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European Journal of Cardiovascular Prevention & Rehabilitation 2011 18: 581 originally published online 31 January 2011
DOI: 10.1177/1741826710389392

Original scientific paper

European Journal of Cardiovascular Prevention & Rehabilitation

EUROPEAN SOCIETY OF CARDIOLOGY®

European Journal of Cardiovascular Prevention & Rehabilitation
18(4) 581–586

DOI: 10.1177/1741826710389392
ejcpr.sagepub.com

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In-patient cardiac rehabilitation versus medical care – a prospective multicentre controlled 12 months follow-up in patients with coronary heart disease

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Abstract

Background: The aim of this study was to evaluate a 3-week inpatient cardiac rehabilitation (Rehab) started early after the index event in patients with coronary heart disease and evidence-based secondary preventive medication.

Method: All patients had acute coronary angiography, 679 were discharged from hospital receiving usual care (Hosp), 795 completed a comprehensive Rehab. Follow-up was 12 months.

Results: Rehab patients were older (64 vs. 62 years; $p < 0.001$), had more multivessel disease (51 vs. 37%; $p < 0.001$), heart failure (64 vs. 40%, $p < 0.001$), ST-segment elevation myocardial infarction (59 vs. 52%, $p = 0.014$), and renal insufficiency (10 vs. 7%, $p = 0.036$). Gender, peripheral artery disease, diabetes, hypertension, and socioeconomic status were similar in groups. Rehab patients had more beta-blockers (88 vs. 75%, $p < 0.001$) and angiotensin-converting enzyme inhibitors (81 vs. 70%, $p < 0.001$), a lower low-density lipoprotein cholesterol (102 vs. 122 mg/dl, $p < 0.001$), and a higher proportion of non-smokers (44 vs. 39%, $p = 0.024$). Primary combined endpoint of mortality, myocardial infarction (MI), revascularization, and hospitalization occurred in 32.6% of Rehab patients and in 38.7% of Hosp patients [$p = 0.014$; absolute risk reduction 0.0615, relative risk reduction 16%, number needed to treat (NNT) 17]. Myocardial infarction (MI) (1.8 vs. 3.8%, $p = 0.015$; NNT 49) and hospitalization (31.8 vs. 38.0%, $p = 0.013$; NNT 17) were reduced. In multivariate analysis, primary endpoint was reduced significantly (OR 0.729; 95% CI 0.585–0.909; $p = 0.005$) giving a relative risk reduction of 27% in favour of Rehab.

Conclusion: Although Rehab patients were sicker at entry, their outcome was substantially improved within 12 months. With very low NNT, Rehab is highly effective and should be advised to all suitable patients with coronary heart disease.

Keywords

Cardiac rehabilitation, coronary heart disease, coronary intervention, follow-up, secondary prevention

Received 17 May 2010; accepted 25 July 2010

Introduction

Cardiac rehabilitation (CR) is recommended for patients with acute coronary syndrome, with stable angina and after coronary artery bypass graft surgery (CABG).[1,2] Meta-analysis consistently show that attendance in CR programmes is able to reduce morbidity and mortality of coronary heart disease (CHD) and to improve cardiac risk factors and quality of life.[3–7] These meta-analyses, however, predominantly included smaller and older trials that preceded contemporary therapy of CHD. Hence, it is questionable, whether

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positive results of CR may be transferred to a modern patient cohort. We therefore evaluated the benefits of CR in CHD patients treated with immediate revascularization and with evidence-based secondary preventive medication.[8,9]

Methods

Data of this study were derived from the multicentre randomized TeleGuard trial.[10] All patients had angiographically proven CHD presenting with acute coronary syndrome, stable stable angina or CABG and all participating hospitals offered 24-h percutaneous coronary intervention (PCI) facilities.[8,9] The study is an analysis of patients who either had cardiac rehabilitation thereafter (Rehab) or were directly discharged from hospital (Hosp) receiving usual care. The only exclusion criteria were ending of health insurance and patient's refusal.[10]

Inpatient rehabilitation started within 14 days after coronary angiography lasting 3–4 weeks. Comprehensive CR was performed with the focus on supervised exercise training, nutrition counselling, lifestyle modification, psychosocial intervention, and assistance regarding work environment including optimization of secondary preventive medication.[11,12]

The primary composite endpoint consisted of all-cause mortality, myocardial infarction, revascularization, and hospitalization. As secondary endpoints, distinct components of the primary endpoint were used. Patients of the Hosp group were recruited on the last day in hospital. Rehab patients were recruited on average 11.3 ± 3 days (median 11 days) later during CR. Hence, endpoint related events in the Hosp group were analysed only from day 12 on for the next 12 months. In the Rehab group, all endpoint-related events were counted from the day of inclusion. Health insurance provided complete endpoint data for all patients.

