

Research report

Type-D personality predicts chronic anxiety following percutaneous coronary intervention in the drug-eluting stent era

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Abstract

Background: Anxiety is an often overlooked risk factor in coronary artery disease (CAD). Hence, little is known about predictors of unremitting chronic anxiety in CAD patients. We examined whether the distressed personality (type-D) predicts chronic anxiety post percutaneous coronary intervention (PCI).

Methods: Unselected patients ($n=167$) treated with PCI using sirolimus-eluting or bare metal stents as part of the RESEARCH registry, who were anxious 6 months post-PCI, qualified for inclusion. Patients completed the Hospital Anxiety and Depression Scale at 6 and 12 months and the Type-D Scale (DS14) 6 months post-PCI.

Results: Of 167 patients anxious at 6 months, 108 (65%) were still anxious 12 months post-PCI. Significant univariable predictors of chronic anxiety were type-D personality (OR: 3.17; 95% CI: 1.64–6.14) and sirolimus-eluting stent implantation (OR: 0.51; 95% CI: 0.27–0.98), with sirolimus-eluting stent showing a protective effect. In multivariable analyses, type-D personality (OR: 3.31; 95% CI: 1.59–6.87) and sirolimus-eluting stent implantation (OR: 0.44; 95% CI: 0.21–0.92) remained significant independent predictors of chronic anxiety adjusting for depressive symptoms at 6 months, demographic and clinical risk factors.

Limitations: All psychological measures were based on self-report, and we had no information on cardiac rehabilitation or use of pharmacotherapy; however our sample represented patients seen in daily clinical practice.

Conclusions: These findings suggest that type-D personality is a risk factor and sirolimus-eluting stent implantation a protective factor for the occurrence of chronic anxiety. The protective effect of sirolimus-eluting stents in relation to anxiety warrants replication in future studies.

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1. Introduction

The impact of depression on the progression of coronary artery disease (CAD) has been studied extensively. Generally, depression has been associated with at least a 2-fold increased risk of mortality, which

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was also confirmed in two recent meta-analyses (Barth et al., 2004; van Melle et al., 2004), although a recent systematic review questions the validity of these findings (Sørensen et al., 2005). Given the wealth of studies on depression and the relative consistency of the results, it is perhaps not surprising that depression may be the first psychosocial factor to gain risk factor status on par with traditional biomedical factors (Rumsfeld and Ho, 2005). In contrast, anxiety is often overlooked as a psychosocial risk factor in CAD (Abbey and Stewart, 2000; Grace et al., 2004; Januzzi et al., 2000), although studying anxiety and depression in concert has been advocated given their frequent co-occurrence (Maser and Cloninger, 1990; Clark and Cook, 1998).

A recent review also emphasizes the importance of studying anxiety in the context of CAD, as anxiety triples the risk of all-cause mortality following myocardial infarction (MI), almost doubles the risk of reinfarction at 5 years follow-up, and the risk of sudden cardiac death by a factor of 6 (Januzzi et al., 2000). It should be noted, however, that not all studies have been able to confirm a link between anxiety and mortality (Lane et al., 2002). Anxiety has also been associated with impaired health status 1 (Lane et al., 2001; Mayou et al., 2000) and 5 years following a cardiac event (Sullivan et al., 2000), and with increased health care consumption post-MI (Strik et al., 2003). Accumulating evidence also indicates that depression in CAD is often accompanied by symptoms of anxiety (Denollet et al., in press), and that anxiety predicts cardiac events in post-MI patients over and above the effect of depression (Grace et al., 2004; Strik et al., 2003). In addition, in a recent study we showed that anxiety enhances the detrimental effect of depressive symptoms on health status post-percutaneous coronary intervention (PCI) (Pedersen et al., in press). Taken together, there is compelling evidence that anxiety should *not* be considered just an epiphenomenon of depression, but should be studied as a risk factor in its own right (Steptoe and Whitehead, 2005; Ballenger et al., 2001).

