Cardiac risk factors, medication, and recurrent clinical events after acute coronary disease

A prospective cohort study

S. N. Willich1, J. Müller-Nordhorn1, M. Kulig1, S. Binting1, H. Gohlke2, H. Hahmann3, K. Bestehorn4, K. Krobot4, H. Vollér5 for the PIN Study Group*

1Institute for Social Medicine and Epidemiology, Charité Hospital, Humboldt University of Berlin, Berlin, Germany; 2Herzzentrum, Bad Krozingen, Germany; 3Waldburg-Zeil Kliniken, Isny, Germany; 4MSD Sharp and Dohme GmbH, Haar, Germany; 5Klinik am See, Rüdersdorf, Germany

Aims Systematic data are sparse on clinical outcome after acute coronary disease followed by cardiac rehabilitation therapy. Therefore, our objective was to determine the long-term development of cardiac risk factors, recurrent clinical events, and cardiac medication in patients undergoing routine inhospital cardiac rehabilitation therapy.

Methods and Results In the prospective PIN Study (Post Infarct Care), 2441 consecutive patients (78% men, 60 ± 10 years, 22% women, 65 ± 10 years) were enrolled in 18 inpatient rehabilitation centres in Germany following myocardial infarction (56%), coronary artery bypass graft (38%) or percutaneous transluminal coronary angioplasty (6%). Cardiac risk factors, pre-specified clinical end-points, and the prescription of cardiac medication were prospectively documented on admission to and at discharge from rehabilitation therapy, and 3, 6 and 12 months later by obtaining information with standardized questionnaires from the patients and their physicians. The cardiac risk factors improved initially during cardiac rehabilitation therapy, but deteriorated within the following 12 months: 39% patients smoked at the beginning vs 5% at the end of inhospital rehabilitation vs 10% at 12 months follow-up (P<0.001). The respective numbers for patients with blood pressure >140 and/or 90 mmHg were 24 vs 8 vs 25% (P<0.01) and with plasma cholesterol >200 mg . dl⁻¹ 57 vs 29 vs 51% (P<0.01). A total of 886 patients experienced one or more recurrent clinical events during the first year, 69% of those within the initial 6 months. At 12 months follow-up, 77% of patients received aspirin, 70% beta-blockers, 62% lipid lowering medication, and 53% angiotensin converting enzyme inhibitors.

Conclusion The present results indicate that the benefit of cardiac rehabilitation therapy following acute coronary events is only partially maintained during the following year. Continuous strategies of medical care need to be developed to improve the long-term outcome in coronary patients. (Eur Heart J 2001; 22: 307–313, doi:10.1053/euhj.2000.2294) © 2001 The European Society of Cardiology

Key Words: Coronary heart disease, rehabilitation, secondary prevention, risk factors.

See page 276 for the Editorial comment on this article

Introduction

Many intervention studies have established the prognostic importance of long-term control of risk factors in patients following acute coronary events[1–5]. Prevention is a cornerstone in the effort to reduce cardiovascular mortality, that is still responsible for over 40% of all deaths in industrialized societies[6–9]. Therefore, several cardiovascular societies have developed and published guidelines for the long-term management of patients with coronary heart disease[10]. However, there have been only a few systematic studies on the development of risk factors and clinical
events in patients after acute coronary events. The EUROASPIRE Study has demonstrated a high prevalence of modifiable risk factors in approximately 3500 patients with coronary heart disease recruited in nine European countries[11]. Grande et al. evaluated the long-term development of cardiac risk factors in 353 patients with myocardial infarction, coronary artery bypass graft (CABG) and percutaneous transluminal coronary angioplasty (PTCA), after in-hospital or ambulatory cardiac rehabilitation therapy[12]. There was only short-term success in the adequate control of cardiac risk factors in patients following in-hospital rehabilitation therapy.

Based on routine standardized in-hospital cardiac rehabilitation therapy offered to patients in Germany after acute coronary disease, a multicentre cohort study was designed to evaluate the long-term changes of risk factors, the natural course of recurrence of clinical events, and the prescription of cardiac medication.

**Methods**

**Patient population**

The PIN Study (Post Infarction Care) was designed as a long-term prospective cohort study in a representative sample of German rehabilitation centres. Patients were consecutively included into the study on admission to one of 18 participating rehabilitation centres if they met the following entry criteria: primary rehabilitation indication due to acute myocardial infarction, CABG, or PTCA. Patients were excluded from study participation if no consent was given, in cases with limited language skills, or if patients were transferred to in-hospital acute care because of recurrent coronary events. The 18 participating hospitals in the present study appear representative of the total 69 inpatient rehabilitation centres in Germany, as indicated by the similar average number of beds (207 vs 178) and the focus on cardiovascular rehabilitation therapy (solely cardiology departments in 71 vs 65%).

