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Prevalence and predictors of depressive symptoms and wellbeing during and up to nine years after outpatient cardiac rehabilitation

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Summary

BACKGROUND AND AIM: Depression is an important independent prognostic variable in cardiac patients. The prevalence and predictors of depressive symptoms up to nine years after cardiac rehabilitation were studied.

METHODS: Follow-up questionnaires were sent to 2199 patients who had completed a 12-week exercise-based outpatient cardiac rehabilitation (OCR) programme between June 1999 and March 2006. Medical outcome, general wellbeing, and depressive symptoms were assessed, the latter by using two screening questions according to Arrol. Patients with incomplete data due to language problems, lack of compliance and non-response were excluded.

RESULTS: Complete data for analysis was available for 710 patients. The median follow up period was 46 months (Interquartile range (IQR) 22-71, min. 6 months). At follow-up, 132 patients (19%) indicated low wellbeing, whereas 81 (11%) were having depressive symptoms.

Multivariate analyses revealed impaired quality of life (p <0.001), diabetes (p = 0.013) and low exercise capacity after OCR (p = 0.003) to be independent predictors of low wellbeing at follow-up. Persistent smoking (p = 0.045) as well as negative mood (p = 0.022) at the end of OCR were independent predictors of depressive symptoms at follow-up.

CONCLUSIONS: In a selected patient population a mean of four years after OCR, persistent smoking, diabetes, low exercise capacity and impaired quality of life at the end of OCR were independent long term predictors of low wellbeing and depressive symptoms, rather than specific cardiac variables. This highlights the need for close cooperation between cardiovascular and psychological specialists in cardiac rehabilitation.

Key words: *depression; late follow-up; cardiac rehabilitation*

Introduction

Depression is known to be present in a substantial number of cardiac patients. Major depression has been found in the range of 20% of patients by several authors [1–3], and minor depression has been described in up to 27% [4].

Clear causal relationships have not been described so far but there is general consensus about the independent prognostic impact of a depressive state on morbidity and mortality after myocardial infarction [5–7].

Among a range of pathophysiological explanations for the inter-relationship between depression and cardiovascular disease are adrenergic activation [8, 9], autonomic imbalance [10] and altered behaviour [11], which in turn may increase the cardiovascular risk profile [4]. In addition, several psychosocial variables and personality traits have been found to be related to depressive symptoms and to independently influence cardiovascular diseases [11–13]. It is therefore of interest to study the course of depressive symptoms during and late after cardiac rehabilitation.

The current study aimed to assess the prevalence of depressive symptoms in patients undergoing outpatient cardiac rehabilitation at three different points in time, namely at the beginning and at the end of a 12 week rehabilitation programme as well as at a late follow-up after several years. Furthermore, predictive variables of late depressive symptoms and low wellbeing were sought.

Methods

From June 1999 through to March 2006, a total of 2199 patients were enrolled in the outpatient cardiac rehabilitation programme of the University Hospitals in Basel.

An estimated 30% of all cardiac patients in the referring hospitals enter this programme, whereas another 30% are referred to an inpatient setting and some 40% follow individual pathways.

Outpatient cardiac rehabilitation programme (OCR)

KARAMBA is an exercise based comprehensive cardiac rehabilitation programme with a 12-week duration mainly for patients with coronary heart disease (acute coronary syndromes mostly with acute revascularisation by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)) [14].

Patients follow a structured exercise programme with a total of 36 exercise sessions under medical supervision, in four levels according to their physical capacity.
Patient education concerning diet, disease knowledge, risk factors, and lifestyle modification and stress management was covered during a total of 10 hours.

Measurements before and after cardiac rehabilitation
For the purpose of this study, measurements at three points in time were used. These time points were at the start of the OCR, at the end of OCR (12 weeks) and at a late follow-up by questionnaires sent out a mean of four years after completion of the OCR (min. 2 years, max. 9 years after completion of OCR).

Medical and demographic variables
Parameters included in the analysis were demographic data, reasons for referral, risk factors, medication, left ventricular ejection fraction (LVEF) (assessed by angiography, szintigraphy or echocardiography), and results of symptom-limited maximal exercise testing at the start and at the end of the OCR. Reasons for discontinuation of the programme and cardiac and non-cardiac complications were noted.

