Attenuated physical exercise capacity in smokers compared with non-smokers after coronary angioplasty despite similar luminal diameters

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Aims To study the impact of smoking on the change in exercise capacity in patients treated with coronary angioplasty.

Methods Three hundred and sixty-eight men below 70 years of age eligible for percutaneous transluminal coronary angioplasty without previous coronary interventions were consecutively enrolled. Of the 334 patients (90·8%) who completed the study 77 (23·1%) were current smokers. Exercise tests were performed before percutaneous transluminal coronary angioplasty, 2 and 19 ± 2·4 weeks after percutaneous transluminal coronary angioplasty. Coronary angiography was done in 333 patients (99·7%) (at mean 19 ± 2·4 weeks). The angiograms were analysed quantitatively.

Results There were no differences in the clinical and angiographic characteristics among the groups except for age. The non-smokers were older than the smokers (55·7 vs 52·4 years (P=0·001)). Exercise capacity was equal before percutaneous transluminal coronary angioplasty in both groups (17·6 vs 16·5 W × min⁻¹ × kg⁻¹). Non-smokers had a significantly higher increase in exercise capacity than smokers from baseline to 2 weeks after percutaneous transluminal coronary angioplasty (mean difference 4·3 W × min⁻¹ × kg⁻¹ (95%CI: 2·3 to 6·2; P<0·001)), and from baseline to 19 weeks after percutaneous transluminal coronary angioplasty (mean difference 3·9 W × min⁻¹ × kg⁻¹ (95%CI: 1·6 to 6·2; P<0·001)).

Conclusion A clinical benefit from percutaneous transluminal coronary angioplasty was seen in both groups as judged from exercise testing. Smokers had a substantially lower increase in exercise capacity than non-smokers, indicating an attenuated benefit from percutaneous transluminal coronary angioplasty among smokers.

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Key Words: Angioplasty, smoking, exercise testing, exercise capacity, coronary artery disease.

Introduction

The goals of coronary angioplasty treatment are relief or reduction of angina pectoris or myocardial ischaemia and an increase in exercise capacity. Clinical improvement after percutaneous transluminal coronary angioplasty can be measured by exercise testing[1–4]. In patients with coronary disease a high exercise capacity signals a lifestyle with minimal physical restrictions. A low exercise capacity is associated with increased cardiovascular mortality[5]. Cigarette smoking is associated with low exercise capacity[6,7]. A decline in exercise capacity with increasing age has been shown to be greater among smokers than non-smokers[8]. This study aims at examining the impact of cigarette smoking on exercise capacity and thereby exercise capacity after percutaneous transluminal coronary angioplasty.

Subjects and methods

From April 1992 to June 1996, patients who participated in a medical intervention trial, the Coronary Angioplasty Amlodipine Restenosis Study (CAPARES), investigating the effect of amiodipine on restenosis[9], were followed with exercise testing. The inclusion criteria were stable angina pectoris, age below 70 years, no previous coronary intervention, and coronary artery stenosis suitable for percutaneous transluminal coronary angioplasty. A total of 368 consecutive male patients were studied, and 34 patients were excluded (angioplasty not performed, unsuccessful angioplasty or the patients denied the second follow-up). The final study population consisted of 334 patients, 77 (23·1%) were current smokers. Smoking habits were recorded on the basis of a
personal interview. All non-smokers were labelled as such regardless of previous smoking habits. After inclusion all patients had a general clinical examination and performed an exercise test 2 weeks prior to percutaneous transluminal coronary angioplasty. The first follow-up exercise test was performed 2 weeks after percutaneous transluminal coronary angioplasty, and the second on average 19 weeks after angioplasty. Amlodipine treatment did not affect the results. Beta-blockers were continued throughout the study to avoid influence on exercise test performance by withdrawal. The study was carried out in accordance with the declaration of Helsinki, and by approval of the local ethical committee.

