Long-Term Effects of Integrated Rehabilitation in Patients with Advanced Angina Pectoris: A Nonrandomized Comparative Study

SOEREN BALLEGAARD, M.D.,¹ E. BORG, M.P.H.,¹ B. KARPATSCHOFF, M.Sc.,² J. NYBOE, M.Act.,³ and A. JOHANNESSSEN, R.N.¹

ABSTRACT

Objectives: An evaluation of Integrative Rehabilitation (IR) of patients with angina pectoris with respect to death rate, the need for invasive treatment, and cost effectiveness.

Design: A report from a clinical database. Death rates were compared to those of the general Danish population matched for age, gender, and observation period, as well as with data from the literature concerning medical and invasive treatments.

Setting: The treatment was carried out as an ambulatory treatment in a private clinic.

Subjects: One hundred and sixty-eight (168) patients with angina pectoris, of whom 103 were candidates for invasive treatment and 65 for whom this had been rejected.

Interventions: Integrated rehabilitation consists of acupuncture, a self-care program including acupressure, Chinese health philosophy, stress management techniques, and lifestyle adjustments.

Outcome measures: Death rate from any cause, the need for invasive treatment, and health care expenses.

Results: The 3-year accumulated risk of death was 2.0% (95% confidence limits: 0.0%–4.7%) for the 103 candidates for invasive treatment, 6.4% for the general Danish population, 5.4% (4.7%–6.1%), and 8.4% (7.7%–9.1%) for patients who underwent percutaneous transluminal balloon angioplasty and coronary artery bypass grafting, respectively, in New York. For the 65 inoperable patients the risk of death due to heart disease was 7.7% (3.9%–11.5%), compared to 16% (10%–34%) and 25% (18%–36%) for American patients, who were treated with laser revascularization or medication, respectively. Of the 103 candidates for invasive treatment, only 19 (18%) still required surgery. Cost savings over 3 years were US $36,000 and US $22,000 for surgical and nonsurgical patients, respectively. These were mainly achieved by the reduction in the use of invasive treatment and a 95% reduction in in-hospital days.

Conclusions: Integrated rehabilitation was found to be cost effective, and added years to the lives of patients with severe angina pectoris. The results invite further testing in a randomized trial.

INTRODUCTION

Great effort has been made to systemize and evaluate the broad spectrum of conventional treatments available for the treatment of angina pectoris (Eagle, 1999; Gibbons 1999). It is evident that invasive treatment provides pain relief. However, the effects on the risk of death and of repeated heart attack are difficult to determine, when compared to aspirin and cholesterol lowering medication. Both have a significant positive effect on the risks mentioned (Eagle et al., 1999; Gibbons et al., 1999).

In the past few decades, a great amount of evidence concerning the effect of lifestyle on heart disease has been published. Smoking, obesity, diet, alcohol, exercise, depression

¹The Ballegaard Acupuncture Center, Klampenborg, Denmark.
²Psychological Department, University of Copenhagen, Denmark.
³Former National Hospital, University of Copenhagen, Denmark.
or social isolation can each affect risk by over 30% (Calle et al., 1999; de Lorgeril et al., 1999; Frasure-Smith et al., 1995; Groenbaek et al., 1995; Hakim et al., 1998; Hasdai et al., 1997; House et al., 1988; Leon et al., 1987).

At the Nordic Heart Center, all heart patients who received integrated rehabilitation (IR) and had been recommended for an operation have been followed since 1991, and the results of our annual quality control review have been published since 1995 (Ballegaard et al., 1996; Ballegaard et al., 1999). The purpose of this study is to provide a reliable basis for further confirmation of the results, preferably in a randomized trial.

**MATERIALS AND METHODS**

**Design and outcome measures**

The report is based on data from a clinical database, derived from questionnaires sent to all our patients once a year. If a patient fails to answer the questionnaire, the relevant information is obtained from the patient's doctor (with the patient's permission). The evaluation of risk is done on an intention-to-treat basis, including the 168 patients who started treatment.