**Study protocol**

The study protocol is depicted in Fig. 1. The patients provided information by standardized questionnaires at admission to and discharge from the rehabilitation hospitals, and 3, 6, and 12 months later. The physicians in the rehabilitation centres provided information at discharge of the patient, as did the patients’ general practitioners, retrospectively, after 12 months. Two of the 18 centres performed a prospective follow-up of the patients by contacting the general practitioners after 3, 6 and 12 months. The information obtained from the physicians included the frequency and values of laboratory testing of total plasma cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, arterial blood pressure values and body weight. The patients’ questionnaires included medical history, risk factors including smoking status, medication prescription, other therapy, recurrent coronary events, quality of life assessed with the SF-36[13], and occupational status. The occurrence of the clinical end-points of the PIN Study including cardiovascular death, myocardial infarction, revascularization with CABG or PTCA, and angina pectoris or congestive heart failure with hospitalization, were assessed using information obtained from the
patients and/or physician. To determine, at least, the survival status and cause of death if data were missing, letters were sent either to the patients and their families, their general practitioners or if necessary to the public vital statistics offices.

**Data management and statistical analysis**

All questionnaires were manually reviewed for completeness and plausibility. A double entry was performed using MS-ACCESS 7.0 software with subsequent manual review where information was conflicting. An independent audit was performed for quality control purposes, including assessment of consecutive and complete patient recruitment and data retrieval and management procedures in a 50% random sample of the participating centres and in the coordinating centre. The audit yielded data errors in less than 1% of the checked data which were subsequently corrected.

Statistical calculations were performed using SAS 6.12 software. For the purposes of the present study, the following upper risk factor levels were defined: blood pressure systolic 140 and/or diastolic 90 mmHg, body mass index (BMI) 30 kg m⁻², total plasma cholesterol 200 mg dl⁻¹, LDL cholesterol 130 mg dl⁻¹, and triglycerides 200 mg dl⁻¹. Cross-sectional prevalence analysis was performed for risk factors and medication. The comparison between patient groups was done with chi-square tests for categorical variables, intra-individual comparisons at two time points were performed using Wilcoxon (continuous data) and McNemar’s (categorical data) tests. Multiple logistic regression was used to estimate the effect of (risk) factors on the recurrence of clinical events. Parsimonious models were derived with stepwise logistic regression adjusting for confounding (age, sex, educational level, smoking) as described by Hosmer and Lemeshow.[14] The statistical significance of a potential risk factor is given as a P-value of the likelihood ratio test statistic relative to the model without the factor in question. P-values <0.05 were considered significant.

**Results**

**Patient selection**

From January to June 1997, a total of 3024 consecutive patients were screened at admission to the rehabilitation centres. Of those, 2441 patients (78% men, 60 ± 10 years, 22% women, 65 ± 10 years) were enrolled in the study. The other 583 patients were excluded because of missing consent by the patient (60%), language or intellectual barriers (13%), retransfer to acute care for recurrent clinical events (7%), severely reduced physical state (3%), or other reasons (17%).

Among the 2441 study patients, the follow-up response was 2233 (91%) at the 6 month and 2069 (85%) at the 12 month follow-up. Among the general practitioners of the 2441 study patients, the follow-up response was 1557 (64%) at 6 months and 1536 (63%) at 12 months, and the main results were similar between the prospective and retrospective follow-up strategies. The survival status could be determined in all but four patients enrolled in the present study (99.8%).

**Baseline characteristics**

The primary indication for inhospital rehabilitation therapy was acute myocardial infarction in 56% of patients, CABG in 38% and PTCA in 6% of patients. Important sociodemographic variables of these patient groups are depicted in Table 1. Among all patients with the primary indication of acute myocardial infarction, 39% had subsequently undergone PTCA, 18% CABG, and 1% both. Among all patients with the primary indication of PTCA, 19% had subsequently undergone CABG. Among all patients with coronary artery disease, 27% had one-vessel, 26% two-vessel, 45% three-vessel disease, and 2% had left main artery disease. The medical history of the patients included hyperlipidaemia (83% of patients), arterial hypertension (56%), overweight (49%), current or former smoking (62%), diabetes mellitus (21%), and family history of cardiovascular disease (31%).