A paucity of studies has also investigated predictors of anxiety, including predictors of chronic anxiety. Knowledge of these predictors is important for secondary prevention, in particular given that anxiety has been associated with increased risk of adverse clinical events (Januzzi et al., 2000) and impaired health status (Lane et al., 2001). A recent report from the National Heart, Lung and Blood Institute in the United States also emphasizes the importance of studying patient-centered outcomes such as anxiety and its determinants, as a means to bridge the gap between research and clinical practice (Krumholz et al., 2005).

Personality may be an important determinant and explanatory factor of individual differences in chronic anxiety in CAD patients. The *distressed* (type-D) personality is an emerging risk factor in CAD that has been associated with a wide range of emotional distress, including anxiety, depression, and post-traumatic stress disorder, and adverse clinical prognosis (Denollet et al., 2000; Pedersen and Denollet, 2003, 2004, 2006). Persons with a type-D personality are characterized by the tendency to experience increased negative affectivity paired with the tendency not to express these emotions in social interactions due to fears of how others may react (Denollet, 2005). In other words, type-D personality is defined by the interaction of these two traits, with social inhibition modulating the effect of negative affectivity on prognosis, as shown in a recent study (Denollet et al., 2006). This supports the notion that type-D personality is more than depression and anxiety, with type-D also referring to how people deal with these increased levels of negative emotions.

To date, no study has looked at the role of type-D personality in chronic, unremitting anxiety in CAD patients in general and in a sample of patients undergoing PCI in particular. Hence, the objective of the current study was to investigate whether type-D personality is a predictor of chronic, unremitting anxiety in consecutive patients treated with PCI in the drug-eluting stent era.

2. Methods

2.1. Study design and participants

Patients ($n=167$) were drawn from a population of unselected patients ($n=875$; response rate=71%) participating in a psychological sub-study of the RESEARCH registry, who were treated with PCI using either sirolimus-eluting stent or bare metal stent implantation. The sirolimus-eluting stent is a drug-eluting stent that has been shown to decrease the risk of restenosis post-PCI substantially (Roiron et al., 2006). However, the use of drug-eluting stents in general and the sirolimus-eluting stent in particular confers no benefits on survival (Roiron et al., 2006). The inclusion criterion for the current study was the presence of anxiety 6 months post-PCI (Fig. 1). Details of the RESEARCH study design (Lemos et al., 2003) and the psychological sub-study have been published previously (Pedersen et al., 2004a). In brief, the registry was set up to evaluate the efficacy of sirolimus-eluting stent implantation. For this purpose, no clinical or anatomical exclusion criteria were applied so as to reflect patients

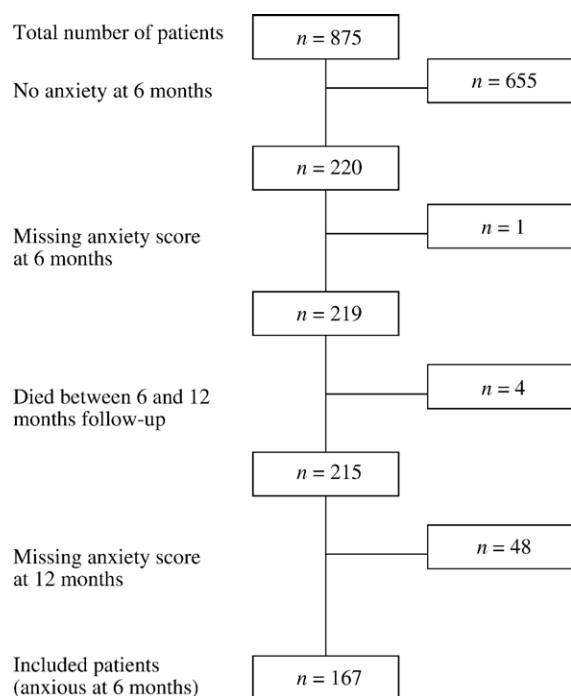


Fig. 1. Flowchart of patient selection.

seen in daily clinical practice. Of the patients included in the RESEARCH registry, 68% would not have qualified for inclusion in clinical trials due to their more complex clinical profile (Lemos et al., 2005).