Quality of life
Quality of life was assessed at the start and at the end of the OCR using the PLC questionnaire. PLC means "Profil der Lebensqualität chronisch Kranker", and was developed and described by Siegrist et al. [15]. This is a generic German questionnaire developed to measure time dependent variables of health in chronic diseases, applicable and validated in a broad spectrum of patients [16]. It is however not a disease-specific instrument for the diagnosis of depression. Measurements can be grouped into three dimensions: somatic, psychological and social. Questions relate to the last 7 days and weighted responses are given between 0 and 4 points. To avoid response biases, the questions are posed negatively or positively in an unsystematic way. There are 40 questions resulting in 6 scales:
Scale 1 subjective physical capacity
Scale 2 psychological functioning (ability to enjoy life and relax)
Scale 3 positive mood
Scale 4 negative mood (inverse scale)
Scale 5 social functioning (ability to relate)
Scale 6 social wellbeing (sense of affiliation)
For the definition of depressive symptoms in this study 8 items of PLC forming scale 4 (negative mood) were used. A value below the 25th percentile was set to classify the patient as "depressive" (i.e., to have depressive symptoms).

Measurements at follow-up
In the year 2008, all patients who could communicate using the German language were sent a questionnaire which included questions on morbid events, hospital admissions, current wellbeing and two screening questions for depression. The diagnostic accuracy of these questions was analysed and described by Arrol [17].

Screening questions according to Arrol:
"During the past month, have you often been bothered by feeling down, depressed or hopeless?"
"During the past month, have you often been bothered by little interest or pleasure in doing things?"

General wellbeing at late follow-up was assessed using the following question
"How did you generally feel in the last days?"
From five possible answers that were offered, the following categories were built:
Very well / well = intact wellbeing
Moderately bad / rather bad / bad = low wellbeing

Statistical analyses and tests
Univariate analyses were made comparing groups of patients with or without depressive symptoms and with low or intact wellbeing respectively. Chi-square and Fisher's exact tests were used to test for statistical significance between the groups.
Multiple logistic regression analyses were performed with both low wellbeing and depressive symptoms at follow-up as dependent variables, using significant variables of the univariate analyses as possible predictors. Odds ratios (OR) with 95% confidence intervals (CI) and *p*-values for significance were calculated.

Results

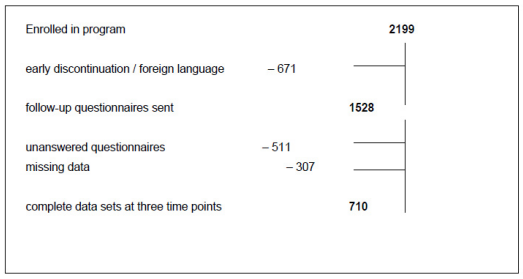

Figure 1
Flow diagram of patient inclusion.

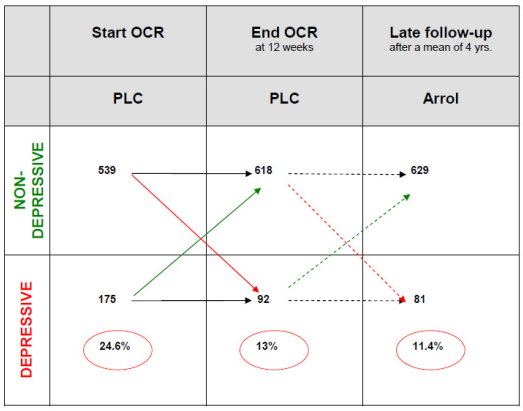

Figure 2
Prevalence of depressive symptoms at three time points in 710 patients undergoing outpatient cardiac rehabilitation (OCR) using two separate instruments of assessment (PLC and Aroll, see text).

Complete data sets at all three time points of measurements were available from 710 patients, which form the basis of the current study. A flow diagram of patient inclusion and reasons for exclusion is shown in figure 1.

The main reasons for the substantial reduction in numbers were a lack of understanding of the German language which excluded the meaningful answering of the follow-up questionnaire, and early drop out of the programme or lack of exercise tests at the end of the programme.

Table 1 shows a comparison of patients included in the follow-up and those not responding at the late follow-up.

Time course of symptoms

At the beginning of outpatient cardiac rehabilitation (OCR), 175 (24.6%) patients were classified as having depressive symptoms (fig. 2). At the end of OCR, the number was reduced to 92 (13%, p <0.001), consisting of 58 patients remaining depressive and 34 patients who were newly classified as depressive, whereas 117 patients improved.