Statistical analysis

Data were analysed by SPSS version 16.0 (Chicago, Illinois, USA). Differences in subgroups were tested by chi-square test for categorical variables and by Mann–Whitney *U*-test for continuous variables. In bivariate analysis absolute and relative risk reductions and number needed to treat (NNT) were computed for the association of treatment modes (Rehab vs. Hosp) with the occurrence of the primary endpoint and the distinct components of this endpoint computing 95% confidence intervals according to Altman.[13] In logistic regression models, the impact of treatment modes on the primary endpoint was assessed including age, sex, telemedicine device, ST-segment elevation myocardial infarction (STEMI), stable angina, ejection fraction, 1–3-vessel disease, CABG, PCI, heart failure, renal failure, carotid stenosis, and medication as confounders in the model.

Results

Of 1500 patients, randomized in the TeleGuard trial,[10] 1474 patients (98.3%) entered this study and were followed for 12 months: 795 patients (53.9%) attended Rehab and 679 patients (46.1%) were directly discharged at home. Rehab patients were older, had more advanced CHD, more pronounced coronary risk factors, and more comorbidities than Hosp patients (Table 1). There was no difference between groups in telemedicine device prescription (49.3% vs. 49.8%), education, marital, socioeconomic, and psycho-social status. In Hosp patients, medication, blood lipids, and smoking habits were evaluated at discharge from hospital. Values of the Rehab group were obtained at discharge from CR (Table 2). The adherence to prescription was not monitored in both groups.

In bivariate analysis, less Rehab patients exhibited the primary endpoint (32.6% vs. 38.7%; $p = 0.014$) as compared to Hosp patients giving a NNT of 17 to prevent one composite endpoint within 12 months (Table 3). This result was driven by a reduction of hospitalization (31.8% vs. 38.0%; $p = 0.013$) and myocardial infarction (1.8% vs. 3.8%; $p = 0.015$), exhibiting a NNT of 17 and 49, respectively. In multivariate analysis, primary endpoint was reduced in Rehab patients (OR 0.729, 95% CI 0.585–0.909; $p = 0.005$; Table 4).

Discussion

Evidence of cardiac rehabilitation (CR) is mainly based on meta-analyses.[3–7] The papers of Oldridge et al.[3] and O'Connor et al.,[4] however, included studies published between 1972 and 1985. Hence, these results may not be generalized to contemporary CHD treatment. In the Cochrane analysis,[5] the latest study included was published in 1999 and the authors state that the incremental benefit of CR in patients with adequate secondary preventive medication has not been studied adequately. In the 2009 edition of their review,[14] no new studies were added. Taylor et al.[6] also stressed the poor methodological quality of many trials and 83% of the studies included were published between 1970 and 1999 preceding contemporary treatment strategies of CHD.

The meta-analysis of Clark et al.[7] reported 63 randomized controlled trials (RCTs) including 21,295 patients. However, two-thirds of the trials were

Table 1. Baseline parameters

	Hosp ($n=679$)	Rehab ($n=795$)	p
Age (years)	62.2 ± 10.3	64.1 ± 9.64	<0.001[a]
Age (years, range)	25–88	33–84	
Females	157 (23.1)	209 (26.3)	0.161[b]
Index diagnosis prior to inclusion			
STEMI	349 (52.2)	461 (58.7)	0.014[b]
NSTEMI	31 (4.6)	46 (5.9)	0.304[b]
Unstable AP	161 (24.1)	191 (24.3)	0.930[b]
Stable AP	148 (22.2)	104 (13.2)	<0.001[b]
Coronary intervention prior to inclusion			
CABG	189 (27.9)	447 (56.4)	<0.001[b]
PCI	425 (62.8)	353 (44.5)	0.001[b]
Coronary heart disease			
1-vessel disease	225 (33.3)	190 (24.0)	<0.001[b]
2-vessel disease	189 (28.0)	194 (24.5)	
3-vessel disease	252 (37.3)	404 (50.9)	
Left ventricular function			
LV-EF (%)	57.7 ± 13.9	54.4 ± 12.7	<0.001[b]
Comorbidities			
Atrial fibrillation	29 (4.3)	48 (6.1)	0.129[b]
Heart failure	268 (39.6)	509 (64.2)	<0.001[b]
Renal failure	46 (6.8)	78 (9.8)	0.036[b]
PAD	40 (5.9)	68 (8.6)	0.051[b]
Carotid stenosis	27 (4.0)	60 (7.6)	0.004[b]
Coronary risk factors			
Hypertension	536 (79.2)	636 (80.2)	0.625[b]
Hyperlipidaemia	503 (74.3)	629 (79.3)	0.023[b]
BMI (kg/m^2)			
<20	14 (2.2)	12 (1.7)	0.154[b]
20–25	131 (20.1)	174 (22.3)	
>25	506 (77.7)	529 (74.0)	
Diabetes mellitus type II	128 (18.9)	180 (22.7)	0.075[b]

