Long-term effects of in-hospital cardiac rehabilitation on the cardiac risk profile

A case-control study in pairs of siblings with myocardial infarction

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Aims In the general population, measures for secondary prevention of myocardial infarction are poorly utilized. Our aim was therefore to analyze whether post-myocardial infarction in-hospital rehabilitation and education programmes improve the subsequent utilization of preventive strategies.

Methods and Results We screened 93,500 patient charts in cardiac rehabilitation clinics to identify a myocardial infarction patient with a sibling, who likewise had a myocardial infarction prior to the age of 60 years but was discordant with respect to the participation in cardiac in-hospital rehabilitation. In 92 such sibling pairs the coronary risk profile was studied by standardized questionnaire, biochemical measurements and physical examination. At the time of the acute myocardial infarction, both groups showed an equal risk factor distribution. However, at follow-up (on average 5.5 years after myocardial infarction), rehabilitation-siblings presented with significantly lower systolic (137 ± 2 vs 150 ± 3 mmHg, P<0.01) and diastolic blood pressure (82 ± 1 vs 89 ± 1 mmHg, P<0.01). Antihypertensive drug therapy resulted more often in effective (≤140/90 mmHg) control of blood pressure (58% vs 29%, P<0.01). Blood lipid levels and smoking prevalence tended to be lower in rehabilitation-siblings. Significantly fewer rehabilitation-siblings presented with two or more modifiable risk factors (OR 0.36 (CI 0.17–0.76), P<0.01). There was a strong tendency towards fewer recurrent cardiac events (re-myocardial infarction, coronary angioplasty, coronary artery bypass grafting) during follow-up in rehabilitation-siblings (OR 0.57 (CI 0.31–1.04); P=0.07).

Conclusion An in-hospital programme for cardiac rehabilitation may successfully encourage therapy to modify risk factors and thus enhance the long-term implementation of secondary prevention.

Introduction

In patients who suffered from myocardial infarction, cardiac rehabilitation represents a multifactorial intervention, that has been shown subsequently to improve quality of life and to carry the potential to reduce recurrent coronary events[1–3]. However, the utilization and structure of cardiac rehabilitation programmes varies widely between Western countries. In the United Kingdom, the participation rate in cardiac rehabilitation programmes was found to be low, possibly due to lack of scientific evidence in favour of long-term benefit of such programmes[4]. By contrast in Germany, a 3- to 4-week in-hospital rehabilitation programme of patients with cardiac disease is widely utilized yet controversial given the unproven long-term benefits.

No controversy exists regarding the benefits of risk factor intervention after myocardial infarction. Indeed, treatment of arterial hypertension and hypercholesterolaemia as well as the motivation to stop smoking may be the most efficacious measures in the prevention of re-infarction[5–9]. However, the implementation of various guidelines for risk factor intervention has been unsatisfactorily low[10–12]. The reasons for this apparent dilemma are complex and may include lack of patient...
information and motivation. Thus, it is crucial to identify interventions that may improve the adherence to guidelines for secondary prevention. We hypothesized that an intensive, several week long, cardiac in-hospital rehabilitation programme enhances compliance with risk factor interventions and thus, potentially, the long-term prognosis after myocardial infarction.

No prospective and randomized study has thus far addressed this question. Such study design, albeit preferable from a scientific point of view, may be difficult to apply given regional differences in the utilization of cardiac rehabilitation\textsuperscript{13,14}, the preferential recommendation of many physicians as well as the patients’ attitude towards such intervention. We therefore designed a case-control study in pairs of siblings who both suffered from myocardial infarction but utilized the cardiac in-hospital rehabilitation programme differentially.

