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Type D personality and diabetes predict the onset of depressive symptoms in patients after percutaneous coronary intervention

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Background Depression is common in cardiac patients and has been associated with adverse clinical outcome. However, little is known about predictors of the onset of depressive symptoms. We examined predictors of the onset of depressive symptoms at 12 months post-percutaneous coronary intervention (PCI) in patients treated in the drug-eluting stent era.

Methods Unselected patients, free from depressive symptoms at 6 months with a depression score at 12 months treated with PCI with either drug-eluting or bare stent implantation as part of the RESEARCH registry qualified for inclusion in the current study. Patients completed the Hospital Anxiety and Depression Scale at 6 and 12 months and the Type D Personality Scale (DS14) at 6 months post-PCI. Six months was used as the baseline assessment.

Results Of 542 patients, 41 (8%) had developed significant depressive symptoms at 12 months. The occurrence of a new cardiac event between 6 and 12 months post-index event did not influence the incidence of depressive symptoms at 12 months. Depressive patients were more likely to have a type D personality (34% vs 16%, $P = .003$) and diabetes (24% vs 11%, $P = .01$) than nondepressive patients. Type D personality (odds ratio 3.04, 95% CI 1.50-6.16) and diabetes (odds ratio 2.75, 95% CI 1.25-6.05) were independent predictors of the onset of depressive symptoms 12 months post-PCI in adjusted analyses. In patients with neither risk factors (type D or diabetes), the incidence of depression was 5.1% with the incidence more than doubling to 13.2% and 30% for each additional risk factor.

Conclusions Type D personality and diabetes comprise risk factors for the onset of depressive symptoms post-PCI. In clinical practice, patients with these risk factors should be identified and considered for psychosocial intervention targeting depression to enhance secondary prevention. (Am Heart J 2006;151:367.e1-367.e6.)

Depression has gained status as an important risk factor for morbidity and mortality in patients with established cardiovascular disease (CVD). Depression is prevalent in approximately 20% to 30% of cardiac patients and has been shown to confer a 2-fold increased risk of adverse clinical outcome adjusting for established risk factors,¹⁻³ which was also confirmed in two recent

meta-analyses.^{4,5} Depression has also been related to nonadherence to medical treatment recommendations,^{6,7} impaired health status,^{8,9} increased risk of rehospitalization,^{10,11} and may also be associated with increased health care consumption although results to date have been mixed.^{12,13}

The recent Enhancing Recovery in Coronary Heart Disease (ENRICH) study and the Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) showed that psychosocial intervention and treatment with selective serotonin re-uptake inhibitors successfully reduce depressive symptoms^{14,15} and improve health status.¹⁶ However, a reduction in depressive symptoms did not lead to a concomitant risk reduction in clinical adverse events.^{14,15} Hence, we are still at large as to which intervention is effective in reducing depressive symptoms while simultaneously leading to improved prognosis in patients with established CVD.

The key to optimizing risk stratification and secondary prevention in clinical practice may lie in the

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identification of factors that predict the onset of depressive symptoms. Lack of social support, hostility, depressive symptoms during hospitalization, exhaustion before myocardial infarction (MI), younger age, smoking, self-reported previous cardiac condition, self-reported history of anxiety and depression, social factors, and impaired health status have all been associated with the development of depressive symptoms, whereas denial has been shown to be protective.¹⁷⁻²⁰

However, a paucity of studies have examined the influence of personality factors on the development of depressive symptoms in cardiac patients, and no study has examined predictors of the onset of depressive symptoms in unselected patients treated with percutaneous coronary intervention (PCI) in the drug-eluting stent era.

The distressed (type D) personality is an emerging risk factor that has been associated with increased psychological distress, symptoms of exhaustion, adverse health status, and adverse clinical outcome despite appropriate treatment.²¹⁻²⁴ Type D is a risk factor on par with established biomedical risk factors with type D patients being above a 4-fold increased risk of adverse clinical outcome.^{21,22} This personality taxonomy is defined as the tendency to experience increased negative emotions paired with the nonexpression of these emotions in social interactions. Although type D is often mistaken for depression, it is more than negative affect because it also includes how patients deal with this affect.²⁵ Because type D personality has been shown to predict depressive affect at 5 years' follow-up in a mixed group of cardiac patients in the pre-drug-eluting stent era,²¹ type D may also be a determinant of the onset of depressive symptoms in post-PCI patients treated in the drug-eluting stent era.

