso-
ciated with, the outcome of the procedure. 
Smokers were younger, more likely to be male, 
to have peripheral vascular disease, and to have 
had a previous myocardial infarct. Conversely, 
they were less likely to have diabetes mellitus 
or a history of hypertension. These differences in 
baseline characteristics may be related to age. 
For example, as smokers tend to develop 
atherosclerosis at a younger age, they would be 
less likely to develop diseases of the older age 
group such as hypertension and diabetes. 
Many epidemiological studies have, however, 
also reported that smokers have significantly 
lower blood pressures than ex-smokers or 
non-smokers,32 but the mechanism for this 
negative relation is unknown. These differences 
in baseline clinical characteristics may have 
influenced clinical and angiographic outcome 
in various ways. For example, diabetic patients 
are more likely to have restenosis than non-diabetes,33 35 while dilatation of a vessel 
supplying previously infarcted territory is more 
likely to result in occlusion at the time of follow 
up angiography.

There were also significant differences in 
baseline haematological characteristics, with 
smokers having a higher haemoglobin, packed 
cell volume, and white cell count than 
non-smokers, and ex-smokers somewhere in 
between. There is evidence that smokers are 
also more likely to have a higher fibrinogen 
concentration and increased blood viscosity.34 
What influence these variables may have on the 
clinical and angiographic outcome after inter-
vention is unclear. Although increased fibrino-
gen concentrations have not been associated 
with a higher restenosis rate in a small series,35 
raised white cell counts36 are known to be 
strong predictors of myocardial infarction37 and 
to be a marker of important cellular injury.

There were also differences in the distribu-
tion of lesions, with smokers having more 
lesions in the right coronary artery and fewer in 
the left anterior descending artery than non-
smokers, ex-smokers being somewhere in 
between. This is in keeping with other 
published reports suggesting a more proximal 
location of coronary lesions in hypercholes-
terolaemic non-smokers, and more distally 
situated lesions in normocholesterolaeic 
smokers.36 The lower incidence of left anterior 
descending coronary artery lesions, with their 
known higher incidence of restenosis,28 may be
Smoking and coronary restenosis

A further possibility is that our study may have been underpowered to detect a small enough difference between the groups. Given the number of patients and the results in the non-smoker group, our study has a power of 90% to detect a difference of 20% in the smoking group for the categorical restenosis rate, and 0.10 mm for the absolute loss. We would consider both of these to be clinically significant, but the fact remains that if the effect of smoking were below these levels we would have been unable to detect it.

We also do not have information on changes in smoking habits during the follow up period and their possible effect on outcome. However, subanalysis of the 1048 patients (taking part in the CARPORT and PARK studies), whose smoking status was ascertained at the one and six month follow up visit, revealed that 64 of the 166 current smokers (38.55%) stopped smoking by the time of the six month follow up visit. Of these, 18 had a clinical end point compared with 25 who continued to smoke. However, the numbers in this subanalysis are too small to allow a meaningful comparison.

Ideally, future studies should include observation of the changes in smoking habits over time as well as intravascular ultrasound assessment of the acute results of intervention and the mechanism of subsequent restenosis; by differentiating between slow recoil, thrombus formation/incorporation, and intimal hyperplasia this would make it easier to show benefit from cessation of smoking.

CONCLUSIONS

Our results indicate that smokers, despite having a lower incidence of known predisposing risk factors for atherosclerosis, require coronary intervention almost six years earlier than non-smokers and three years earlier than ex-smokers. This is on a background of increased risk of previous myocardial infarction and peripheral vascular disease. According to our results, however, there appears to be no evidence that smoking at the time of the procedure affects the six month outcome. Therefore, smoking should not of its own be a contraindication for coronary angioplasty.

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Influence of a history of smoking on short term (six month) clinical and angiographic outcome after successful coronary angioplasty

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