Nonischemic Chest Pain Induced by Coronary Interventions
A Prospective Study Comparing Coronary Angioplasty and Stent Implantation
Allen Jeremias, MD; Sven Kutscher, MD; Michael Haude, MD; Dagmar Heinen; Gerald Holtmann, MD; Wolfgang Senf, MD; Raimund Erbel, MD

Background—Chest pain frequently occurs without any signs of ischemia within the first 24 hours after coronary interventions. To test the hypothesis that this pain may be due to local vessel injury (“stretch pain”), we performed a prospective study enrolling patients after PTCA, stent implantation, or diagnostic coronary angiography alone.

Methods and Results—A total of 145 patients after coronary angiography were evaluated by a validated questionnaire for quantifying postinterventional chest pain within 24 hours. To detect myocardial ischemia, all patients were evaluated with a 12-lead ECG and cardiac isoenzymes immediately after the procedure and the morning after. After stent implantation, 21 of the 51 patients (41.2%) developed chest pain, compared with 4 of the 33 patients (12.1%) undergoing PTCA and 6 of the 61 patients (9.8%) with a diagnostic angiography (P<0.001). Of these 31 patients who developed chest pain, only 3 (9.7%) felt that the pain was similar to previously experienced angina pectoris. The minimal lumen diameter after intervention was significantly larger in the stent group than in the PTCA group (3.14±0.75 versus 1.95±0.67 mm; P<0.001). No patient had changes in the ECG compared with before intervention, but 3 patients after stent implantation had a rise in cardiac isoenzymes. No other major adverse cardiac events occurred until discharge.

Conclusions—Nonischemic chest pain develops in almost half of all patients undergoing stent implantation and seems to be related to vessel overexpansion caused by the stent in the diseased vessel segment. (Circulation. 1998;98:2656-2658.)

Key Words: coronary disease ■ angina ■ angioplasty ■ stents

Various studies have focused on recurrent chest pain after PTCA1 that may be due to abrupt vessel closure2 or coronary artery vasoconstriction3 or may simply represent a focal trauma to the coronary artery (“stretch pain”). It is critical to distinguish between these entities, because the former needs urgent repeat coronary angiography, whereas the latter represents a benign condition without the need for intervention. In recent years, various new devices have been introduced in addition to balloon angioplasty. Coronary stenting, in particular, is routinely used, with >500,000 coronary stent procedures this year alone. In a retrospective study reviewing 410 patients after stenting, chest pain occurred in 23% of all patients, of whom 31% underwent a repeat coronary angiography.4 The majority of patients who experienced chest pain, however, did not have any kind of complication related to the procedure. On the basis of this evidence and of our observation that patients undergoing stent implantation frequently complain of chest pain without any signs of ischemia, we performed a prospective trial evaluating the frequency of nonischemic postprocedural chest pain in patients after stent implantation compared with patients undergoing PTCA or diagnostic coronary angiography.

Methods

Patient Selection and Study Design
From March 1997 until August 1997, all patients undergoing elective stent implantation (group A) or PTCA (group B) of a single lesion of a native coronary artery, as well as patients undergoing a diagnostic coronary angiography (group C), were included in the trial, except for patients with interventions to multiple target lesions or simultaneous PTCA and stent implantation and patients after heart transplantation. One investigator, blinded to the treatment assignment, questioned all patients included in the trial within 24 hours after the procedure. Patients who experienced chest pain were followed daily until the pain resolved to determine its duration. For assessment of postprocedural chest pain, the Seattle Angina Questionnaire (SAQ) and a rating scale for quantification of chest pain were used. To detect myocardial ischemia, an ECG was performed immediately after the procedure and the morning after, and serial measurements of creatine kinase (CK) were made. Major adverse cardiac events were recorded during the entire hospital course. Informed consent was obtained from all patients.
TABLE 1. Demographic and Clinical Data for Each Patient Group

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>59.8±9.4</td>
<td>60.8±10.6</td>
<td>57.5±10.7</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>42/9</td>
<td>27/6</td>
<td>45/16</td>
<td>NS</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>24 (47.1%)</td>
<td>18 (54.5%)</td>
<td>23 (37.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>AP class (CCS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCS I</td>
<td>13 (25.5%)</td>
<td>15 (45.5%)</td>
<td>17 (27.9%)</td>
<td>NS</td>
</tr>
<tr>
<td>CCS II</td>
<td>11 (21.6%)</td>
<td>5 (15.2%)</td>
<td>20 (32.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>CCS III</td>
<td>21 (41.2%)</td>
<td>8 (24.2%)</td>
<td>18 (29.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>CCS IV</td>
<td>6 (11.7%)</td>
<td>5 (15.2%)</td>
<td>6 (9.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>34 (66.6%)</td>
<td>24 (72.7%)</td>
<td>40 (65.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>32 (62.7%)</td>
<td>19 (57.6%)</td>
<td>32 (52.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>18 (35.3%)</td>
<td>13 (39.4%)</td>
<td>15 (24.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (7.8%)</td>
<td>4 (12.1%)</td>
<td>4 (6.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Target vessel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>11 (21.6%)</td>
<td>10 (30.3%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>LCx</td>
<td>22 (43.1%)</td>
<td>11 (33.3%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>18 (35.3%)</td>
<td>12 (36.4%)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Group A received stents (n=51); B, PTCA (n=33); and C, angiography (n=61). CCS indicates Canadian Cardiovascular Society; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; and RCA, right coronary artery. Values are mean±SD for age and n (%) for other parameters.