Surviving patients at 6 and 12 months post-PCI were asked to complete a set of psychological questionnaires. The 6 months time point was chosen in order for patients to be in a stable medical condition. In addition, assessment of psychological symptoms at the time of PCI has not been shown to be a good indicator of later psychological symptomatology (Poston et al., 2003). Others have adopted a similar approach (Rumsfeld et al., 2003). Type-D is a stable personality construct rendering the time point for assessment of the construct of less importance (Denollet, 2005). Clinical variables were also obtained at 6 months.

The protocol for the RESEARCH registry was approved by the local medical ethics committee and was conducted in accordance with the Helsinki Declaration. All patients provided written informed consent.

2.2. Materials

2.2.1. Demographic and clinical variables

Demographic variables included sex and age. Information on clinical variables was obtained from the medical records. Variables included prior MI, prior coronary artery bypass graft surgery (CABG), prior PCI,

sirolimus-eluting versus bare metal stent implantation, multi-vessel disease, hypertension, dyslipidemia, renal impairment, diabetes mellitus, and smoking. Since clinical variables were also assessed at 6 months, the 6 months assessment will be referred to as baseline in the remainder of the article.

2.3. Psychological variables

2.3.1. Type-D personality

Type-D personality was assessed at 6 months post-PCI using the 14-item Type-D Scale (DS14) (Denollet, 2005). The scale consists of two subscales, negative affectivity (e.g. “I often feel unhappy”) and social inhibition (e.g. “I am a closed person”). Responses are indicated on a 5-point Likert scale from 0 to 4 (score range 0–28 for each subscale). A standardized cut-off ≥ 10 on both subscales indicates type-D personality caseness. The DS14 has good psychometric properties with Cronbach’s $\alpha=0.88/0.86$ and test–retest reliability $r=0.72/0.82$ for the negative affectivity and social inhibition sub-scales, respectively (Denollet, 2005). Type-D is often mistaken for depression or negative affect, but it is more than negative affect since it also includes how patients deal with these negative emotions (Denollet, 2005). In addition, type-D has been shown to exert a deleterious effect on prognosis, independent of mood states (Pedersen and Denollet, 2006).

2.3.2. Anxiety and depression

Anxiety and depressive symptoms were assessed at 6 and 12 months post-PCI using the 7-item anxiety subscale and the 7-item depression subscale of the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983). Responses to both subscales are indicated on a four-point Likert Scale from 0 to 3 (score range 0–21). A cut-off score ≥ 8 was used for both subscales to identify patients with anxiety and depressive symptomatology. This cut-off has been shown to balance sensitivity and specificity optimally (Bjelland et al., 2002). The HADS has been shown to be a valid and reliable instrument (Bjelland et al., 2002; Herrmann, 1997) and to predict mortality in patients referred for exercise testing (Herrmann et al., 2000). Patients with anxiety scores above the cut-off at both 6 and 12 months post-PCI were considered to suffer from unremitting, chronic anxiety.

2.4. Statistical analyses

Discrete variables were analyzed using the chi-square test (Fischer’s exact test when appropriate) and are

