Predictive Relationship Between Depression and Physical Functioning After Coronary Surgery

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Background: Depression is a prevalent condition in patients undergoing coronary artery bypass graft surgery (CABG) and is often associated with a less favorable health status. The aim of this study was to investigate the relationship between depression and physical functioning in patients undergoing CABG.

Methods: The analyses were based on a sample of 883 consecutive subjects (aged 35-93 years; 19.8% women) undergoing CABG. Depression was assessed using the Patient Health Questionnaire (PHQ); the subscale “physical functioning” was taken from the 36-Item Short-Form Health Survey. Questionnaires were administered 1 to 3 days before surgery (T1) and 2 months (T2) and 1 year (T3) after surgery.

Results: A cross-lagged path analytic model showed that an increase in depressive symptoms predicted a decrease in physical functioning ($\beta_{T1,T2} = -0.15$ [P < .001]; $\beta_{T2,T3} = -0.17$ [P < .001]), but not the other way around. Multigroup comparisons revealed one moderator effect: in patients with systolic heart failure (left ventricular ejection fraction [LVEF], ≤45%), the effect of depression on physical functioning from T2 to T3 was significantly stronger than in patients with preserved LVEF ($\beta_{T2,T3} = -0.30$ [P < .001] vs $\beta_{T2,T3} = -0.14$ [P < .001]; $\chi^2_{diff}=3.885$ [P = .049]).

Conclusions: More attention should be paid to diagnosis and treatment of depression in patients undergoing CABG. After surgery, patients with systolic heart failure and depressive symptoms in particular seem at risk of a deterioration of their physical functioning.

Arch Intern Med. 2010;170(19):1717-1721
The cross-lagged panel design showing cross-lagged longitudinal (a), cross-sectional (b), and longitudinal (c) paths. PF indicates physical functioning; T1, 1 to 3 days before surgery; T2, 2 months after surgery; and T3, 1 year after surgery.

**Figure 2.** Flowchart of participants.

dictive inference has not yet been clarified for this context: Is depression predictive of a deterioration in health status after the surgery or is a change in health status for the worse predictive of an increase in depression? To answer this question, we tested the longitudinal, cross-lagged associations between depressive symptoms and physical functioning within a single model. In addition, we sought to explore whether the relationship between depression and physical functioning was moderated by gender, age, partner status, or HF.

**METHODS**

After the institutional review board approved the study protocol, potential candidates were identified through daily screening of the admission records. The initial sample consisted of 1570 consecutive patients undergoing CAGB at the Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum (German Heart Institute) Berlin, Berlin, Germany, between January 1, 2005, and July 31, 2008. Exclusion criteria were (1) inability to read or answer the study questionnaires (eg, dementia, difficulties with the language) and (2) age younger than 18 years. All patients participating provided written consent. Questionnaires were administered 1 to 3 days before surgery (T1), 2 months after surgery (T2), and 1 year after surgery (T3). Clinical and sociodemographic data were abstracted from case report forms.

The depression module of the 9-Item Patient Health Questionnaire (PHQ-9) was used to assess depressive symptoms. The sum score ranges from 0 to 27, with higher values indicating higher levels of depression. The German version has shown excellent reliability, validity, and sensitivity. The subscale “physical functioning” (PF) from the 36-Item Medical Outcomes Study Short-Form health survey (SF-36) was used to assess the subjective PF. The scale consists of 10 items eliciting concrete subjective responses about physical limitations due to health, such as using stairs and lifting objects. The raw score was transformed to a score ranging from 0 (severe impairment) to 100 (no impairment). Excellent psychometric properties have been reported for the German version of the SF-36.

**STATISTICAL ANALYSES**

Structural equation modeling was used to estimate and evaluate the cross-sectional and prospective associations of depression and PF. For correlative data in panel studies, cross-lagged panel designs allow for a direct test of the predictive relationship between 2 variables. This method takes into account time precedence and controls for multivariate dependencies of the antecedent predictor variables. Therefore, in addition to the cross-lagged paths between depression and PF and between PF and depression (Figure 1, path a), the longitudinal structural paths reflecting changes in depression and PF, respectively (Figure 1, path c) as well as the cross-sectional covariances between depression and PF (Figure 1, path b) were taken into account. The predictive priority of either PF or depression could be assumed only if the respective predictor (depression or PF) made an independent contribution to the crossed criterion (PF or depression, respectively) after controlling for the effects at earlier time points and cross-sectional associations.

Because cross-lagged path models are based on continuous variables, the scales for depression and PF were used in their continuous form. Depression and PF were understood as latent constructs, which were estimated by 2 randomly selected split-half “subtests” at all 3 measurement points. To detect moderator effects, constraints that required the cross-lagged paths to be equal were imposed on the model and tested through hierarchical model comparisons. The following subgroups were tested for differences in the cross-lagged paths: (1) patients with systolic HF, as defined by a left ventricular ejection fraction (LVEF) below 45%, vs preserved LVEF; (2) age below vs above the median of 67 years; (3) men vs women; and (4) patients living alone vs living with a partner.