Design of the SAQ
The SAQ is a disease-specific, functional-status measure to quantify the physical and emotional effects of coronary artery disease. It is a 19-item questionnaire resulting in 5 scales that measure clinically important dimensions of coronary artery disease. The SAQ has been extensively validated and has been shown to correlate with other measures of diagnosis and patient function.

Catheterization Procedure and Quantitative Coronary Angiography
Siemens HICOR biplane catheterization equipment was used for coronary angiography. All angiographic cine films were analyzed off-line on the Cardiovascular Measurement System. For calibration, the inner contours of the contrast-filled catheter were used. Automatic edge detection based on the first and second derivatives of the x-ray equipment were the same before and after the procedure.

Statistical Analysis
All data are reported as mean±SD or frequencies. Group means of ratio scale variables of the groups were compared by ANOVA and Yates’s corrected χ² analysis. Data not normally distributed between two different patient populations were compared by the Mann-Whitney rank sum test. A value of P<0.05 was considered statistically significant.

Results
Angiographic and Procedural Characteristics
A total of 145 patients were divided into 3 groups according to treatment regimen: group A consisted of 51 patients with stent implantation, group B of 33 patients with PTCA, and group C of 61 patients with diagnostic coronary angiography. Baseline characteristics and quantitative angiographic data are shown in Tables 1 and 2.

Evaluation of Chest Pain
The mean time of questioning was 12.97±8.4 hours. Chest pain was reported by 21 patients in group A (41.2%), 4 patients in group B (12.1%), and 6 patients in group C (9.8%; P<0.001; Figure 1). Chest pain lasted for a mean time of 23.29±24.29 hours after the procedure. Among all reported cases of chest pain, only 3 patients stated that the pain was similar to angina pectoris. All patients in groups B and C had mild to moderate pain (scores 2 to 5 on a scale from 1 to 10 [1=mild; 10=extreme]), whereas 19% of the patients in group A experienced severe chest pain (scores ≥6). The majority of the patients (76.2%) described the pain as continuous, squeezing pain located deep in the chest. Functional measurements of physical limitation, anginal stability, and frequency before angiography were comparable in all groups.

Chest Pain Related to Ischemia
CK elevation occurred in 3 patients after stent implantation, of whom 2 had chest pain. No ECG changes were detected, and no patient underwent urgent repeat coronary angiography.

Discussion
This is the first study to focus on local vessel injury (stretch pain) induced by stent implantation as a possible cause of chest pain after coronary intervention. The main findings include:

- Development of postprocedural chest pain according to treatment group:
  - Group A: 21.2% (n=51)
  - Group B: 12.1% (n=33)
  - Group C: 9.8% (n=61)
  - P<0.001

Shaded bar denotes percentage of patients with pain similar to previously experienced angina pectoris.
demonstrate that chest pain after intervention is common and occurs significantly more often after stent implantation than after PTCA or coronary angiography alone. This may be a result of the larger minimal lumen diameter achieved after stent implantation and the consecutively higher degree of circumferential stretching as the elastic recoil is minimized.

Multiple studies have analyzed the frequency of ischemic chest pain after coronary interventional procedures. As previously shown by Mansour et al., chest pain after atherectomy and after coronary stenting occurred in 23% of patients, but only a minority of those patients had an ischemic event. The authors concluded that chest pain after coronary procedures may simply reflect local coronary artery trauma. In our subgroup of patients who underwent stent implantation, chest pain after the procedure was found significantly more often (41%) than after PTCA (12%). Therefore, we believe that the pain is not so much due to local trauma as it is associated with a continuous stretch of the treated vessel segment, because stents are shown to prevent the early recoil that usually occurs after PTCA and leads to resolution of the overexpansion.

Chest pain may derive from sensory nerves located in the adventitia. The use of an antiserum to the general neuronal marker protein gene revealed that the proximal part of epicardial arteries possessed a supply of nerve fibers that formed a loose network in the adventitia. In a recent study, Sharf et al. demonstrated a significant change in spectral line shapes for coronary arteries exposed to longitudinal strain. The effect of the elongation of the spectra was assigned to the adventitia, whereas spectral line shapes that originated from the intima and media were almost insensitive to strain. Therefore, continuous stretch to the adventitia may lead to a local injury, resulting in chest pain.

Peripheral embolization by plaque material or thrombus may occur after PTCA and stent implantation and lead to CK elevation. In fact, non-Q-wave myocardial infarctions are reported in 8% to 15% of patients undergoing PTCA. In the present study, however, a rise in CK after the procedure occurred in only 3 patients and can therefore be ruled out as a source of chest pain in the majority of the patients. Another possible cause of chest pain is coronary vasoconstriction. The acute trauma caused on the atherosclerotic arterial wall by balloon inflation is thought to trigger complex vascular reactions. Fischell et al. demonstrated that coronary artery vasoconstriction follows PTCA. If vasoconstriction had caused the symptoms in our patients, the incidence of chest pain should be similar after stenting and PTCA. Therefore, we suggest that the continuous overexpansion of the vessel wall caused by the stent is responsible for the symptoms.

Chest pain after coronary interventional procedures may potentially be hazardous when due to myocardial ischemia. However, especially after coronary stent placement, cardiologists must consider in the differential diagnosis stretch pain due to the overdilation and stretch of the artery. This pain typically lasts for \( \approx 1 \) day, is of benign character, and can be safely monitored without the need for an urgent repeat coronary angiography.

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**References**


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