The median follow-up was 46 months (Interquartile range (IQR) 22-71; min. 6, max. 108 months). At the late follow-up after a mean of four years, the number of patients suspected to be depressive (both Arrol questions positive) was 81 (11.4%). These consisted of 32 patients already classified as depressive by the PLC-scale at the end of OCR and 49 patients newly classified as depressive. In 60 patients an improvement was noted.

Predictors for depressive symptoms and wellbeing at late follow-up

Several variables from the initial data set were used in a univariate analysis of the Arrol classification at late follow-up (table 2).

In the univariate analysis, the following variables were significantly more prevalent in depressive versus non-depressive patients: post coronary bypass surgery, persistent smoking at the end of OCR, and worse PLC-scores for psychological function and negative mood at the beginning of OCR.

The same univariate analysis was performed for general wellbeing at late follow-up (table 3). Lower general wellbeing was significantly correlated to lower exercise capacity at the end of OCR, to the presence of peripheral arterial occlusive disease (PAOD), diabetes and to worse scores for all parameters of quality of life before and immediately after OCR.

After the univariate analysis, a multivariate analysis for depressive symptoms and wellbeing at late follow-up was performed, and the results are given in tables 4 and 5.

Significant independent predictors of depressive symptoms at late follow-up (according to both Arrol's questions being positive) were persistent smoking at the end of OCR (OR: 1.827, 95% -CI: 1.014–3.293, p-value: 0.045) and PLC-scale 4 (negative mood) before OCR (OR: 0.711, 95% -CI: 0.532–0.952, p-value: 0.022).

Significant independent predictors of intact wellbeing at late follow-up were: high PLC-scale 2 prior to OCR (ability to enjoy life and relax) (OR: 0.32, 95% -CI: 0.217–0.472, p-value: <0.001); high PLC-scale 1 after OCR (subjective physical performance) (OR: 0.319, 95% -CI: 0.224–0.454, p-value: <0.001); peak exercise capacity (OR: 0.99, 95% -CI: 0.984–0.997, p-value: <0.003) as well as the absence of diabetes mellitus (OR: 2.105, 95% -CI: 1.17–3.786, p-value: <0.013).

Discussion

The current study shows that low quality of life scores, diabetes and low exercise capacity during OCR were independent predictors of *low general wellbeing* a mean of four years after OCR. Persistent smoking and negative mood after OCR independently predicted *depressive symptoms* at late follow-up. It seems plausible that these results would have been even stronger if the drop outs comprising of more smokers and depressive patients (as shown in table 1) could have been included in the final analysis. Negative mood, smoking and diabetes as well as low exercise capacity in most cases are premorbid characteristics, thus highlighting the fact that a pre-morbid state is often more important for the late psychological outcome than the acute cardiac event itself. Only few studies have been published covering such a long follow-up, and one of them confirms the crucial role of general wellbeing and psychosocial care for long term survival of chronic cardiac patients [18]. It is of note that in our study, the predictive variables for long term wellbeing and state of mood were independent of and more important than some of the known medical variables such as LVEF, a fact which is also known for endpoints such as morbidity and mortality late after myocardial infarction [12].

Table 1: Comparison of responders and non-responders at late follow-up.

Variables (end OCR) % (except age)	Responders (N = 1017)	Non-responders (N = 511)	p-value (Fisher's exact test)
Age (mean years, +SD)	61.7 ± 10.6	54.7 ± 11.2	< 0.0001
Female gender	13.3	16.5	= 0.06
Postop CABG	28.0	20.2	< 0.0001
Watt >150	47.0	46.1	n.s.
Persist. smoking	12.9	27.4	< 0.0001
BMI >25	62.8	67.1	= 0.056
Stable Partnership	89.5	81.0	= 0.001
Depression	30.4	38.3	= 0.027

OCR = outpatient cardiac rehabilitation
CABG = coronary artery bypass grafting
BMI = Body mass index

Methods of assessment

Arrol screening questions

For the purpose of the follow-up, a condensed questionnaire had to be developed asking for a host of different variables and end-points and therefore a simple tool for assessing depressive symptoms was incorporated. In the publication by Arrol et al. [17] data are given to highlight the diagnostic accuracy of the two questions. Among 421 participants screened in 15 general practices in New Zealand and compared to extensive validated diagnostic interviews, the sensitivity was 95% (CI 83–99%) and the specificity was 67% (CI 62–72%). Most cases of depression were therefore correctly identified in a general practice population.