A randomized trial has not been possible in Denmark, and comparable data for Danish patients receiving invasive or medical treatment are not available. Consequently, we compare death rates to those of the general Danish population. Each of the computed death rates is based on data from approximately 35,000 Danes with the same age, gender, and observation period, as our patients. (www.danmarksstatistik.dk). We also compared our death rate to the results from the New York clinic database concerning percutaneous transluminal balloon angioplasty (PTCA) and coronary artery bypass grafting (CABG) (Hannan et al., 1999). According to the American Heart Association and the American College of Cardiology, they provide a reliable evaluation (Eagle et al., 1999), using the 3-year risk of death from any cause, as we do. With regard to the patients rejected for invasive treatment, we compared our results with an American study comparing medication with myocardial laser revascularization (Schofield et al., 1999), using the accumulated 3-year risk of death from heart disease, and so do we.

For the 161 patients who completed the program, the expenses related to treatment were calculated in the year prior to onset of integrative rehabilitation (IR), and in the 3 years following. The rates used to estimate the expenses were US $15 and US $30 for consulting a general practitioner and a cardiologist, respectively; and US $230 and US $615 per day for ambulatory treatment and hospitalization, respectively. The exchange rate in 1999 was DKK 6.50 for US $1.00. Expenses related to angioplasty and bypass operations have been calculated based on an American study (Halky et al., 1997).

**The patients**

We included 168 consecutive patients who had clinical angina pectoris and objective proven myocardial ischemia: 103 were candidates for invasive treatment, while this had been rejected for the remaining 65 patients, either because of high risk ($n = 17$) or because the operation or, more often, reoperation, was not possible on technical grounds ($n = 48$). Patient data are summarized in Table 1. These patients originated from a total population of 340 patients with clinical angina pectoris; 172 were excluded either because myocardial ischemia was not confirmed by clinical tests ($n = 102$), myocardial ischemia was confirmed, but was so mild that invasive treatment was not suggested ($n = 65$), or because IR was used as a supplement to an invasive treatment which was already planned and performed immediately after the IR ($n = 2$).

**The intervention: Integrated rehabilitation**

Each patient had 12 consultations over 3–4 weeks, in which they received acupuntsure and education in the self-care program. The program has been described earlier (Ballegaard et al., 1999). The 3-year accumulated risk was calculated by Kaplan-Meier's analysis (SPSS for Windows).

**RESULTS**

The patients were followed for 3–162 months (mean, 32 months) from the beginning of treatment and until the occurrence of death or cardiac surgery.

**Risk evaluation**

Two (2) of the 103 candidates for invasive treatment died within the 3 years of observation, i.e. an accumulated risk of death of 2.0% (95% confidence limits: 0.0%–4.7%), compared to 6.4% for the general Danish population. At no time during 3 years of observation was the survival curve for our group below that of the general population (Fig. 1). For angioplasty and bypass operations in New York, the risks were 5.4% (4.7%–6.1%) and 8.4% (7.7%–9.1%), respectively. If we divide our 103 patients into three equal sized groups based on onset of treatment, the 2-year accumulated risk of operation, myocardial infarction, or death declined in each successive group. For the first one third of patients, the accumulated risk was 33% (95% confidence limits: 25%–41%), compared to 21% (14%–28%) for the middle one third of patients, and 10% (5%–15%) for the last one third ($p$ for trend <0.05; Fig. 2). Four of the 65 inoperable patients died from heart disease within 3 years of observation, corresponding to an accumulated risk of 7.7% (3.9%–11.5%), compared to 16% (10%–34%) and 25% (18%–36%) among patients who had either laser treatment or drug, respectively.
### Table 1. Demographic Profile of the 161 Patients Who Completed the Program at the Commencement of Treatment