The aim of the current study was to determine predictors of the onset of depressive symptoms at 12 months post-PCI in patients treated in the drug-eluting stent era who were not depressed at 6 months.

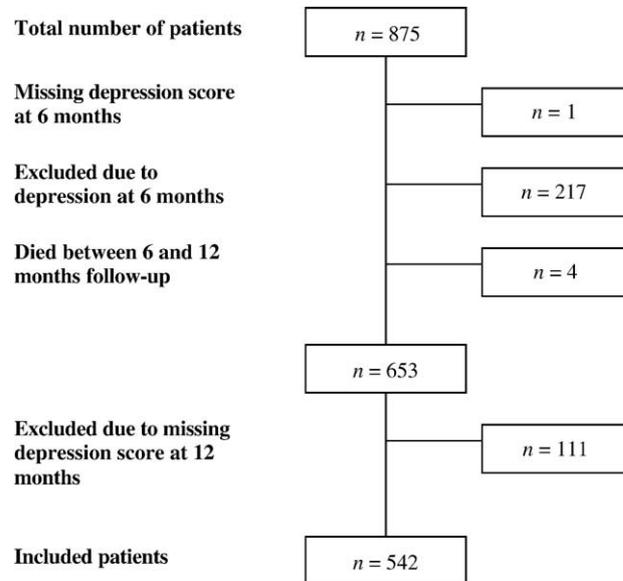
Methods

Study design and participants

Of 875 (71%) unselected patients participating in a psychological substudy of the RESEARCH registry, patients ($n = 542$) who were free from depressive symptoms at 6 months and had a depression score at 12 months qualified for inclusion in the current study. A flowchart of the patient selection for the current study is shown in Figure 1. Details of the RESEARCH study design²⁶ and the psychological substudy have been published elsewhere.²² In brief, the registry was set up to evaluate the efficacy of the sirolimus-eluting stent. For this purpose, no clinical or anatomical exclusion criteria were applied so as to reflect patients seen in daily clinical practice. Of note, 68% of the patients included in the RESEARCH registry would not have qualified for inclusion in clinical trials.²⁷

Surviving patients at 6 and 12 months post-PCI were asked to complete the Hospital Anxiety and Depression Scale (HADS) and the Type D Personality Scale. Questionnaires were

Figure 1



Flowchart of patient selection.

administered at 6 months post-PCI in order for patients to be in a stable medical condition and to avoid measuring psychological distress related to the procedure; a similar approach has been adopted by others.^{28,29} Type D is a stable personality construct²⁵ rendering the time point for assessment of the construct of less importance. Clinical variables were also obtained at 6 months.

The study was approved by the local medical ethics committee and conducted in accordance with the Declaration of Helsinki. Every patient provided written informed consent.

Materials

Sociodemographic and clinical variables. Sociodemographic variables included sex and age. Clinical variables included prior MI, prior PCI, prior coronary artery bypass graft (CABG) surgery, recent cardiac event (defined as MI, PCI, or CABG between 6 and 12 months post-PCI), sirolimus-eluting or bare metal stent implantation, multivessel disease, diabetes mellitus (defined as receiving oral hypoglycemic agents or insulin), dyslipidemia (indicated by total cholesterol levels >240 mg/dL or on lipid-lowering medication), hypertension (defined as being on antihypertensive therapy), renal impairment (indicated by creatinine clearance ≤ 60 mL/min), and smoking status (assessed by means of self-report).

Depressive symptoms. The 7-item depression subscale of the HADS was used to evaluate depressive symptoms.³⁰ The items are answered on a 4-point Likert scale from 0 to 3 (score range 0-21). We used a cutoff score ≥ 8 to quantify patients with depressive symptoms, as this cutoff yields an optimal balance between sensitivity and specificity.³¹ The HADS is a valid and reliable instrument³¹ and has been shown to predict mortality in patients referred for exercise testing.³² The HADS was administered at 6 and 12 months post-PCI.