Table 1
Patient characteristics stratified by chronic anxiety

	Anxious (n=108)	Non- anxious (n=59)	OR	[95% CI]	p
<i>Demographics</i>					
Females, n (%)	41 (38)	24 (41)	1.12	[0.59– 2.14]	0.73
Age, mean (SD)	61 (11)	59 (11)	1.02	[0.99– 1.05]	0.31
<i>Psychological variables</i>					
Depression at 6 months, n (%)	70 (65)	33 (56)	1.45	[0.76– 2.78]	0.26
Type-D personality, n (%)	74 (69)	24 (41)	3.17	[1.64– 6.14]	0.001 [‡]
Anxiety at 6 months, mean (SD)	11 (2.5)	9.6 (1.8)	–	–	–
Anxiety at 12 months, mean (SD)	10 (2.3)	5.3 (1.8)	–	–	–
<i>Clinical variables</i>					
Sirolimus-eluting stents, n (%)	48 (44)	36 (61)	0.51	[0.27– 0.98]	0.042 [†]
Prior cardiac event ^a , n (%)	55 (51)	27 (46)	1.23	[0.65– 2.32]	0.52
Multi-vessel disease, n (%)	52 (48)	33 (52)	0.73	[0.39– 1.38]	0.34
Diabetes mellitus ^b , n (%)	20 (19)	10 (17)	1.11	[0.48– 2.57]	0.80
Hypertension ^b , n (%)	53 (49)	26 (44)	1.22	[0.65– 2.31]	0.54
Dyslipidemia ^c , n (%)	85 (79)	46 (78)	1.04	[0.48– 2.25]	0.91
Renal impairment ^d , n (%)	35 (33)	20 (35)	0.90	[0.46– 1.77]	0.76
Current smoking ^e , n (%)	45 (42)	28 (48)	0.79	[0.42– 1.50]	0.47

[†] $p < 0.05$, [‡] $p < 0.01$.

^a MI, CABG, or PCI prior to the index PCI.

^b Present if being treated for the condition.

^c Total cholesterol levels >240 mg/dl or on lipid lowering medication.

^d Indicated by creatinine clearance <61 ml/min.

^e Based on self-report.

presented as percentages. Continuous variables were analyzed with the Student's *t*-test and are presented as means \pm standard deviations. Univariable and multivariable logistic regression analyses were performed to identify predictors of chronic anxiety. In multivariable analysis, we entered type-D personality and depressive symptoms at 6 months together with all demographic and clinical baseline characteristics. Results are presented as odds ratio (OR) with 95% confidence intervals (CI). All tests were two-tailed, and $p < 0.05$ was considered to be statistically significant. All statistical analyses were performed using SPSS 13.0 for Windows.

3. Results

3.1. Baseline characteristics stratified by anxiety symptoms

The mean (SD) score for HADS-anxiety at baseline for the total sample was 10.37 (2.37). Of the 167 patients who were anxious at baseline (6 months), 108 (65%) were still anxious at 12 months (mean (SD) = 10.48 (2.27)), whereas in 59 (35%) the anxiety symptoms had remitted (mean (SD) = 5.25 (1.17)). A comparison of baseline characteristics stratified by anxiety at 12 months is presented in Table 1 (columns 1–2). Those who remained anxious were more likely to have a type-D personality, but less likely to have received a sirolimus-eluting stent implantation during PCI. No other statistically significant differences were found between the two groups on baseline characteristics.

We also examined whether patients with chronic anxiety at 12 months were more likely to have experienced a new cardiac event (defined as MI, CABG or PCI) between 6 and 12 months post-PCI. However, chronically anxious patients were not more likely to have had an event during follow-up than patients whose anxiety remitted prior to 12 months (10% vs. 2%; $p = 0.06$), although there was a trend.

3.2. Predictors of chronic anxiety

In univariable analysis, type-D personality was associated with an increased risk of unremitting chronic anxiety at 12 months post-PCI (OR: 3.17; 95% CI: 1.64–6.14) (Table 1, columns 3–5). In contrast, sirolimus-eluting stent implantation was found to buffer the occurrence of chronic anxiety at 12 months (OR:

Table 2
Independent predictors of chronic anxiety post-PCI (adjusted analysis)

Variable	OR [95% CI]	p
Type-D personality	3.31 [1.59–6.87]	0.001 [‡]
Sirolimus-eluting stents	0.44 [0.21–0.92]	0.029 [†]
Age	1.03 [0.98–1.07]	0.28
Sex	1.03 [0.48–2.19]	0.95
Depression at 6 months	0.99 [0.48–2.07]	0.98
Prior cardiac event ^a	1.04 [0.48–2.22]	0.93
Multi-vessel disease	0.69 [0.34–1.41]	0.31
Diabetes mellitus	1.01 [0.40–2.59]	0.98
Hypertension	1.16 [0.55–2.44]	0.70
Dyslipidemia	1.10 [0.45–2.71]	0.83
Renal impairment	0.53 [0.22–1.26]	0.15
Current smoking	0.70 [0.30–1.61]	0.40

[†] $p < 0.05$, [‡] $p < 0.01$.