PLC

The PLC questionnaire developed by Siegrist et al. [15] has several advantages.

Patients themselves rate their quality of life (QoL) in different ways and it is one of the few validated questionnaires available in the German language without translation.

According to the results of this questionnaire it seems possible to gain a better understanding of the expectations of patients and the reasons for their low satisfaction in order to improve their motivation and compliance with changes in life style.

We fully recognise that there is a gap between the diagnosis of depression using a disease-specific questionnaire and our definition of "depressive symptoms". For the sake of clinical applicability in a multidisciplinary setting like cardiac rehabilitation, the use of PLC seems appropriate and justified. In order to maximise the response rate at follow-up the two very short screening questions (Arrol) were used in addition to a series of other more medical follow-up questions (on morbidity, medication and risk factors).

The prevalence of patients with depressive symptoms in patients with heart disease was comparable to the figures generally found in the literature [2–4] and the figures slightly declined over time, although there were some patients newly classified as depressive at the late follow-up only. This is however no stringent comparison, since the screening questions used at follow-up must have included some other individuals than the classification by the PLC as used during OCR. For comparison it is interesting to note that the lifetime prevalence in a sample of the general population in Switzerland was 18% for major depression and 35% for all forms of minor depression [19] which is in the

Table 2: Univariate analysis for depressive symptoms at late follow-up.

Variable	Depressive according Arrol	Non-depressive	*p-value*
N	81	629	
Age (years)	62.3 ± 9.2	62.6 ± 9.8	*0.792*
Female gender	11.1%	16.9%	*0.261*
Exercise capacity at end of OCR (Watt)	160 ± 54.4	152 ± 46.6	*0.187*
Exercise capacity % target	100.8 ± 30.8	99.2 ± 26.6	*0.643*
LVEF (%)	58 ± 12.6	57 ± 13.3	*0.368*
Post CABG	31 (38.3%)	177 (28.1%)	*0.069*
PAOD	6 (7.4%)	35 (5.6%)	*0.452*
Hypertension	40 (49.4%)	359 (57.1%)	*0.193*
Diabetes	6 (7.4%)	82 (13%)	*0.208*
BMI	26.1 ± 2.7	26.3 ± 3.6	*0.451*
Persist. smoking at end of OCR	17 (21%)	77 (12.2%)	*0.036*
Stable partnership	76 (93.8%)	555 (88.7%)	*0.185*
PLC scale 1 start OCR	2.18 ± 0.8	2.28 ± 0.8	*0.306*
scale 2	2.59 ± 0.7	2.73 ± 0.6	*0.111*
scale 3	2.18 ± 0.8	2.27 ± 0.7	*0.319*
scale 4	2.76 ± 0.8	2.97 ± 0.8	*0.028*
scale 5	2.69 ± 1.7	2.66 ± 0.7	*0.869*
scale 6	3.11 ± 0.8	3.25 ± 0.6	*0.154*
PLC scale 1 end OCR	2.86 ± 0.8	2.97 ± 0.7	*0.247*
scale 2	2.99 ± 0.7	3.05 ± 0.6	*0.442*
scale 3	2.59 ± 0.8	2.61 ± 0.7	*0.773*
scale 4	3.11 ± 0.8	3.24 ± 0.7	*0.171*
scale 5	3.02 ± 0.7	3.07 ± 0.6	*0.564*
scale 6	3.22 ± 0.6	3.25 ± 0.6	*0.65*

Abbreviations: LVEF= left ventricular ejection fraction;
PAOD = peripheral arterial occlusive disease;
PLC = "Profil der Lebensqualität Chronischkranker" (quality of lfe scores);
Scale 1 subjective physical capacity
Scale 2 psychological functioning (ability to enjoy and relax)
Scale 3 positive mood
Scale 4 negative mood (inverse scale)
Scale 5 social functioning (ability to relate)
Scale 6 social wellbeing (sense of affiliation)

Other abbreviations see table 1

same range as the figures for cardiac patients, whereas depression as a comorbid condition was found in up to 23% of patients in large WHO surveys [20]. However, prevalence figures assessed by specific diagnostic tools may differ considerably from those found by the instruments used in the current study.

The interdependence of smoking and depression is well known [21]. Antidepressant effects of nicotine have been described [22, 23] and smoking may therefore partly be seen as an attempt of self-healing in depressive patients [24]. As cessation of smoking is one of the most important measures in secondary prevention of atherosclerotic diseases it seems worthwhile to address the proper identification and treatment of depressive patients in order to improve smoking cessation rates [25–30].