Exercise test

The exercise tests were performed in the upright position, on an electrically braked ergometer bicycle (Ergoline 900) throughout the study. The ergometer bicycle was controlled by a computer (Siemens MegaCart® Siemens-Elema AB, Electrocardiography Division Solna, Sweden) with regard to workload in watts and stage due to the pre-programmed protocol. The starting load was 50 watts (2·94 kJ . min\(^{-1}\)) with regard to workload in watts and stage due to the pre-programmed protocol. The exercise test was stopped earlier if one of the following events occurred: increasing angina, severe dyspnoea, sudden dizziness, headache or nausea, more than three couplet ventricular beats, atrial fibrillation or flutter, a drop in systolic blood pressure more than 20 mmHg or a rise in systolic blood pressure above 300 mmHg. Exercise capacity was defined as the cumulated work (workload in watts times duration of exercise in minutes), divided by the individual weight in kilograms[9].

Coronary angioplasty and angiographic analysis

Angioplasty was performed according to standard clinical practice by the femoral approach. Intracoronary stents were implanted in 52 patients. Successful angioplasty was defined as an angiographically satisfactory post-percutaneous transluminal coronary angioplasty result, as judged by the operator, and without clinical complications (myocardial infarction or need for an urgent re-percutaneous transluminal coronary angioplasty or bypass surgery during the hospital stay). Complete revascularization was defined as a patient with a successful angioplasty and no diameter stenosis ≥50% at the major coronary arteries not treated with percutaneous transluminal coronary angioplasty.

Identical angiographic views were taken immediately before and after percutaneous transluminal coronary angioplasty, and at follow-up. All angiograms were analysed by Cardiovascular Angiography Analysis System (CAAS II) (Pie Medical Imaging, Maastricht, Netherlands). Quantitative analysis was carried out as described by Serruys and co-workers[10].

Statistical analysis

Continuous variables are expressed as means ± SD. Differences between means are tested with a two-tailed Student’s t-test, with an alpha level of 0·05. Ninety-five percent confidence intervals are given. Discrete variables are expressed as numbers and percentages. The chi-square test was used to compare proportions. Multivariate linear regression analysis was done to evaluate the association between smoking, age, previous myocardial infarction, diabetes, hypertension, total cholesterol, implantation of a stent and complete revascularization on the change in exercise capacity from before to after percutaneous transluminal coronary angioplasty.

Results

Of the 368 patients who performed an exercise test before percutaneous transluminal coronary angioplasty, 334 (90·7%) performed the first and second follow-up exercise test. Table 1 shows the baseline clinical and angiographic characteristics for both groups. The smokers were significantly younger than the non-smokers (mean difference 3·3 years; 95%CI: 1·4 to 5·9). There were no significant differences between the two groups, as regards the other variables.

Exercise test

The duration of exercise and exercise capacity at baseline, and at the first and second follow-up investigations, are shown in Table 2. At baseline, there were no differences between the groups. The non-smokers had a 30·2% increase in exercise duration from baseline to the first follow-up, and a 24·8% increase from baseline to the second follow-up vs 18·6% and 15·2% for the smokers, respectively. The non-smokers had a 50·3% increase in exercise capacity from baseline to the first follow-up, and a 43·4% increase from baseline to the second follow-up vs 27·3% and 21·8% for the smokers, respectively. (Fig. 1). The smokers had a 48·8% lower increase in exercise capacity from baseline to the first follow-up, and a 43·4% increase from baseline to the second follow-up, vs 27·3% and 21·8% for the smokers, respectively. (Fig. 1). The smokers had a 48·8% lower increase in exercise capacity from baseline to the first follow-up and a 53·3% lower increase in exercise capacity from baseline to the second follow-up investigation compared with the non-smokers. From the multivariate regression analysis, smoking was significantly and negatively associated with increase in exercise capacity (coefficient: -3·86; \(P=0·0007\)).

Quantitative coronary analysis

Quantitative coronary analysis (Table 3) revealed no significant differences in minimal luminal diameters and
reference diameters pre- and post-PTCA and at follow-up between the two groups.