<table>
<thead>
<tr>
<th></th>
<th>Candidates for Operation $n = 99$</th>
<th>Patients denied an operation $n = 62$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (% female)</td>
<td>42%</td>
<td>26%</td>
</tr>
<tr>
<td>Average age (years)</td>
<td>62</td>
<td>63</td>
</tr>
<tr>
<td>Over 70 years old</td>
<td>27%</td>
<td>21%</td>
</tr>
<tr>
<td>&lt;55 years</td>
<td>24%</td>
<td>14%</td>
</tr>
<tr>
<td>55–64 years</td>
<td>36%</td>
<td>51%</td>
</tr>
<tr>
<td>65–74 years</td>
<td>32%</td>
<td>27%</td>
</tr>
<tr>
<td>&gt;74 years</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Previous myocardial infarction (heart attack)</td>
<td>49%</td>
<td>64%</td>
</tr>
<tr>
<td>Previous PTCA (angioplasty)</td>
<td>22%</td>
<td>31%</td>
</tr>
<tr>
<td>Previous CABG (bypass)</td>
<td>13%</td>
<td>60%</td>
</tr>
<tr>
<td>3-vessel or proximal left anterior descending artery disease</td>
<td>17%</td>
<td>16%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>37%</td>
<td>15%</td>
</tr>
<tr>
<td>NYHA classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>20%</td>
<td>5%</td>
</tr>
<tr>
<td>II</td>
<td>49%</td>
<td>20%</td>
</tr>
<tr>
<td>III-IV</td>
<td>31%</td>
<td>65%</td>
</tr>
<tr>
<td>Actual medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta blockers</td>
<td>44%</td>
<td>43%</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>64%</td>
<td>69%</td>
</tr>
<tr>
<td>Nitrates with prolonged effect</td>
<td>45%</td>
<td>65%</td>
</tr>
<tr>
<td>Cholesterol lowering medication</td>
<td>23%</td>
<td>39%</td>
</tr>
<tr>
<td>Consumption of nitroglycerine tablets per week$^a$</td>
<td>2 (0–41)</td>
<td>4 (0–55)</td>
</tr>
<tr>
<td>Medically treated hypertension</td>
<td>24%</td>
<td>30%</td>
</tr>
<tr>
<td>Medically treated diabetes</td>
<td>8%</td>
<td>14%</td>
</tr>
<tr>
<td>Medically treated congestive heart failure</td>
<td>9%</td>
<td>19%</td>
</tr>
<tr>
<td>Aspirin</td>
<td>68%</td>
<td>71%</td>
</tr>
<tr>
<td>Ace-inhibitor</td>
<td>11%</td>
<td>24%</td>
</tr>
<tr>
<td>Social status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>75%</td>
<td>76%</td>
</tr>
<tr>
<td>Social class 4 or 5</td>
<td>35%</td>
<td>21%</td>
</tr>
<tr>
<td>BMP</td>
<td>25.9 (19.9–32.5)</td>
<td>26.9 (20.6–36.1)</td>
</tr>
<tr>
<td>Total cholesterol ((\mu\text{mol/l}))^b</td>
<td>6.0 (4.3–8.0)</td>
<td>4.9 (3.2–8)</td>
</tr>
<tr>
<td>HDL cholesterol ((\mu\text{mol/l}))^b</td>
<td>1.2 (0.9–2.2)</td>
<td>1.2 (0.8–4.7)</td>
</tr>
<tr>
<td>LDL cholesterol ((\mu\text{mol/l}))^b</td>
<td>3.4 (1.8–5.0)</td>
<td>2.8 (1.9–6.1)</td>
</tr>
<tr>
<td>Triglycerides ((\mu\text{mmol/l}))^b</td>
<td>1.4 (0.4–3.5)</td>
<td>1.6 (0.4–9.9)</td>
</tr>
<tr>
<td>Blood pressure$^a$</td>
<td>140 (110–170)</td>
<td>130 (110–180)</td>
</tr>
<tr>
<td></td>
<td>80 (65–110)</td>
<td>80 (60–106)</td>
</tr>
</tbody>
</table>

$^a$Median (5th–95th percentiles).