Values are *n* (%) or mean ± standard deviation unless otherwise indicated. [a]Mann–Whitney *U*-test. [b]Chi-squared test. AP, angina pectoris; BMI, body mass index; CABG, coronary artery bypass graft surgery; Hosp, patients directly discharged from hospital, receiving usual care; LV-EF, left ventricular ejection fraction; NSTEM, non ST-segment elevation myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; Rehab, patients with cardiac rehabilitation subsequent to hospital stay; STEMI, ST-segment elevation myocardial infarction.

Table 2. Medication, blood lipids, and smoking habits

	Hosp ($n=679$)	Rehab ($n=795$)	p
Medication			
Beta-blockers	503 (75.1)	691 (87.5)	<0.001[a]
ACE inhibitors	472 (70.4)	640 (81.0)	<0.001[a]
Nitrates	112 (16.7)	30 (3.8)	<0.001[a]
Statins	529 (79.0)	638 (80.8)	0.391[a]
Platelet aggregation inhibitors	653 (97.5)	760 (96.2)	0.174[a]
Blood lipids			
Total cholesterol (mg/dl)	200 ± 49.9	174 ± 47.7	<0.001[b]
LDL-C (mg/dl)	122 ± 47.4	102 ± 35.5	<0.001[b]
LDL-C (mg/dl, median)	116	96	
HDL-C (mg/dl)	52.9 ± 37.3	42.2 ± 13.3	<0.001[b]
HDL-C (mg/dl, median)	44	40	
Triglycerides (mg/dl)	169 ± 127	145 ± 84.6	0.001[b]
Triglycerides (mg/dl, median)	139	125	
Smoking habits			
Non-smokers	262 (38.6)	353 (44.4)	0.024[a]

Values are *n* (%) or mean ± standard deviation unless otherwise indicated. ACE, angiotensin-converting enzyme; HDL-C, high-density lipoprotein cholesterol; Hosp, patients directly discharged from hospital, receiving usual care; LDL-C, low-density lipoprotein cholesterol; Rehab, patients with cardiac rehabilitation subsequent to hospital stay. [a]Chi-squared test. [b]Mann–Whitney *U*-test.

published until 1999, only 29% of patients were treated in the year 2000 or later and the studies of this latter era were rather small (median of 146 patients).[7] Nevertheless, the authors state that mortality benefits were of similar magnitude in recently published trials and in trials published more than two decades before. Again, methodological problems of the studies included were emphasized.[7] Invasive treatment strategies of acute CHD were not mentioned in these publications.[3–7] As a consequence, it is questionable, whether data derived from these meta-analyses may still be transferred to contemporary patients treated by rapid coronary revascularization during acute CHD including evidence-based secondary preventive medication in chronic disease.[5]

In this study, all participating hospitals offered 24-h PCI facilities. All patients had coronary angiography receiving adequate revascularization by PCI/CABG or a conservative approach, whichever was appropriate.[8,9] Secondary preventive medication was on a very high level in Rehab patients and Hosp patients showing no difference concerning antiplatelet drugs and statins. Whereas angiotensin-converting enzyme inhibitors and beta-blockers were prescribed significantly more often in Rehab patients (Table 2). The difference in medication might be one explanation for the better

Table 3. Clinical outcomes at 12 months

				Bivariate analysis		
	Hosp ($n = 679$)	Rehab ($n = 795$)	p	ARR (%)	RRR (%)	NNT
Primary endpoint	263 (38.7)	259 (32.6)	0.014	6.15	16	17
Hospitalization	258 (38.0)	253 (31.8)	0.013	6.17	16	17
AMI	26 (3.8)	14 (1.8)	0.015	2.07	54	49
Revascularization	37 (5.4)	33 (4.2)	0.243	1.30	24	77
All-cause mortality	16 (2.4)	17 (2.1)	0.778	0.22	9	455

Values are *n* (%). AMI, acute myocardial infarction; ARR, absolute risk reduction; Hosp, patients directly discharged from hospital, receiving usual care; NNT, number needed to treat; Rehab, patients with cardiac rehabilitation subsequent to hospital stay; RRR, percentage relative risk reduction.