**Table 1** Baseline clinical and angiographic characteristics of non-smokers and smokers. Values are means ± SD and numbers (percentages)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-smokers (n=257)</th>
<th>Smokers (n=77)</th>
<th>Mean difference</th>
<th>95% CI of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55·6 ± 8·2</td>
<td>52·2 ± 7·7*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>82·3 ± 10</td>
<td>83·5 ± 13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg . m⁻²)</td>
<td>26·0 ± 2·9</td>
<td>26·4 ± 3·4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (percent)</td>
<td>73·1 ± 11·1</td>
<td>74·1 ± 8·8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>11 (4·3)</td>
<td>4 (5·2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>107 (41·6)</td>
<td>34 (44·2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>55 (21·4)</td>
<td>21 (27·3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol . l⁻¹)</td>
<td>5·59 ± 1·02</td>
<td>5·74 ± 1·01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of angina (month)</td>
<td>27·3 ± 42·8</td>
<td>24·6 ± 43·9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Angina status (CCS)†

- I: 42 (16·9) vs 15 (21·1)
- II: 133 (53·4) vs 31 (43·7)
- III–IV: 74 (29·7) vs 25 (35·2)

Medication
- Beta-blocker: 235 (91·4) vs 71 (91·9)
- Calcium channel antagonist: 129 (50·2) vs 43 (55·8)

Number of vessels diseased
- One vessel: 145 (56·4) vs 48 (62·3)
- Two vessels: 94 (36·6) vs 27 (35·1)
- Three vessels: 18 (7·0) vs 2 (2·6)

Artery dilated
- Left anterior descending: 170 (66·1) vs 49 (63·6)
- Left circumflex: 99 (38·5) vs 26 (33·8)
- Right coronary artery: 116 (45·1) vs 33 (42·9)
- Complete revascularization: 156 (61·7) vs 49 (63·6)
- Stents implanted: 36 (14·0) vs 13 (17·1)

*P<0·05
†According to the Canadian Cardiovascular Society (CCS) classification system.

**Table 2** Exercise duration and exercise capacity in non-smokers and smokers at baseline, first and second follow-up. Values are means ± SD

<table>
<thead>
<tr>
<th>Exercise duration (min)</th>
<th>Non-smokers (n=257)</th>
<th>Smokers (n=77)</th>
<th>Mean difference</th>
<th>95% CI of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline exercise test</td>
<td>14·9 ± 4·9</td>
<td>14·5 ± 5·1</td>
<td>0·4</td>
<td>−0·8 to 1·7</td>
</tr>
<tr>
<td>Follow-up exercise test 1</td>
<td>19·3 ± 4·4</td>
<td>17·2 ± 4·3**</td>
<td>2·1</td>
<td>1·0 to 3·2</td>
</tr>
<tr>
<td>Follow-up exercise test 2</td>
<td>18·5 ± 5·7</td>
<td>16·6 ± 4·9*</td>
<td>1·9</td>
<td>0·5 to 3·3</td>
</tr>
<tr>
<td>Exercise capacity (W · min⁻¹ · kg⁻¹)</td>
<td>17·6 ± 9·9</td>
<td>16·6 ± 8·5</td>
<td>1·0</td>
<td>−1·4 to 3·5</td>
</tr>
<tr>
<td>Follow-up exercise test 1</td>
<td>26·2 ± 10·5</td>
<td>21·0 ± 7·8**</td>
<td>5·2</td>
<td>2·6 to 7·8</td>
</tr>
<tr>
<td>Follow-up exercise test 2</td>
<td>25·1 ± 12·3</td>
<td>20·1 ± 8·7*</td>
<td>5·0</td>
<td>2·0 to 7·9</td>
</tr>
</tbody>
</table>

*P<0·01; **P<0·001 non-smokers compared with smokers.

Discussion

These data show that both smokers and non-smokers had a significant increase in exercise capacity from before to after percutaneous transluminal coronary angioplasty, in agreement with other studies. In the ACME trial, 99 patients underwent exercise testing before and after percutaneous transluminal coronary angioplasty and showed a 24% increase in exercise duration after 6 months; of these, 29% were smokers\(^{[11]}\).

A 23% increase one month after percutaneous transluminal coronary angioplasty and a 27% increase after 6 months was found in the RITA trial\(^{[12]}\). Ernst et al. reported a 34% increase in exercise workload early after percutaneous transluminal coronary angioplasty and a 30% increase late after this intervention\(^{[13]}\).