^a MI, PCI or CABG prior to the index PCI.

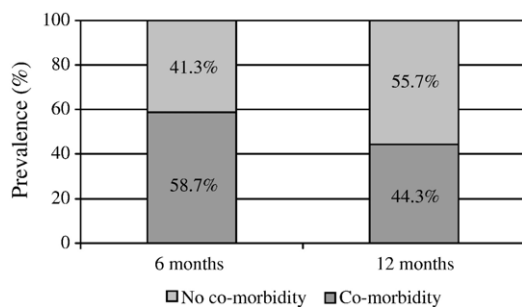


Fig. 2. Prevalence of co-morbidity between type-D personality and anxiety at 6 and 12 months.

0.51; 95% CI: 0.27–0.98). This effect was not only statistically significant, but also clinically relevant, as the risk of chronic anxiety was lowered by 50% for patients with sirolimus-eluting stent implantation. No other demographic, psychological or clinical factors were predictive of chronic anxiety 12 months post-PCI, including depressive symptoms.

Type-D personality (OR: 3.31; 95% CI: 1.59–6.87) and sirolimus-eluting stent implantation (OR: 0.44; 95% CI: 0.21–0.92) remained significant independent predictors of chronic anxiety in multivariable analysis, adjusting for all demographic and clinical factors and depressive symptoms at 6 months (Table 2). Type-D was associated with more than a 200% increased risk of chronic anxiety, whereas sirolimus-eluting stent implantation was associated with a 50% protective effect.

To rule out the possibility that the predictive value of type-D in relation to anxiety was due to co-morbidity between type-D and anxiety, we examined the levels of co-morbidity at both 6 and 12 months. Of the 167 patients, 58.7% of patients had a type-D personality and experienced significant levels of anxiety at 6 months, whereas at 12 months the prevalence of co-morbidity was 44.3% (Fig. 2). Taken together, this shows that the relationship between type-D personality and anxiety at 12 months cannot be attributed to their co-morbidity, supporting the independent impact of type-D on anxiety at 12 months post-PCI.

4. Discussion

To our knowledge, this is the first study to examine predictors of chronic anxiety in PCI patients in general and in the drug-eluting stent era in particular. Of note, 65% of patients who were anxious at 6 months continued to be anxious at 12 months, suggesting a high risk of subsequent chronicity if anxious 6 months post-PCI. Type-D personality and sirolimus-eluting stent implantation were independent predictors of unremitting,

chronic anxiety post-PCI, with sirolimus-eluting stent implantation showing a protective effect.

Type-D personality was associated with above a 3-fold increased risk of chronic anxiety adjusting for depressive symptoms at 6 months and demographic and clinical factors. Previous studies have shown that this personality taxonomy is related to increased anxiety in patients with an implantable cardioverter defibrillator (Pedersen et al., 2004b) and first MI patients (Pedersen and Denollet, 2004), and to the onset of depressive symptoms at 12 months in patients free of depressive symptoms at 6 months post-PCI (Pedersen et al., 2006). Patients with this personality structure are very likely to experience increased anxiety due to their high levels of negative affectivity, and paired with diminished coping abilities due to high levels of social inhibition these patients have no real means of relieving their negative affectivity.