The statistical analyses were performed using AMOS 7.0 for structural equation modeling. Statistical software SPSS 16.0 was used to conduct t tests for independent samples; if the variables were categorical, χ² tests were used. Changes in depression and PF over time were tested by ANOVAs. For all analyses, P < .05 was considered statistically significant.

**MISSING DATA ANALYSIS**

Of 1917 consecutive patients, 1610 consented to the study; 1570 patients fulfilled the inclusion criteria and returned the questionnaire at the first measurement point (Figure 2). Of these patients, 112 (7.1%) died during the 1-year follow-up. For all patients who were not identified as deceased, we were able to confirm vital status by directly contacting the patient or his or her general practitioner. A total of 883 patients (56.2%) responded at all 3 time points (“continuer sample”).

Missing data due to item nonresponse were estimated using the expectation maximization algorithm. To show potential effects of attrition on a unit level, Table 1 gives all study variables for the full sample as well as for continuers and noncontinuers separately. A higher proportion of noncontinuers compared with continuers were living without a partner, were more...
Table 1. Baseline Characteristics for Full Sample, Continuers, and Noncontinuers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Full Sample (N=1570)</th>
<th>Continuers (n=883)</th>
<th>Noncontinuers (n=687)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66.91 (9.04)</td>
<td>66.74 (8.40)</td>
<td>67.13 (9.82)</td>
<td>.41</td>
</tr>
<tr>
<td>Living alone, %</td>
<td>26.94</td>
<td>22.0</td>
<td>33.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female, %</td>
<td>23.25</td>
<td>19.7</td>
<td>27.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>54.47 (13.97)</td>
<td>56.33 (13.28)</td>
<td>52.0 (14.48)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>5.99 (4.61)</td>
<td>5.38 (4.09)</td>
<td>6.76 (5.09)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>52.20 (27.03)</td>
<td>56.29 (26.07)</td>
<td>46.1 (27.32)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: LVEF, left ventricular ejection fraction.

Descriptive data are presented in Table 1. The following results are presented for the continuer sample (n=883; 19.8% women) unless otherwise specified. Mean age was 66.74 years (range, 35-93 years), mean LVEF was 56.29%. The prevalence for major depression in our patient population was 8.5%, compared with a rate of 3.8% obtained from a German representative sample also using the PHQ-9.22 Over 1 year, PF improved significantly (main effect for time, F<sub>2,882</sub>=80.809; P<.001). Accordingly, there was a decline in depressive symptoms (main effect for time, F<sub>2,882</sub>=3.132; P=.04).

**PREDICTIVE RELATIONSHIP OF DEPRESSION AND PF**

**Figure 3** displays the empirical estimates for the cross-lagged panel model, which allows the identification of the predictive directionality between the constructs “depression” and “PF” (overall model fit, χ²=275.28; P<.001). Indices of approximate fit that are robust to sample size showed a sufficiently close fit of model variables (CMIN/df [minimum value of the discrepancy function divided by degrees of freedom], 6.714; RMSEA [root mean square error of approximation], 0.08; CFI [comparative fit index], 0.98; and NFI [normed fit index], 0.97). The model fit can thus be classified as acceptable to good. Controlling for the respective cross-sectional and baseline scores, depressive symptoms showed a pronounced predictive priority over PF. This predictive priority could be demonstrated for both time intervals: from baseline (T1) to 2 months after surgery (T2) and from 2 months (T2) to 1 year after surgery (T3). In contrast, the paths from prior PF to later depression were not significant (Figure 3).

Nested multigroup model comparisons were conducted to detect moderator effects. Standardized regression weights (β) for all subgroups are given in Table 2. Assuming group independent model parameters by simultaneously restricting all model paths to be equal between patients with systolic HF and patients with preserved LVEF, no overall group differences could be found (χ²diff=8.712; P=.07). However, on a path-specific level the path leading from depression 2 months after surgery to PF 1 year after surgery indicated significant group differences (χ²diff=3.885; P=.049). Thus, in patients with systolic HF, changes in depression over this period were significantly more closely related to changes in PF compared with patients with preserved LVEF (Table 2). No moderator effects were found for gender (χ²diff=4.393; P=.36), age (χ²diff=1.876; P=.76), and partner status (χ²diff=2.009; P=.73). For these groups, the unconstrained initial model was valid.