Subjects and Methods

Rehabilitation programme

The in-hospital rehabilitation programme comprised a residential stay in a specific rehabilitation clinic including cardiological management, psychological and social interventions\textsuperscript{15}. Patients are usually referred to this specialized rehabilitation clinic by the hospital physician responsible for the treatment of acute myocardial infarction. In Germany, overall utilization depends on age and gender. It ranges from 80\% in employees younger than 55 years of age to 50\% in older, mostly retired patients. No more than 14 days are allowed to elapse between the two in-hospital stays for acute treatment and rehabilitation, respectively. It is based on the individual’s requirements aiming at the improvement of the quantity and quality of life by means of: reduction (or abolition, when possible) of the classical risk factors as well as medical therapy, modification of dietary habits, physical exercise, increase and maintenance of endurance training, psychological support, stress management, and guidance on returning to work. The average cost of the cardiac rehabilitation is 130 Euros per day. For employees, such a programme is reimbursed by retirement funds; for non-employees funding is via health insurance.

Study population

Families with two siblings who survived a myocardial infarction were identified by screening of more than 93 500 patient charts in nine cardiac rehabilitation centres. All the siblings of these families were contacted and invited to participate in the study. All patients gave written informed consent. Ninety two sibling pairs out of 850 families with two myocardial infarction patients in a ‘sibship’ met the following criteria\textsuperscript{13}: both siblings had suffered from myocardial infarction prior to the age of 60 years; one sibling underwent a 3- to 4-week in-hospital rehabilitation programme immediately after the acute hospitalization, whereas the control sibling did not participate in such a programme.

Medical records from the acute care hospital were analysed retrospectively in order to obtain baseline data at the time of the acute myocardial infarction. Patients who were not treated clinically for the acute myocardial infarction (e.g. silent myocardial infarction) did not enter the study. After hospitalization followed or not followed by the cardiac rehabilitation programme, siblings were subjected to usual care by their primary care physician.

The present examination was carried out after identification of a respective sibling pair during the retrospective chart review in the rehabilitation centre. On average 5-5 years after myocardial infarction, a standardized questionnaire was obtained by specially trained telephone interviewers regarding medical and social history, medication, and clinical events. All patients underwent measurements of weight, height, heart rate, and blood pressure as well as a venipuncture to obtain a blood sample during a visit scheduled at their primary care doctors’ office. Blood pressure was measured at rest in the sitting position using a standard mercury sphygmomanometer. Serum samples were centrifuged immediately and sent to a central laboratory for lipid analysis (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) and for measurement of glucose and glycosylated haemoglobin (HbA1c). As the time between the acute cardiac event and the follow-up study is of importance for this evaluation, we formed three subgroups with about equal sizes in the rehabilitation and the control groups: (1) myocardial infarction ≤1 year ago, (2) myocardial infarction between 1 and 5 years ago, (3) myocardial infarction >5 years ago.

Risk factors

According to the guidelines of the European Society of Cardiology (ESC) for secondary prevention, cardiovascular risk factors were defined as follows: arterial hypertension was considered when systolic blood pressure was above 140 mmHg and/or diastolic blood pressure was above 90 mmHg or when subjects were currently using antihypertensive medication or had a known history of arterial hypertension (as defined by The Fifth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure of the NIH, JNC-V\textsuperscript{16}). Antihypertensive medication was defined as the regular intake of drugs known to lower blood pressure (diuretics, beta-blockers, vasodilators, ACE inhibitors or AT-1 blockers, alpha blockers, calcium channel blockers). Hypercholesterolaemia was diagnosed when the total cholesterol level was above 190 mg . dl\^{-1} and/or LDL cholesterol was above 115 mg . dl\^{-1} or when lipid lowering therapy was administered. LDL cholesterol levels were determined...
using the Friedewald formula when triglycerides were below 400 mg . dl$^{-1}$ (4·52 mmol . l$^{-1}$). Lipid lowering therapies were considered when fibrates, nicotinic acid, cholestyramine, or cholesterol synthase enzyme inhibitors were taken on a regular basis.

Diabetes mellitus was considered with the history of diabetes or the intake of antidiabetic medication. Only individuals currently smoking cigarettes were classified as smokers. Obesity was defined according to National Institutes of Health Consensus Development Panel criteria as an elevated body mass index greater than 27·5 kg . m$^{-2}$ calculated as weight in kilograms divided by the square of the height in metres.