Table 4. Predictors of primary composite endpoint at 12 months

	Odds ratio	95% confidence interval		p
		Lower limit	Upper limit	
Rehabilitation	0.729	0.585	0.909	0.005
STEMI	1.313	1.049	1.643	0.018
Age	1.015	1.003	1.026	0.012
Renal failure	1.498	1.026	2.188	0.036
Absolute term	0.212			<0.001

Odds ratios and *p*-values were calculated by multivariate analysis after being adjusted for age, sex, telemedicine device prescription, STEMI, stable angina, ejection fraction, 1-3-vessel disease, coronary artery bypass graft surgery, percutaneous coronary intervention, heart failure, renal failure, carotid stenosis, and medication with beta-blockers and angiotensin-converting enzyme inhibitors relative to outcome not being observed. STEMI, ST-segment elevation myocardial infarction.

outcome of Rehab patients as suggested by other studies.[15,16]

However, CR encompasses more than the sole prescription of evidence-based medication. Taking in mind, that medication with statins was similar in both groups, CR led to significantly lower levels of low-density lipoprotein cholesterol and triglycerides, the latter being influenced directly by nutrition habits. In addition, CR significantly increased the proportion of non-smokers (Table 2). As a result of the whole rehabilitation process, primary endpoint was significantly reduced with an absolute risk reduction of 6.2% within 12 months (Table 3). A NNT of 17 for the prevention of one primary endpoint or one hospitalization and a NNT of 49 to prevent one myocardial infarction show that CR was highly effective in reducing clinical events within the first year.

As these data are derived from bivariate analysis, it is possible that the higher proportion of CABG surgery in the Rehab group and the higher proportion of PCI in the Hosp group might have influenced the results. In the literature, however, the reported incidence of nonfatal myocardial infarction is inhomogeneous showing a similar incidence after CABG and PCI,[17–20] a lower incidence after CABG,[21] or a lower incidence after PCI.[22] Hence, the reduction of recurrent nonfatal myocardial infarction in this study is not necessarily caused by a selection bias towards CABG surgery in the Rehab group. In addition, patients in the Rehab group had significantly more three-vessel disease, heart failure, renal failure, generalized atherosclerosis, and a lower ejection fraction (Table 1). The index diagnosis of a STEMI, which was an independent negative outcome parameter (Table 4), was present significantly more often in the Rehab group. Hence, even though Rehab patients were older and sicker at entry, CR significantly reduced recurrent myocardial infarction within 1 year.

In multivariate analysis, CR reduced the primary endpoint as well (Table 4). This reduction was achieved on top of very high treatment rates for platelet inhibition, statins, angiotensin-converting enzyme inhibitors, and beta-blockers (Table 2) and in addition to a 100% coronary revascularization by PCI or CABG in the acute phase of CHD. Hence, this study shows that CR is able to generate an incremental benefit in contemporary patients with CHD, which had been questioned before.[5] Results of this study underscore the importance of lifestyle and nonpharmacological intervention in the treatment scenario of CHD.[23]

So far, CR regimes are not standardized across countries concerning type (inpatient vs. outpatient), length (3–4 weeks vs. 12–16 weeks) and main focus of therapy (exercised based vs. comprehensive counselling). In Germany, CR is usually offered on an inpatient basis with intensive rehabilitative activity on 6 days a week for 3–4 weeks duration starting no later than 14 days after the index event.[24] This is different from international studies.[3–7] where CR is

performed on an outpatient basis once or twice a week for 12–16 weeks duration. So far, there is only very limited data comparing these two systems.[25,26] Following a standard CR of 4-weeks duration after myocardial infarction, 3241 patients were randomized to receive further rehabilitative interventions monthly from month 1 to month 6, then every 6 months for 3 years.[27] This study failed to decrease the primary endpoint significantly assuming that an intervention of approximately 2 h every 6 months might be not enough to sustain the benefits of an early short-term CR during long-term follow-up.[27] Hence, positive results obtained with one particular type of CR must be transferred very carefully to other rehabilitative settings.

Limitations

This is a non-randomized study comparing patients attending CR or not. The results of this multicentre cohort study, however, reflect current management of CR in a large and unselected population in Germany. Results of this study represent a post-hoc analysis of the TeleGuard RCT.[10] Hence, primary and secondary endpoints were the same as in the TeleGuard trial and no subgroup analysis was prespecified for the particular CR setting. However, all data were prospectively assessed in the RCT, no patient was lost and health insurance provided complete data of all patients.

Conclusion

This study suggests a significant reduction of clinical endpoints by 3–4 weeks of inpatient CR started within 14 days after the index event in patients with CHD. This benefit was obtained in addition to rapid coronary revascularization and on top of an evidence-based preventive medication within 1 year. With a NNT between 17 and 49, CR is highly effective and should be offered to all suitable patients. However, the convincing advice to the patient to take part in CR is essential as personal factors rather than health status may still predict referral for CR.[28] Despite current recommendations, underutilization of CR is still common.[1,2] A sufficiently powered randomized trial is still required as non-randomized studies might exaggerate intervention benefits.

Acknowledgement

This study has been presented in part at the American Heart Association scientific sessions 2007.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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