Surprisingly, we found that sirolimus-eluting stent implantation was associated with a 50% decreased risk of developing chronic anxiety. Although sirolimus is an immunosuppressant drug that may have anxiolytic effects, the amount of drug eluted at the site of the stent is not sufficient for such effects to be present. A more plausible explanation may be that the introduction of sirolimus-eluting stents at our institution was associated with a considerable amount of positive publicity in the press. Furthermore, the treating cardiologists stressed the innovative quality and safeguarding effects of sirolimus-eluting stents to patients. Taken together, this may have strengthened the patient's belief in the drug-eluting stent as a miraculous form of treatment safeguarding against adverse prognosis, in turn leading to reduced levels of anxiety. It is possible that the drug-eluting stent reinstated a sense of perceived control in these patients due their belief in its efficacy. Perceived control has been shown to reduce emotional distress in patients with heart failure (Dracup et al., 2003).

Our results have some bearing on research and clinical practice. Type-D personality was associated with a more than 3-fold increased risk of chronic, unremitting anxiety. In contrast, using sirolimus-eluting stent implantation showed a clinically relevant decrease (by almost 50%), suggesting that using the latest innovation in the treatment of CAD is not sufficient to buffer against anxiety post-PCI. In order to enhance risk stratification, it is also necessary to screen for psychosocial factors, since they may have a profound impact on psychological outcome. In addition, anxiety has been shown to affect benefits following cardiac rehabilitation (Rafanelli et al., 2003). The presence of psychosocial risk factors also impact on disease progression, with both anxiety and

type-D having been associated with adverse prognosis in patients with established CAD independent of traditional biomedical risk factors (Denollet et al., 2000; Pedersen and Denollet, 2003).

Although personality is considered to exert a stable influence on behavior, this does not imply that the distress of these patients cannot be modified. Traditional cardiac rehabilitation has shown positive results in terms of decreasing levels of anxiety, improving health status, and the overall risk profile of cardiac patients (Lavie and Milani, 2004). However, generally a combination of psychological interventions and traditional rehabilitation programs including education and exercise has been superior to standard rehabilitation (Lane et al., 1999). It has been suggested that type-D personality interacts negatively with a person's ability to cope adequately (Doering et al., 2004), and therefore that patients with this personality taxonomy may need interventions specifically targeting their impaired coping skills, an aim that may go beyond the scope of traditional behavioral interventions. Future intervention trials focusing on type-D are needed in order to examine how the deleterious effect of this risk profile can be reduced.

The results of the current study should be interpreted with some caution. First, questions may be raised as to the appropriateness of using 6 months as a baseline measure for the HADS. However, the aim of the study was to identify predictors of chronic anxiety in post-PCI patients and not anxiety related to the PCI procedure. Baseline assessment of psychological symptoms in PCI patients has been shown not to be a good predictor of later psychopathology, as symptoms at the time of the PCI may reflect distress related to the procedure (Grace et al., 2004; Rumsfeld et al., 2003). Furthermore, a 6 months assessment ensures that patients are medically stable. Second, we used a self-report measure of anxiety rather than a diagnostic interview. However, the HADS has been shown to be both valid and reliable in assessing anxiety caseness in somatic patients (Bjelland et al., 2002; Herrmann, 1997). Furthermore, HADS-depression has been shown to be superior to the BDI fast scale at identifying patients with acute coronary syndrome at increased risk of 1-year mortality (Doyle et al., 2006). Although using HADS is not equivalent to performing a diagnostic interview, these results support the use of HADS-anxiety when assessing clinically relevant anxiety in cardiac patients. Third, we had no information on participation in cardiac rehabilitation and the use of pharmacotherapy, which may have influenced our results. Despite these limitations, advantages of the current study are the serial assessment of anxiety and that patients represent those seen in daily clinical practice.

In conclusion, the results of the current study showed that 65% of patients who were anxious 6 months post-PCI also suffered from anxiety at 12 months, showing a high level of chronicity. Type-D personality increased the risk of developing chronic anxiety in excess of 200%, whereas the use of sirolimus-eluting stents reduced the risk by 50%. Although sirolimus-eluting stent implantation had a significant protective effect, this needs to be replicated in future studies as it may be an artifact of the PR surrounding the use of this new drug-eluting stent. However, the risk associated with type-D points to the importance of including psychosocial factors in risk stratification in research and clinical practice despite new interventions in the treatment of CAD.

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