Table 1. Patient characteristics stratified by depressive symptoms* at 12 months

	Depressed (n = 41)	Nondepressed (n = 501)	OR	95% CI	P
Demographics					
Males (%)	63	75	0.58	0.30-1.13	.11
Age, mean (SD)	64 (12)	62 (10)	1.02	0.99-1.05	.19
Personality					
Type D (%)	34	16	2.81	1.41-5.60	.003†
Clinical variables					
Sirolimus-eluting stent (%)	37	42	0.80	0.41-1.55	.51
Prior cardiac event‡	59	51	1.37	0.72-2.62	.34
Multivessel disease (%)	59	50	1.44	0.76-2.75	.27
Diabetes mellitus§ (%)	24	11	2.67	1.24-5.75	.01
Dyslipidemia¶ (%)	73	81	0.65	0.31-1.34	.24
Hypertension# (%)	44	36	1.37	0.72-2.61	.34
Renal impairment** (%)	39	30	1.53	0.79-2.95	.20
Current smoking‡‡ (%)	39	30	1.47	0.76-2.83	.25
Medication					
β-Blockers (%)	95	99	0.28	0.06-1.38	.12
Calcium antagonists (%)	56	46	1.49	0.79-2.84	.22
Nitrates (%)	10	9	1.12	0.38-3.30	.83
ACE inhibitors (%)	22	25	0.85	0.39-1.82	.67
Statins (%)	61	69	0.69	0.36-1.34	.27

*A cutoff ≥ 8 on the HADS was used to denote those with depressive symptoms.

† $P < .01$.

‡MI, CABG, or PCI before the index PCI.

§Receiving oral hypoglycemic agents or insulin.

|| $P < .05$.

¶Total cholesterol levels >240 mg/dL or on lipid-lowering medication.

#Being on antihypertensive therapy.

**Indicated by creatinine clearance ≤ 60 mL/min.

‡‡Based on self-report.

Type D personality. The 14-item Type D Personality Scale (DS14) was used to assess type D personality.²⁵ Items are answered on a 5-point Likert scale from 0 to 4 with a score range of 0 to 28 for each subscale. The scale consists of two subscales: negative affectivity (eg, “I often feel unhappy”) and social inhibition (eg, “I am a ‘closed’ person”); patients who score high on both components—as determined by a standardized cutoff ≥ 10 —are categorized as type D. The psychometric properties of the DS14 are good with Cronbach $\alpha = .88/.86$ for the negative affectivity and social inhibition subscales, respectively.²⁵ Type D is a stable personality construct, as indicated by a test-retest reliability over a 3-month period ($r = 0.72/0.82$ for the negative affectivity and social inhibition subscales, respectively) and because it has been shown to be independent of mood and health status.²⁵ The DS14 was administered 6 months post-PCI.

Statistical analyses

Discrete variables were compared with the χ^2 (Fisher exact test when appropriate) and are presented as percentages. Continuous variables were compared with the Student *t* test and are presented as mean \pm SD. Univariable and multivariable logistic regression analyses were performed to delineate predictors of the development of depressive symptoms 12 months post-PCI. The multivariable analyses were performed in two steps due to the relatively small number of patients with depressive symptoms. In the first step, we entered type D personality, sex, age, stent type, prior cardiac event, multivessel disease, diabetes, dyslipidemia, hypertension, renal impairment, and smoking in a multivariable model with a

backward selection using a liberal *P* value criterion (entry criteria *P* = .05 and removal criteria *P* = .50). This procedure is considered one of the least harmful of the stepwise procedures, given that a liberal *P* value criterion compensates by making more likely that truly important predictors will be retained in the model.⁵³ In the second step, all significant variables from the first analysis were included using an enter procedure adding sex, age, multivessel disease, and stent type (sirolimus-eluting or bare metal stent) irrespective of whether the latter covariates were significant in the first model. We chose to adjust for these covariates, as sex and age are included standardly in multivariable models in psychosomatic research and have been associated with depressive symptoms; multivessel disease was included to adjust for disease severity, ruling out the possibility that onset of depressive symptoms could be due to more severe cardiac disease; stent type was included as there is as yet no knowledge of the impact of drug-eluting stents on psychological outcome. All tests were 2-tailed. A *P* value $< .05$ was considered to be statistically significant. Odds ratios (ORs) with 95% CIs are reported. All statistical analyses were performed using SPSS 12.0.1 for Windows.