**Cardiac risk factors**

Several of the major cardiac risk factors improved markedly during inhospital rehabilitation therapy, but worsened within the first 3 months following discharge, almost back to baseline levels (Table 2). Accordingly, the prevalence of conventionally defined cardiac risk factors was reduced during inhospital treatment, but increased already within a few months of discharge.

---

**Table 1 Sociodemographic variables of patient population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Myocardial infarction (n=1379)</th>
<th>CABG (n=916)</th>
<th>PTCA/CAD (n=146)</th>
<th>Total (n=2441)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (%)</td>
<td>78</td>
<td>79</td>
<td>74</td>
<td>78</td>
</tr>
<tr>
<td>Average age (mean ± SD, years)</td>
<td>57 ± 11</td>
<td>59 ± 10</td>
<td>62 ± 9</td>
<td>60 ± 10</td>
</tr>
<tr>
<td>Women (%)</td>
<td>22</td>
<td>21</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>Average age (women) (mean ± SD, years)</td>
<td>65 ± 11</td>
<td>63 ± 10</td>
<td>65 ± 10</td>
<td>65 ± 10</td>
</tr>
<tr>
<td>Single (%)</td>
<td>27</td>
<td>22</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>College/University degree (%)</td>
<td>12</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>
The relative changes in the prevalence of conventionally defined cardiac risk factors were similar for male and female patients, and for patients over 60 years of age.

### Clinical events

A total of 886 patients (43% of all patients with complete follow-up information) experienced one or more recurrent clinical events during the follow-up; 69% of those occurred within the initial 6 months after discharge from the rehabilitation centre. Cardiovascular death occurred in 1% of all patients, acute myocardial infarction in 15%, congestive heart failure with hospitalization in 12%, angina pectoris with hospitalization in 19% and revascularization with PTCA or CABG in 24%. In a multivariate model for the risk (odds ratio including 95% confidence interval) for recurrent clinical events, patients with a primary indication of acute myocardial infarction or PTCA experienced odds ratios for recurrent events of 2.0 and 2.4, respectively, compared to patients with CABG (Table 3). Furthermore, heart failure, and episodes of angina pectoris during cardiac rehabilitation therapy were predictors for recurrent clinical events, whereas education of more than 10 school years was associated with an odds ratio of 0.7, i.e. was a protective factor. Other variables including age and sex of patients were no significant predictors of recurrent clinical events.

### Medication

Among all patients, 84% received aspirin therapy on admission to the rehabilitation hospital, 86% at discharge, 83% 3 months later, 81% 6 months later and 77% 12 months later (Fig. 3, P<0.05 for the comparison

---

Table 2  Cardiac risk factors during the course of the study

<table>
<thead>
<tr>
<th></th>
<th>Admission Mean ± SD</th>
<th>Discharge Mean ± SD</th>
<th>3 Months Mean ± SD</th>
<th>6 Months Mean ± SD</th>
<th>12 Months Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure syst./diast. (mmHg)</td>
<td>129 ± 21/78 ± 12 *</td>
<td>121 ± 16/73 ± 10 *</td>
<td>132 ± 16/79 ± 8 *</td>
<td>131 ± 17/81 ± 9 ns</td>
<td>133 ± 17/80 ± 9 ns</td>
</tr>
<tr>
<td>Body mass index (kg . m$^{-2}$)</td>
<td>27.0 ± 3.7 *</td>
<td>26.7 ± 3.4 *</td>
<td>26.9 ± 3.6 *</td>
<td>27.2 ± 3.8 *</td>
<td>27.4 ± 3.8 *</td>
</tr>
<tr>
<td>Cholesterol (mg . dl$^{-1}$)</td>
<td>213 ± 51 *</td>
<td>183 ± 47 *</td>
<td>200 ± 43 ns</td>
<td>202 ± 42 ns</td>
<td>205 ± 52 ns</td>
</tr>
<tr>
<td>LDL cholesterol (mg . dl$^{-1}$)</td>
<td>145 ± 44 *</td>
<td>118 ± 34 *</td>
<td>125 ± 39 ns</td>
<td>125 ± 37 ns</td>
<td>127 ± 35 ns</td>
</tr>
<tr>
<td>HDL cholesterol (mg . dl$^{-1}$)</td>
<td>39 ± 14 ns</td>
<td>39 ± 13 *</td>
<td>46 ± 27 ns</td>
<td>47 ± 25 ns</td>
<td>47 ± 18 ns</td>
</tr>
<tr>
<td>Triglycerides (mg . dl$^{-1}$)</td>
<td>163 ± 114 *</td>
<td>143 ± 78 *</td>
<td>170 ± 120 ns</td>
<td>180 ± 133 ns</td>
<td>181 ± 135 ns</td>
</tr>
</tbody>
</table>

*P<0.001

---

(Fig. 2). The relative changes in the prevalence of conventionally defined cardiac risk factors were similar for male and female patients, and for patients ≤ 60 and over 60 years of age.