There was a slight decrease in exercise duration and exercise capacity for both groups from the first to the second follow-up. This reduction may reflect the natural course of the coronary artery narrowing after...
percutaneous transluminal coronary angioplasty treatment in that approximately one third of dilated lesions are prone to restenosis within 4 months\(^{[14,15]}\). This study showed that smokers had a substantially lower increase in exercise capacity compared with non-smokers, thereby attenuating the advantage of the percutaneous transluminal coronary angioplasty treatment. Smokers were younger than non-smokers. Regression analysis revealed that older age was associated with lower exercise capacity and shorter exercise duration. This is in agreement with Leon et al. who studied 175 men, in whom cigarette smoking was also an independent predictor of shorter exercise duration\(^{[7]}\). The fact that the smokers were younger than the non-smokers in our study implies that if the age in both groups was equal, the differences in exercise duration and exercise capacity should be even greater.

The reason for the lower increase in exercise capacity in smokers may be multifactorial. It has been shown that during exercise smokers have a smaller increase in heart rate and achieve a lower maximal heart rate compared with non-smokers\(^{[6,16,17]}\). Furthermore, smoking considerably accelerates the sequential decline in lung function\(^{[18]}\). Smoking is associated with impairment of pulmonary oxygen exchange, that may explain a reduced maximum oxygen consumption\(^{[19]}\). In a 7 year follow-up of 1393 healthy middle aged men, it was found that a decline in exercise capacity and lung function (measured as forced expiratory volume in one second) was considerably greater among smokers than non-smokers\(^{[9]}\). Impairment of oxygen transport may be another possible factor. Smokers have been shown to have elevated carboxyhaemoglobin levels compared with non-smokers, and evidence supports impaired endothelial control of vascular tone in smokers\(^{[20,21]}\).

The low exercise capacity seen in both groups before angioplasty is due to the significant stenoses in the major coronary arteries reducing the myocardial blood supply. The extent of coronary disease in the major coronary arteries was the same for both groups. After dilatation of these stenoses, both groups achieved the same increments in luminal diameters, but smokers had a substantially attenuated increase in exercise capacity compared with non-smokers. This attenuation may be explained by a more disseminated progression of the atherosclerotic disease into the coronary microvascular bed, combined with impairment of cardiac, endothelial and lung functions. The fact that this study does not account for the presence of previous smoking in the non-smoker group, suggest that the toxicity of ongoing cigarette smoking affects exercise capacity. Several studies have addressed the importance of low exercise

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\begin{array}{c|c|c}
\text{Reference diameter (mm)} & \text{Non-smokers} & \text{Smokers} \\
\text{Before angioplasty} & 2.68 \pm 0.57 & 2.63 \pm 0.45 \\
\text{After angioplasty} & 2.74 \pm 0.51 & 2.69 \pm 0.44 \\
\text{At follow-up} & 2.65 \pm 0.50 & 2.58 \pm 0.44 \\
\text{Obstruction diameter (mm)} & \text{Before angioplasty} & 0.95 \pm 0.38 & 1.00 \pm 0.32 \\
\text{After angioplasty} & 1.90 \pm 0.43 & 1.84 \pm 0.42 \\
\text{At follow-up} & 1.60 \pm 0.53 & 1.65 \pm 0.48 \\
\text{Percentage stenosis (%)} & \text{Before angioplasty} & 64.3 \pm 12.5 & 61.5 \pm 11.7 \\
\text{After angioplasty} & 30.4 \pm 10.0 & 31.2 \pm 10.3 \\
\text{At follow-up} & 39.9 \pm 14.7 & 35.8 \pm 16.2 \\
\end{array}
\]

capacity assessed by exercise testing as an independent predictor of cardiovascular mortality[22].

Our findings show a reduced improvement in exercise capacity in smokers compared with non-smokers after angioplasty, and this may be included in the total evaluation when considering benefits and risks in patients referred for percutaneous transluminal coronary angioplasty.

References