PTCA, percutaneous transluminal balloon angioplasty; CABG, coronary artery bypass grafting; NYHA, New York Heart Association; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

### Need for an Operation

Among the 103 operation candidates, only 19 (18\%) required operation during the observation period.

### Economics

In the year before they began IR, the 99 operation candidates who completed the treatment had an average of 6.1 days in hospital, 1.9 visits to an outpatient clinic, 2.7 visits to their general practitioner, 1.7 visits to a cardiologist, and medication expenses of US $800. In the 3 years that followed, hospitalization was reduced by 96\%, the number of ambulatory hospital visits by 88\%, visits to their family doctor by 76\%, visits to a heart specialist by 84\%, and expenses for heart medication consumption fell by 78\% (Fig. 3). In order to estimate the economic consequences, we have compared the cost of operating on all of the 99 patients with that of treating them with IR and operating on only 19\%. The result is savings of US $12,000 per annum, per patient.
FIG. 1. Comparison of 3-year survival curves for 103 candidates for invasive treatment receiving integrated rehabilitation (IR), matched to the general Danish population for age, gender, and observation periods.

In the year prior to treatment, the 62 patients rejected for invasive treatment and who completed the treatment had an average of 11.3 days in hospital, 2.7 visits to an outpatient clinic, 5.0 visits to their general practitioner, 1.1 visits to a cardiologist, and medication expenses of US $1350. In the 3 years that followed, the number of days in hospital was reduced by 95%, the number of visits to outpatient clinics by 82%, and medication expenses fell by 73%. The number of visits to a cardiologist and general practitioner were reduced by 67% and 68%, respectively. Based on these reductions in the use of health care services, the total savings for this patient category were US $7,500 yearly per patient.

DISCUSSION

Our results illustrate that IR is beneficial for patients with severe heart disease and reduces medical expenses. However, it is necessary to discuss whether the findings are specific to particular patients, or generally applicable, and how well the control groups used match our patients.

Many factors, such as lifestyle, exercise, psychologic treatment, massage, and hence also IR, can influence the course of illness, even though randomized double-blind trials are not possible. However, observational studies can be used, and recent reviews concerning treatment of heart disease arrive at the same conclusion (Benson and Hartz, 2000; Concato et al., 2000; Ioannidis et al., 2001). This is similar to the recommendations of the American Heart Association and American College of Cardiology (Eagle et al., 1999), concerning the use of clinical databases for quality control comparisons between hospitals. Furthermore, an editorial in JAMA (Radford and Foody, 2001) points out that observational studies suffice to support practical recommendations when the effect size is large and the risk is low, as for example with advice to stop smoking. The same may be true for IR.

The present results are drawn from a patient database and information from annual questionnaires. Any quality control review has limitations such as expectation bias (because neither the patient nor the therapist can be blinded), selection bias (as patients are not randomly allocated to a treatment or a control group), lack of a control group, and because evaluation of the effect applies to the whole treatment and not to the individual components.

For IR and acupuncture, the patients and the therapist cannot be blinded. Patient and doctor expectations are known to influence the outcome in a large variety of trials (Rosenthal, 1969). However, in the present investigation patients rarely saw their doctors and still avoided operation and death. Accordingly, such sources of bias cannot explain the findings of this study.

Selection bias occurs when the clinician excludes too many patients from a trial (Economist, 1995). Moreover, selection bias occurs when some patients do not want to participate in the trial. Thus, in any study, population selection bias occurs. Nevertheless, conclusions from such studies have been applied to the patient population as a whole.