---

Figure 2  Prevalence of the conventionally defined cardiac risk factors, blood pressure, smoking, body mass index (BMI), cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides at admission to and discharge from inpatient rehabilitation therapy and at 3 (except for smoking status), 6 and 12 months follow-up. Statistical comparisons were made between the values of admission vs discharge and discharge vs 12 months follow-up (*P<0.001). □=admission; □=discharge; □=3 months; □=6 months; □=12 months.

---

admission vs discharge and P<0.001 for the comparison discharge vs 12 months follow-up). The respective numbers for beta-blockers are 61 vs 77 vs 75 vs 73 vs 70% (P<0.001), for lipid lowering agents 33 vs 69 vs 67 vs 65 vs 62% (P<0.001), and for angiotensin converting enzyme (ACE) inhibitors 51 vs 57 vs 56 vs 55 vs 53% (P<0.001 and P<0.01, respectively). In addition to medication, therapeutic strategies between discharge from inpatient rehabilitation and 12 months follow-up included physical therapy (32% of patients), patient seminars (21%), and psychotherapy (10%).

Table 3  Predictive model for risk of recurrent clinical events

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference</th>
<th>Odds ratio*</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary indication</td>
<td>ACVB</td>
<td>2.4</td>
<td>1.6-3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PTCA</td>
<td>2.0</td>
<td>1.6-2.4</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td>1.3</td>
<td>1.0-1.6</td>
</tr>
<tr>
<td>NYHA I</td>
<td></td>
<td></td>
<td>1.5</td>
<td>1.2-2.0</td>
</tr>
<tr>
<td>NYHA II</td>
<td></td>
<td></td>
<td>3.0</td>
<td>1.5-6.3</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td></td>
<td></td>
<td>3.0</td>
<td>1.8-5.1</td>
</tr>
<tr>
<td>Angina pectoris during in-hospital cardiac rehabilitation</td>
<td></td>
<td></td>
<td>1.0</td>
<td>0.8-1.2</td>
</tr>
<tr>
<td>Education &gt;10 years</td>
<td>≤10 years</td>
<td>0.7</td>
<td>0.5-0.9</td>
<td>0.0255</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age, smoking.

Figure 3  Prevalence of the prescription of cardiac medication, aspirin (ASA), beta-blockers, lipid lowering drugs, angiotensin converting enzyme (ACE) inhibitors, calcium (Ca) antagonists, and heart glycocides at admission to and discharge from inpatient rehabilitation therapy and at 3, 6 and 12 months follow-up. Statistical comparisons were made between the values of admission vs discharge and discharge vs 12 months follow-up (*P<0.05, **P<0.01, ***P<0.001). □=admission; □=discharge; □=3 months; □=6 months; □=12 months.

Discussion

The results of the present study demonstrate that the adequate reduction of cardiac risk factors in many patients during inhospital rehabilitation therapy after acute coronary events is not satisfactorily maintained during the following 12 months. The insufficient long-term control of cardiac risk factors following discharge from inpatient coronary rehabilitation is associated with a decline in the prescription rate of cardiac medication and recurrent clinical events in over one third of the patient population.
The PIN study was designed to provide representative insight into the medical care of patients following acute coronary events and cardiac rehabilitation therapy in Germany. Patients are legally entitled to undergo inpatient rehabilitation therapy after coronary events usually for 3 to 4 weeks. The inpatient rehabilitation centres provide essentially standardized care. This situation was ideal for the purposes of the present study. Furthermore, since the German policy of cardiac rehabilitation is different from many other countries in Europe, the present data might be expected to represent not only usual but rather ‘best’ general practice.