Results

Patient characteristics stratified by depressive symptoms

Of the 542 patients who were not depressed at 6 months, 41 (8%) developed significant depressive

Table II. Independent predictors of depressive symptoms 12 months post-PCI (multivariable analysis)

Variable	OR	95% CI	P
Type D personality	3.04	1.50-6.16	.002*
Diabetes mellitus†	2.75	1.25-6.05	.012‡
Male sex	0.62	0.31-1.24	.18
Age	1.02	0.99-1.05	.25
Multivessel disease	1.34	0.69-2.63	.39
Sirolimus-eluting stent	0.72	0.37-1.43	.35

* $P < .01$.

†Receiving oral hypoglycemic agents or insulin.

‡ $P < .05$.

symptoms at 12 months. Characteristics at 6 months comparing those who developed depressive symptoms at 12 months versus those who did not are presented in Table I (columns 1 and 2). Depressed patients were more likely to have a type D personality (34% vs 16%, $P = .003$) and diabetes (24% vs 11%, $P = .01$) than nondepressed patients. No other statistically significant differences were found between the two groups on characteristics at 6 months, including on cardiac medication.

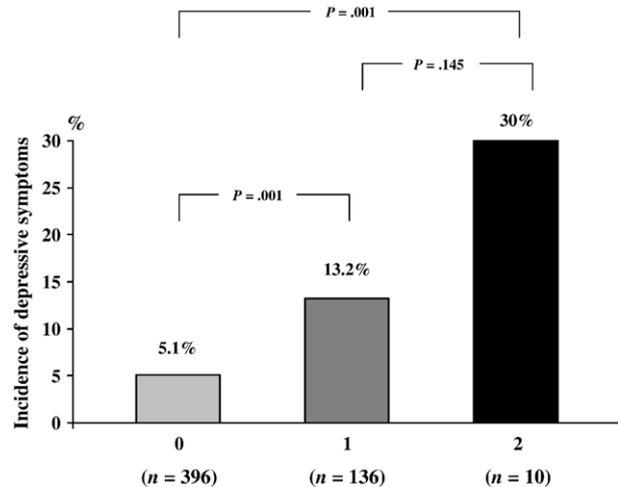
We also examined whether the occurrence of a new cardiac event (defined as MI, CABG, or PCI) between 6 and 12 months post-index event influenced the incidence of depressive symptoms. However, depressed patients were not more likely to have had a recent event between 6 and 12 months compared with nondepressed patients (7.3% vs 5.2%, $P = .47$).

Predictors of depressive symptoms

Type D personality and diabetes were predictors of the onset of depressive symptoms 12 months post-PCI in univariable analyses (Table I, columns 3-5). No demographic or other clinical risk factors were associated with the onset of depressive symptoms.

In a stepwise model using a backward selection with a liberal P value for removal ($P = .50$), we entered all baseline characteristics listed in Table I except for cardiac medication. Type D personality (OR 3.29, 95% CI 1.60-6.80, $P = .01$) and diabetes (OR 2.76, 95% CI 1.25-6.10, $P = .12$) were the only significant predictors of the onset of depressive symptoms. In a subsequent multivariable analysis using the enter procedure, type D personality and diabetes remained independent predictors of depressive symptoms 12 months post-PCI adjusting for sex, age, multivessel disease, and stent type (Table II). The risk associated with type D (OR 3.04, 95% CI 1.50-6.16) and diabetes (OR 2.75, 95% CI 1.25-6.05) was of a similar magnitude.

In patients with neither risk factors (type D or diabetes), the incidence of depression was 5.1% with the incidence more than doubling to 13.2% and 30% for

Figure 2

Incidence of depressive symptoms at 12 months stratified by number of risk factors* (*type D personality and diabetes).

each additional risk factor, showing a graded relationship (Figure 2). Although the incidence in depressive symptoms did not differ significantly for patients with one versus both risk factors ($P = .145$), this is likely due to reduced statistical power given that only 10 patients had two risk factors.

Discussion

This is the first study to examine predictors of the onset of depressive symptoms in unselected post-PCI patients in general and in the drug-eluting stent era in particular. Type D personality and diabetes were both associated with close to a 3-fold increased risk of developing depressive symptoms 12 months post-PCI.