From our findings, we conclude that further specialist evaluation of patients with depressive symptoms emerging from screening questions or generic instruments assessing quality of life during cardiac rehabilitation is recommended, be it by disease-specific questionnaires or by personal intervention. It seems highly important that cardiologists cooperate closely with psychotherapists and psychiatrists to make best use of cognitive behavioural and pharmacological antidepressant therapies in selected patients. As to how many of the patients with depressive symptoms in our population of outpatient cardiac rehabilitation ultimately benefit from this type of care is not exactly known. In our experience, only a minority of patients with depressive symptoms currently benefit from specialist evaluation and care.

Limitations

The patients included in this analysis certainly represent some positive selection. This can be seen from the comparison of baseline characteristics between responders and non-responders to the follow-up questionnaire in table 1. Another substantial number of patients were not included in the follow-up because they were judged unable to respond to a complex German questionnaire.

Table 3: Univariate analysis for global wellbeing at late follow-up.

Variable	Low wellbeing	Intact wellbeing	*p*-value
N	132	576	
Age (years)	63.4 ± 9.6	62.3 ± 9.7	*0.271*
Female gender	20.5%	15.3%	*0.151*
Exercise capacity end OCR (Watt)	128.7 ± 36.9	158.7 ± 48.1	*<0.001*
Exercise. capacity % target	85.5 ± 21.4	102.6 ± 27.3	*<0.001*
LVEF (%)	45 (34.1%)	162 (28.1%)	*0.203*
Post CABG	57 ± 14.1	58 ± 12.4	*0.478*
PAOD	16 (12.1%)	25 (4.3%)	*0.001*
Hypertension	70 (53%)	327 (56.8%)	*0.439*
Diabetes	26 (19.7%)	61 (10.6%)	*0.008*
BMI	26.6 ± 3.3	26.2 ± 3.6	*0.242*
Persist. smoking end OCR	20 (15.2%)	73 (12.7%)	*0.475*
Stable Partnership	113 (85.6%)	518 (90.2%)	*0.12*
PLC scale 1 Start OCR	1.8 ± 0.7	2.37 ± 0.7	*<0.001*
scale 2	2.25 ± 0.6	2.82 ± 0.6	*<0.001*
scale 3	1.79 ± 0.7	2.37 ± 0.7	*<0.001*
scale 4	2.47 ± 0.8	3.06 ± 0.7	*<0.001*
scale 5	2.23 ± 0.7	2.76 ± 0.9	*<0.001*
scale 6	2.9 ± 0.7	3.31 ± 0.6	*<0.001*
PLC scale 1 end OCR	2.4 ± 0.6	3.09 ± 0.6	*<0.001*
scale 2	2.6 ± 0.6	3.15 ± 0.5	*<0.001*
scale 3	2.12 ± 0.6	2.72 ± 0.7	*<0.001*
scale 4	2.76 ± 0.8	3.34 ± 0.6	*<0.001*
scale 5	2.65 ± 0.7	3.16 ± 0.5	*<0.001*
scale 6	2.9 ± 0.8	3.33 ± 0.6	*<0.001*
Abbreviations see table 2.			

Table 4: Multivariate analysis of predictors of depressive symptoms at late follow-up.

	OR	95%-CI	*p-value*
Persistent smoking at end of OCR	1.827	1.014–3.293	*0.045*
PLC neg. Mood	0.711	0.532–0.952	*0.022*

Table 5: Multivariate predictors of low wellbeing at late follow-up.

	OR	95%-CI	*p-value*
PLC scale 2 start (high)	0.32	0.217–0.472	*<0.001*
PLC scale 1 end OCR (high)	0.319	0.224–0.454	*<0.001*
Diabetes mellitus	2.105	1.17–3.786	*0.013*
High exercise capacity (Watt)	0.99	0.984–0.997	*0.003*

A second point was the fact that we assessed depression (i.e., depressive symptoms) by two different methods during OCR and at late follow-up for practical reasons (length of questionnaire), and therefore a direct comparison of prevalence at all three measurement points is not meaningful. The use of a generic rather than a disease-specific questionnaire also prohibits the strict comparison of prevalence rates of depression in other populations. This does however not influence the analysis of predictors for depressive symptoms and wellbeing at the long term follow-up, which was the main aspect of this study.

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