**Statistical evaluation**

Analyses were performed using JMP® Statistical Software (SAS Institute Inc, Cary, NC) with a two-sided standard t-test or analysis of variance for normally distributed continuous variables and with a Wilcoxon rank sum test for variables not normally distributed. Categorical characteristics of the patients in the two groups were compared by Fisher’s exact test. Multivariate logistic regression analyses were conducted, and Wald chi-square values were calculated to study the significance of predictors of outcome and to adjust simultaneously for potential confounding variables (age, gender, educational level, time between myocardial infarction and time of interview, body mass index, hypercholesterolaemia, diabetes, nicotine consumption). Using a backward selection, only the factors which were significant at $a=0·10$ remained in the model. For the multivariable analysis the patient was only mentioned once if an event occurred. The goodness of fit of the logistic regression model was tested by a chi-square statistic. Odds ratios were calculated to approximate relative risks and are present with 95% confidence interval. A value of $P<0·05$ was considered to indicate statistical significance.

**Results**

**Baseline characteristics at the time of myocardial infarction**

Table 1 displays the mean values of age, educational level, blood pressure, lipid levels as well as the prevalence of traditional risk factors at the time of acute myocardial infarction in siblings subsequently participating in the in-hospital rehabilitation programme (rehab-siblings) or their siblings not participating in such programme (control-siblings). In addition, localization and extension (maximal creatine kinase levels) of...
Cardiac risk profile at the follow-up

This follow-up study took place on average 5.5 years after the acute myocardial infarction or, if applicable, the cardiac rehabilitation programme. The average time of follow-up was similar in both groups (5.3 ± 0.3 years in rehab-siblings and 5.7 ± 0.4 years in control-siblings).

Arterial hypertension

In general, systolic and diastolic blood pressures were significantly lower in siblings who participated in the in-hospital rehabilitation programme (rehab-siblings) as compared to those siblings not undergoing the rehabilitation programme (control-siblings, Table 2). Yet, the number of individuals with hypertension was similar (rehab-siblings 82.6% vs control-siblings 81.5%). Accordingly, the number of individuals taking antihypertensive medication and displaying effective antihypertensive treatment success, significantly different between rehab-siblings and control-siblings were observed up to 5 years after myocardial infarction (Table 2).

Hypercholesterolaemia

Siblings who participated in the rehabilitation programme had subsequently significantly lower levels of total cholesterol than siblings without rehabilitation (223 ± 5 mg. dl⁻¹ vs 239 ± 6 mg. dl⁻¹, P<0.05; Table 2), HDL-, LDL- and triglyceride levels as well as the LDL/HDL ratio also tended to be lower in these siblings (not significant). The prevalence of treatment with lipid lowering drugs was comparable in both groups (65% vs 52%, not significant; Fig. 2). Effective treatment (total cholesterol <190 mg. dl⁻¹ and LDL cholesterol

Table 2  Blood pressure and lipid levels in different subgroups with respect to the time difference between the acute myocardial infarction (MI) and the follow-up: MI <1 year (n=57), MI between 1 and 5 years (n=54), MI >5 years (n=73)