The present results are consistent with prior studies on the development of cardiac risk factors in patients with coronary heart disease. In the EUROASPIRE study, approximately 50% of patients with coronary artery disease were not adequately controlled for high blood pressure and plasma cholesterol, and approximately 20% were not adequately controlled for smoking, body mass index, or diabetes[11]. To our knowledge, there is only one study, with a relatively small sample size, that compares patient populations in terms of inpatient vs ambulatory rehabilitation therapy[12]. In this study, both treatment strategies revealed the same lack of adequate long-term control of cardiac risk factors.

In our study, long-term lipid metabolism control appears insufficient. The guidelines of the European Society of Cardiology recommend an LDL cholesterol of less than 130 mg. dl⁻¹ for secondary prevention[10]. This is in noticeable contrast to 61% of our patients with LDL levels of 130 mg. dl⁻¹ or higher at admission to the rehabilitation centres in the present study. During inpatient rehabilitation the proportion of patients with elevated LDL cholesterol was markedly reduced, but this beneficial effect was only partially maintained during the subsequent 12 months. It is of note, that HDL cholesterol levels increased significantly during follow-up, contributing to the patients’ prognostic benefit. Given the clear prognostic importance of plasma lipids, LDL and HDL cholesterol development after coronary events warrants a continuous and rigid therapy regimen[15,16].

The blood pressure control in the present study appears somewhat better than the lipid control, but was still far from adequate with approximately 25% of patients demonstrating values of 140/90 mmHg or higher at admission to the rehabilitation centre. Given the prognostic importance of blood pressure, stringent high blood pressure therapy is needed[17]. Only the long-term development of smoking among patients appears relatively low with a 10% prevalence, but this rate may be under-estimated since it is based solely on information from the patients and their physicians without validation by objective markers.

The potential underlying reasons for this inadequate risk factor control include lack of coordination of treatment strategies between the hospital rehabilitation centres and the private practitioner of the patients[18,19]. Inadequate prevention efforts on the part of the physicians — perhaps in part due to increasing budget constraints in the health care system — and patient compliance. Although some patients may have a definite contraindication or no need for the use of aspirin, beta-blockers, lipid lowering medication, and ACE-inhibitors, the percentage of patients in the present study receiving prognostically relevant medication still appears too low. Even in the case of lipid lowering medication, the present rate of approximately 60% long-term prescription — to our knowledge the highest published rate after coronary events— leaves room for improvement. Particularly in the light of the present adverse risk factor development, better long-term adherence to treatment recommendations of secondary prevention is needed.

In the present study, there was a cardiovascular mortality rate of approximately 1% during the first year following discharge from inpatient cardiac rehabilitation. This surprisingly low cardiovascular mortality may be associated with the beneficial overall effect of inpatient rehabilitation therapy. It may also, in part, reflect that patients with acute clinical deterioration during rehabilitation and subsequent retransfer to acute inpatient care were not included in the present analysis.

Furthermore, at least 30% to 40% of patients usually choose not to undergo inpatient rehabilitation therapy following acute coronary events[20], and this group may have a relatively worse clinical outcome.

Our results also demonstrate a high rate of recurrent clinical events, including revascularization procedures and hospitalization for heart failure or angina pectoris. Since altogether almost 30% of the PIN patients received PCTA after the acute coronary event and 20% had a history of diabetes, the recurrent morbidity reflects, at least in part, the adverse prognosis known in these patient groups[21,22]. The recurrence of clinical events is of concern not only regarding the long-term outcome, but also considering the enormous cost associated with rehospitalization in the light of current attempts to limit further increases of health care budgets.

### Limitations

Some limitations of the present study should be noted. The PIN study appears representative of a large patient population and reflects the natural cause of therapy, risk factor development, and recurrent clinical events. However, since there was no systematic treatment protocol, the study cannot prove efficacy of rehabilitation therapy.

The legal regulations regarding inpatient cardiac rehabilitation therapy in Germany does not allow for randomized trials to directly determine the efficacy of inpatient vs ambulatory or even no rehabilitation therapy. Furthermore, because of the specific German legislation, the present results may not generally reflect the situation in other countries. The information on the prescription of cardiac medication may not reflect the actual medication use due to compliance issues.

The detailed 12 months follow-up data were available.
for 85% of the total patient population. This may be associated with potential selection and perhaps also information bias.

**Conclusion**

The results of the PIN study indicate the need to develop better long-term secondary prevention. Continuous preventive treatment strategies, physician efforts, even in light of budget constraints in the current health care situation, as well as patients' knowledge, compliance, and lifestyle changes are important factors that will eventually provide better long-term control of cardiovascular disease.

**References**