Personality factors are known to increase the risk of developing depressive symptoms in the general population.^{34,35} As such, personality may be construed as a vulnerability factor. Type D personality has previously been identified as an important explanatory factor of individual differences in distress^{23,24} and clinical outcome in patients with established CVD.^{21,22} In the current study, we found that type D also comprises a risk factor for the onset of depressive symptoms in unselected patients post-PCI. This supports the notion that personality comprises a vulnerability factor for the onset of depressive symptoms not only in the general population but also in patients with established CVD.

Diabetes was also an independent risk factor for the development of depressive symptoms on par with the risk associated with type D. We found no relationship between disease severity and the development of

depressive symptoms at 12 months, which is consistent with the results of previous studies.^{17,20}

Similar to Havranek et al,²⁰ we found a graded relationship between depressive symptoms and risk factors with the incidence of depression increasing to >2-fold with the addition of each risk factor (ie, type D and diabetes). Psychosocial risk factors are known to cluster together within individuals³⁶ and also to act in synergy with traditional biomedical CVD risk factors in producing adverse clinical outcome.³⁷ In a population-based study, patients with concomitant diabetes and CVD who were depressed were almost two times more likely to have three or more known CVD risk factors compared with the nondepressed.³⁸ Using poor clinical outcome and health care costs as end points, type D has also been shown to act in synergy with age and left ventricular dysfunction in the pre-drug-eluting stent era.²¹

This study has some limitations. First, we used a self-report measure rather than a diagnostic interview to assess depression. However, the HADS, which was the measure used in the current study, has good sensitivity and specificity indicating that it is a reasonable predictor of a clinical diagnosis of depression.³¹ Although we also had no information about history of depression, patients only qualified for inclusion in this substudy if they were not depressed at 6 months. In other words, patients who developed depressive symptoms at 12 months were incident cases. Second, the number of depressed patients was relatively small, limiting the number of covariates that we could adjust for in multivariable analyses. Although some steps were undertaken to limit overfitting in the regression model, we cannot rule out that overfitting may have influenced our results. Third, 17% (111/653) of the patients with no depression at 6 months were excluded because they had dropped out during follow-up. Fourth, we had no information on treatment for depressive symptoms. Finally, depressive symptoms and type D personality were evaluated at 6 months rather than at the time of the index PCI. This time point was chosen to ensure that patients were in a stable medical condition and that psychological symptoms did not reflect symptoms related to the index procedure. However, the 6-month time gap may have been unnecessarily wide given that assessment at 1 month postprocedure has been shown to comprise a sufficient time frame.²⁸ The time point for assessing type D personality is of less importance given that it is a stable personality construct.²⁵

Nevertheless, a strength of the current study is that it consisted of unselected patients, as no patients were excluded due to clinical or anatomical criteria. Hence, the patients represent those seen in daily clinical practice. In addition, this study points to two potentially important risk factors for the onset of depressive symptoms, namely, type D personality and diabetes. If these findings can be confirmed in future studies, it

may be important to screen for type D personality and diabetes, as these patients should be considered for psychosocial intervention to prevent the development of depressive symptoms. This would also lead to efficient and cost-effective allocation of health care resources, as most patients (73%) in the current study had neither of the risk factors. Moreover, the presence of CVD and depression has been associated with significantly increased health care costs in patients with diabetes³⁹ and depression¹³ and the convergence of type D, sex, and left ventricular dysfunction with increased health care costs in patients with CVD.²¹ Hence, screening may not only lead to gains for patients in terms of increased survival, less psychological distress, and improved health-related quality of life, but there may also be gains to society in terms of reduced health care costs. Taken together, these results indicate that the use of algorithms, as suggested by Rozanski et al³⁶ already in 1999, that also include psychosocial risk factors may improve risk stratification in clinical practice.

In conclusion, this preliminary study showed that type D personality and diabetes predict the onset of depressive symptoms 12 months post-PCI in unselected patients. We found a graded relationship between depressive symptoms and the risk factors type D and diabetes, with the incidence of depressive symptoms increasing in an almost exponential fashion with the addition of each risk factor. Additional studies are warranted to confirm these findings, as knowledge of risk factors for depression onset may point to targets for psychosocial intervention.

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