<table>
<thead>
<tr>
<th></th>
<th>Rehabilitation-siblings (n=92)</th>
<th>Control-siblings (n=92)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI &lt;1 year ago</td>
<td>140 ± 3</td>
<td>154 ± 6</td>
<td>0.038</td>
</tr>
<tr>
<td>MI 1–5 years ago</td>
<td>133 ± 4</td>
<td>152 ± 4</td>
<td>0.003</td>
</tr>
<tr>
<td>MI &gt;5 years ago</td>
<td>138 ± 5</td>
<td>148 ± 3</td>
<td>ns</td>
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<tr>
<td>Mean</td>
<td>137 ± 2</td>
<td>150 ± 3</td>
<td>0.0002</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI &lt;1 year ago</td>
<td>82 ± 2</td>
<td>89 ± 3</td>
<td>0.030</td>
</tr>
<tr>
<td>MI 1–5 years ago</td>
<td>82 ± 2</td>
<td>88 ± 2</td>
<td>0.034</td>
</tr>
<tr>
<td>MI &gt;5 years ago</td>
<td>84 ± 2</td>
<td>88 ± 2</td>
<td>ns</td>
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<tr>
<td>Mean</td>
<td>82 ± 1</td>
<td>89 ± 1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol (mg. dl⁻¹)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MI &lt;1 year ago</td>
<td>221 ± 13</td>
<td>225 ± 21</td>
<td>ns</td>
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<tr>
<td>MI 1–5 years ago</td>
<td>222 ± 16</td>
<td>258 ± 16</td>
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<tr>
<td>MI &gt;5 years ago</td>
<td>264 ± 17</td>
<td>233 ± 11</td>
<td>ns</td>
</tr>
<tr>
<td>Mean</td>
<td>223 ± 5</td>
<td>239 ± 6</td>
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<tr>
<td>LDL/HDL ratio</td>
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<tr>
<td>MI &lt;1 year ago</td>
<td>3.4 ± 0.3</td>
<td>3.3 ± 0.5</td>
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<tr>
<td>MI 1–5 years ago</td>
<td>3.8 ± 0.4</td>
<td>4.4 ± 0.4</td>
<td>ns</td>
</tr>
<tr>
<td>MI &gt;5 years ago</td>
<td>3.3 ± 0.4</td>
<td>3.6 ± 0.3</td>
<td>ns</td>
</tr>
<tr>
<td>Mean</td>
<td>3.5 ± 0.2</td>
<td>3.8 ± 0.2</td>
<td>ns</td>
</tr>
</tbody>
</table>

*To avoid confounding by age and sex, we adjusted for these variables in the statistical model. ns=not significant.
<115 mg . dl \(^{-1}\)) was observed in only 21% of rehab-siblings and 16% of control-siblings (not significant; Fig. 2).

**Cigarette smoking, obesity and diabetes mellitus**

The prevalence of current smoking was reduced from 37% at the time of myocardial infarction to 13% at the time of the interview in siblings participating in the rehabilitation programme and from 38% to 22% in control-siblings. Thus, participation in rehabilitation stimulated slightly more smokers to quit (not significant). At the time of the interview the body mass index was identical in both groups (27·2 kg . m \(^{-2}\)). Moreover, the prevalence of diabetes mellitus (35% vs 25%, not significant) and the level of HbA1c in diabetics (7·1 ± 0·3% in rehab-siblings vs 7·7 ± 0·6% in control-siblings) were similar in both groups.

**Cardiac events during follow-up**

Cardiac events after the initial myocardial infarction (re-infarction, coronary angioplasty, coronary artery bypass grafting) are shown in Fig. 3. The number of re-infarctions during the time period between initial myocardial infarction and follow-up was significantly lower in patients who had participated in a rehabilitation programme (7% vs 17%, \(P<0·05\)). Additionally, a slightly decreased rate of further interventions (coronary angioplasty) was observed in patients joining the rehabilitation programme (14% vs 26%, not significant); no difference was seen regarding subsequent coronary artery bypass grafting.

**Multivariate analysis**

The multivariate odds ratios of prevalent modifiable risk factors adjusted for potentially confounding variables are shown in Fig. 4. With the exception of obesity the odds to present with a modifiable risk factor or to present with equal or more than two modifiable risk factors were lower in rehab-siblings. Interestingly, we also observed a lower risk of experiencing a subsequent cardiac event, especially myocardial infarction and coronary angioplasty, in rehab-siblings (Fig. 4).

**Discussion**

In Europe, an enormous potential exists for lowering the high burden of modifiable risk factors in patients with myocardial infarction\(^{[10]}\). In fact, effective treatment strategies for hypertension and hypercholesterolaemia\(^{[5,6,9,10,18]}\) contrast with poor utilization of these measures\(^{[19,20]}\). Thus, identification of factors that may
improve adherence to current guidelines for secondary prevention is of potential interest. Here, we show long-term salutary effects of a cardiac rehabilitation programme with respect to risk factor modification and subsequent clinical events. Specifically, we observed a significant reduction in systolic and diastolic blood pressure and non-significant trends towards higher success rates in smoking cessation and treatment of hyperlipidaemia. These effects were evident up to 5 years after myocardial infarction (respectively participation in the rehabilitation programme). Finally, a slightly decreased rate of further cardiac events was observed in patients joining the rehabilitation programme, supporting its long-term benefit. These effects can be reasonably demonstrated by more prevalent and more effective medical treatment during follow-up, especially antihypertensive drug therapy in participants of the rehabilitation programme.