To avoid interpretation bias caused by dropout of patients, the analyses were repeated on the full sample (N=1570) (see “Methods” section). Again, standardized regression weights indicated that depressive symptomatology was related to deterioration of PF (β<sub>T1-T2</sub>=−0.12 [P<.001]; β<sub>T2-T3</sub>=−0.18 [P<.001]; continuer sample, β<sub>T1-T2</sub>=−0.15 [P<.001]; and β<sub>T2-T3</sub>=−0.17 [P<.001]), whereas there was no evidence for a predictive inference from PF to depressive symptomatology (β<sub>T1-T2</sub>=−0.01 [P=.71]; β<sub>T2-T3</sub>=−0.04 [P=.26]; continuer sample, β<sub>T1-T2</sub>=−0.03 [P=.44]; and β<sub>T2-T3</sub>=−0.01 [P=.74]). Model fits were also good (CMIN/df, 3.934; RMSEA, 0.04; CFI, 0.98; and NFI, 0.97). In accordance with the analyses based...
The present study provides strong support for the assumption that depression may lead to a deterioration of PF in patients after CABG, but a bad health status is not predictive of an increase in depression in this context. The influence of depression on the course of recovery after cardiac events or a bypass operation has been the object of intense debate over the past few years. Findings of Rumsfeld et al. and Mallik et al. showed that depression appeared to be a strong inverse risk factor for worse quality of life after CABG. In a study testing the opposite path, post-CABG depression status was predicted by somatic factors such as chronic noncardiac illnesses, postoperative fatigue, and shortness of breath.

Surprisingly, to our knowledge, no study to date has assessed the bidirectional influences of depression on PF and PF on depression in the context of CABG. To meet the methodological challenge that is connected to this question, the present study applied a cross-lagged panel design. Three associations were possible: (1) poorer PF could be predictive of an increase in depressive symptoms, (2) a higher level of depression could be predictive of a deterioration in PF, or (3) there could be a reciprocal relationship with no superiority of either path. In the present study, depressive symptoms clearly predicted PF, but PF did not predict depressive symptomatology. The predictive priority of depression over PF could be demonstrated for both time intervals of inter-est: from baseline to 2 months after surgery and from 2 months to 1 year after surgery. With the use of multi-group comparisons in structural equation modeling, it was also possible to directly compare several subgroups with respect to the previously described longitudinal paths. The strength of these paths did not differ with respect to gender, thus departing from the results of other studies, which reported a stronger relationship between depression and PF in women than in men.

It should be noted that comparison with these studies is of limited value, because none of these studies controlled for the cross-sectional and cross-lagged relationships. Our results indicate that only in the subgroup of patients with systolic HF did the paths differ from that of patients without HF. Two months after surgery, there was a significant effect from depression on PF in patients with systolic HF, which could not be shown in patients with preserved LVEF. Several studies have explored the relationship between depression and self-reported quality of life or risk of functional decline in patients with HF. In patients undergoing bypass surgery, longstanding HF may have already led to a reduction of resources and may thus amplify the stress that is induced by the surgery, whereas patients without a history of HF may have psychological resources that enable them to cope better with the additional stressor of a CABG surgery.

Several psychological mechanisms by which depression may produce increased risk for patients with CHD have been studied. For example, depression is associated with a number of behavioral risk factors and non-adherence to medication. How these mechanisms influence the relationship between depression and PF is not yet clear. As our study was not experimental in design, the existence of additional variables influencing the association between depression and PF cannot be excluded and should be subject to further studies. Further studies are also needed to elucidate possible behavioral and pathophysiological pathways for the association of depression and PF in CABG patients.

There are possible limitations to this study, which should be taken into account when interpreting the results. First, the PHQ-9 is a brief screening instrument to assess severity of depressive symptoms and cannot replace a formal clinical diagnosis of depression. However, since there is strong evidence for both high sensitivity and specificity when diagnosing major depression, this instrument seems appropriate for the investigation of epidemiological questions. Second, with respect to the first measurement point, it cannot be excluded that anxiety and the exceptional mental state before surgery may have influenced the response to the depression items at the first measurement point. Third, the study had to face a substantial dropout rate owing to mortality and morbidity. In addition, we cannot exclude minor associations between cognitive impairment and completion of questionnaires. To avoid a systematic bias by interpreting results based on the reduced sample, all analyses were repeated using the full data set, estimating the missing units. These analyses provide additional support for our main finding that depression is predictive for PF. Fourth, all patients were recruited at a single center, the Deutsches...
Herzzentrum Berlin. Given the high reputation of this institution, it is possible that more complicated cases may have been referred to this hospital and thus the study sample may represent a less healthy population.

Our results emphasize the vitally important role depression plays in the CABG recovery process. This was confirmed by evidence of a unidirectional relationship of depression with PF. On the basis of these results, screening for depression should be recommended both before and after CABG treatment. After surgery, this seems to be particularly important for patients with heart failure.

Accepted for Publication: July 30, 2010.
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Financial Disclosure: None reported.

Funding/Support: This study was funded by the German Federal Ministry of Education and Research (BMBF).

Additional Contributions: Elizabeth Morrison and Anna Jonen provided editorial assistance.

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