In a quality-control review, selection is unavoidable, since the patients have chosen the treatment or the hospital themselves. Evidence suggests that in angina pectoris patients, there is no significant bias due to patient choice of a particular treatment or from the referral factor (Morrison et al., 2002). There is no evidence to suggest that paying for a given treatment has an impact on the prognosis. We examined whether social selection had an effect on the results. As shown in Table 1, one third of our patients belonged to the lowest two social groups (4 and 5); 75% were married or had a partner (i.e. they did not differ from the Danish heart patients). In respect of baseline variables and the use of health care services in the year prior to treatment, our patients were not different from other Scandinavian heart patients (Andersson and Kartman, 1995). As we assume that
any possible and unintended selection bias must be constant during the observation period, the fact that the results improved significantly over time (Fig. 2), suggests an independent treatment effect, because although all patients received acupuncture, the self-care training program was changed significantly over time, with an increased emphasis on the preventive effect from acupuncture.

When comparing our patients to those 60,000 in New York who received invasive treatment, some differences in patient characteristics should be considered. In the New York study, patients who had had previous invasive treatment, with main stem stenosis, or who were admitted to other open-heart surgery procedures during the same admission, were excluded. Such patients have an increased death rate (Morrison et al., 2002; Savage et al., 1997), and 40% of our operation candidates belonged to one of these groups. The age and gender distribution between the groups showed no substantial differences. Concerning the anatomy of the coronary disease, an angiogram was not performed in 77% of our patients, as the treatment was initiated before this examination was planned to be performed, and the improvement associated with the treatment made the examination unnecessary. Thus, the presence of significant stenoses were not confirmed in this group. However, 90% of other Danish angina pectoris patients with positive exercise electrocardiograms (ECGs) were found to have significant stenoses (Madsen et al., 1997). In conclusion, an increased risk was to be expected among our patients. Yet the opposite was observed.

If evidence for the effectiveness of a treatment is only valid when based on a comparison between two identical groups in terms of all factors that can influence prognosis, this requirement has not been fulfilled with respect to invasive treatment of heart disease. Factors like smoking, weight, social conditions, depression, diet, alcohol, exercise, intake of aspirin, and cholesterol lowering medication have not been taken into account, and each of these factors can affect the prognosis for heart disease by more than 30% (Calle et al., 1999; de Lorgeril et al., 1999; Frasure-Smith et al., 1995; Groenbaek et al., 1995; Hakim et al., 1998; Hasdai et al., 1997; He et al., 1998; House et al., 1988; Leon et al., 1987; Pedersen et al., 1996).

We tried to compensate for bias by (1) using the toughest possible yardstick for comparison—the general population, and (2) using death rate as the effect variable, as death rate is not substantially affected by methodological limitations (Wulf, 1981), and by comparing with control groups consisting of thousands of patients in order to reduce the confidence limits. Finally, we have calculated the economic consequences of the treatment, which are unaffected by methodological limitations. Accordingly, we believe that this study offers reliable evidence of the positive effects of IR.

The benefit of conventional rehabilitation has been calculated to be a 20% reduction in the risk of death over a 3-year period, and savings in health expenses of US $110 per patient per annum (Taylor and Kirby, 1997). Others have shown that intensive lifestyle adjustments lead to regression of atherosclerosis, weight loss, decreased hospitalization, and need for invasive treatment (Ornish et al., 1990b; Ornish et al., 1998). However, risk of myocardial infarction and death were not affected in the study.
of Ornish et al. (1998). In comparison, our results appear significantly better than those for conventional rehabilitation and intensive lifestyle adjustments, as our patients obtained a lower risk of death than the general population.

In conclusion, IR reduced the risk of dying and the need for invasive treatment among patients with severe angina pectoris. Health care costs were also reduced. When compared to contemporary treatments, with respect to benefits, risk, and economic factors, the results invite further research, ideally testing in a randomized trial.

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Ornish D, Scherzitz LW, Billings JH, Brown SE, Gould KL, Merrill TA, Sparler S, Armstrong WT, Ports TA, Kirkeide RL,


Address reprint requests to:
Soeren Ballegaard, M.D.
Lenschovvej 1
DK 2900 Hellerup
Denmark

E-mail: sb@drballegaard.com