Several data indicate that non-compliance is crucial for the lack of adherence to long-term implementation of secondary prevention[21]. A higher level of awareness and information may improve compliance and result in better risk factor control by patients and primary care physicians reflecting better attention to respective guidelines [22]. Cardiac rehabilitation is a multidisciplinary activity that brings together medical treatment, education and information on coronary risk factors; individual counselling as well as encouragement with exercise training and lifestyle modification may improve an individual’s beliefs or perceptions about the illness [23]. These multiple factors in combination appear to play a pivotal role in health behaviour, motivation and thus,
compliance\textsuperscript{21,22}. Based on the present data, it can be assumed that a cardiac rehabilitation programme will improve patients’ long-term compliance with medication adherence and other essential secondary preventive strategies.

In Germany, the post-myocardial infarction rehabilitation programme that is used most predominantly involves 3- to 4-weeks’ in-hospital treatment. By study design, all rehabilitation patients studied in the present investigation adhered to this in-hospital programme. We therefore cannot provide any information on potential alternative rehabilitation methods, e.g. repeated outpatient consulting. Likewise, we are not in a position to provide data on effort tolerance or fitness levels, although exercise programmes constitute an important component of the multifactorial rehabilitation programme. Unfortunately, however, stress tests were not performed in non-rehabilitation siblings. Thus, data concerning this pertinent issue are lacking and further studies should address the question as to whether inpatient and out-patient rehabilitation programmes are equally effective with respect to risk factor modification and costs.

Several limitations of the study should be emphasized. Most significantly, this study like many others in the field\textsuperscript{23,24} was carried out retrospectively in a non-randomized fashion. The potential for selection, referral and confounding bias should therefore be discussed. We aimed to address these limitations by designing a case-control study in pairs of siblings who both suffered from myocardial infarction. While one of the siblings attended the cardiac rehabilitation programme (considered almost a legal right in Germany\textsuperscript{14}), the second sibling did not.

Studying such sibling pairs with myocardial infarction, we intended to achieve the best potential matching for familial, including genetic as well as environmental and social, factors. Indeed, at the time of myocardial infarction the two groups were highly comparable. Moreover, in order to further decrease selection bias, adjustment for potential confounding factors was conducted. Yet, participation in the rehabilitation programme was a persistent predictor of better control of modifiable risk factors and a higher prevalence of appropriate drug intake. Thus, differences in the risk profile during follow-up may reflect enhanced compliance with medical recommendations in those who participated in the rehabilitation programme.

The most common reason for non-participation in the in-hospital rehabilitation programme was lack of recommendation by hospital physicians. This reflects limited acceptance and conviction of the efficacy and efficiency of such a programme. The fact that hospital physicians are responsible for the referral to the rehabilitation programme is also of importance in the consideration of referral bias as a potential explanation for our results. However, further out-patient care and thus the modification of the risk profile observed here was provided in general by practitioners and internists in private practice, i.e. physicians who were not involved in the referral to the cardiac rehabilitation. Thus, referral bias seems to be an unlikely explanation for the improved risk factor modification in the rehabilitation group.

In conclusion, the results of this sibling pair study indicate favourable long-term effects of cardiac in-hospital rehabilitation regarding risk factor modification, improvement of medical treatment as well as reduction of further cardiac events. Thus, a programme intended to educate patients on coronary risk factors and to encourage therapy of modifiable risk factors as well as appropriate physical activity may enhance compliance resulting in a better long-term implementation of secondary prevention.

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References


\textsuperscript{[4]} Cardiac rehabilitation is performed poorly in the UK. BMJ 1998; 316(7141): F.


