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## Type-D personality exerts a stable, adverse effect on vital exhaustion in PCI patients treated with paclitaxel-eluting stents

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### Abstract

**Objective:** Vital exhaustion is associated with the pathogenesis of cardiovascular disease (CVD), but its prevalence after percutaneous coronary intervention (PCI) with drug-eluting stent implantation, as well as the impact of personality on exhaustion, is not known. In PCI patients, we examined (a) the prevalence of exhaustion, (b) the impact of type-D personality on exhaustion over time, and (c) the clinical significance of type-D personality compared with gender and age as predictors of exhaustion. **Methods:** Consecutive patients ( $n=419$ ) with stable or unstable angina treated with PCI with drug-eluting stent implantation completed the Type-D Scale (DS14) at baseline and the Maastricht Questionnaire (which assesses exhaustion) at baseline and at 1 year. **Results:** Of all patients, 53% were exhausted at baseline and at 1 year, with 41% experiencing chronic symptoms. Type-D patients [ $F(1, 417)=98.688$ ;  $P<.001$ ] had significantly higher exhaustion levels than non type-D patients both at the time of the index PCI

and at 1 year. There was a general improvement in symptoms of exhaustion over time [ $F(1, 417)=5.005$ ;  $P=.03$ ], but type-D exerted a stable effect on exhaustion ( $P=.06$ ). In multivariable analysis, type-D (OR=3.53; 95% CI=1.88–6.64) remained an independent predictor of exhaustion at 1 year, adjusting for demographic and clinical risk factors and exhaustion at baseline. The impact of type-D on exhaustion was large compared with a small effect for gender and age, as measured by Cohen's effect size index. **Conclusions:** Symptoms of exhaustion were still highly prevalent in PCI patients 1 year post-PCI despite treatment with the latest technique in interventional cardiology. Type-D exerted a large and stable effect on exhaustion compared with that of gender and age. CVD research and clinical practice may benefit by adopting a personality approach in order to identify high-risk patients.

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**Keywords:** Cardiovascular disease; Drug-eluting stent; Revascularization; Type-D personality; Vital exhaustion

### Introduction

Vital exhaustion is a mental state characterized by unusual fatigue, demoralization, and increased irritability [1]. Exhaustion is an etiological risk factor for ischemic heart disease and all-cause mortality in healthy individuals [2] and

a prognostic risk factor for adverse health outcomes in patients following percutaneous coronary intervention (PCI) and myocardial infarction (MI) [3–6]. The risk associated with exhaustion in patients with established cardiovascular disease (CVD) ranges from two- to three-fold [3,5], making it a risk factor on par with traditional biomedical risk factors [6,7]. Of note, exhaustion is not merely a marker of subclinical CVD but a risk factor in its own right [3].

Symptoms of exhaustion have been linked to inflammation [8,9], cytomegalovirus, *Chlamydia pneumoniae* [9,10], lower levels of cortisol and adrenocorticotropic hormones [11,12], impaired fibrinolysis [13], and low vagal tone [14],

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all of which have been associated with the pathogenesis of CVD. Conceptually, exhaustion shares several features with depression, and results are conflicting as to their independence [15,16]. Hence, this is the subject of an ongoing debate. To fuel the debate, a recent study found that exhaustion and self-rated health, but not depression, were associated with increased inflammation in women with CVD [17].

The recent Exhaustion Intervention Trial (EXIT) showed that although symptoms of exhaustion were reduced by 55% following a behavioral intervention, this benefit was only seen in patients without a previous history of CVD [18]. Similarly, only patients without a previous history of CVD experienced a 60% reduction in the risk of adverse health outcomes, whereas the intervention did not lead to overall enhanced survival at 2 years follow-up [18].

Although the EXIT increases our knowledge of factors that may impede changes in exhaustion and subsequent benefits to survival, little is known about the impact of personality on exhaustion. Knowledge of the predictors of exhaustion may lead to more successful intervention trials in the future. In addition, focus on patient-centered outcomes, such as exhaustion and its determinants, may bridge the gap between research and clinical practice [19].

In a previous study conducted in the pre-drug-eluting stent era, we identified type-D personality as a predictor of exhaustion in a mixed group of cardiac patients pre- and post-treatment with PCI, coronary artery bypass graft (CABG) surgery, or conservative treatment [20]. Type-D is defined as the tendency to experience increased negative emotions paired with the non-expression of these emotions in social interactions [21]. Type-D is an emerging risk factor in CVD that has been associated with an increased risk of adverse prognosis [22–26]. However, given that the use of drug-eluting stents has been associated with a significant decrease in the risk of restenosis and the need for repeat revascularization [27] and that exhaustion plays a role in the etiology of restenosis post-PCI, it is not clear whether exhaustion remains a problem in the drug-eluting stent era.

The current study was conducted in a series of consecutive PCI patients treated with the paclitaxel-eluting stent (PES) as the default stent. The aims were to (a) evaluate the prevalence of symptoms of exhaustion, (b) examine the impact of type-D personality on exhaustion at the time of the index PCI and at 1 year, and (c) compare the clinical significance of type-D personality with gender and age as predictors of exhaustion.

## Materials and methods

### Study design and participants

Consecutive patients with stable or unstable angina, treated with PCI at the Erasmus Medical Center Rotterdam using PES as the default strategy between July 1, 2003, and

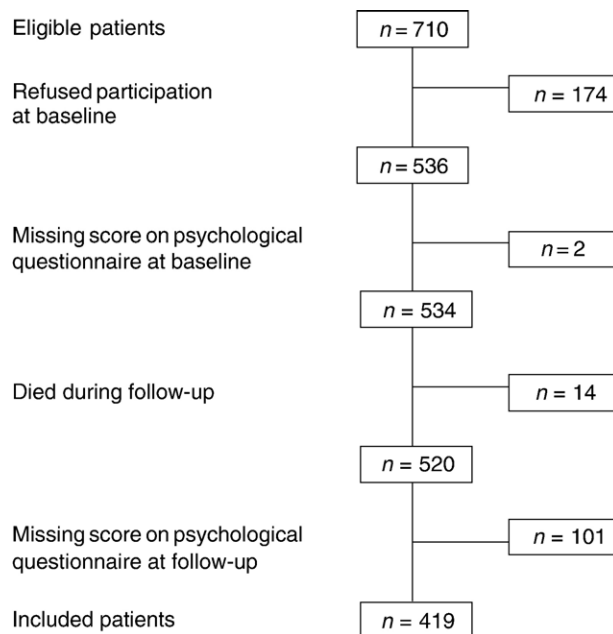


Fig. 1. Flowchart of patient selection.

July 1, 2004, qualified for inclusion in the current study. Of the 845 patients treated during this period, 19 patients died within the first month and 116 were excluded due to insufficient knowledge of the Dutch language. The remaining 710 patients were approached and asked to complete a number of psychological questionnaires 4 weeks post-PCI, of whom 536 (75%) agreed. In the remainder of the article, we will refer to this assessment as baseline. Although assessment at 4 weeks was adapted for logistic reasons, preliminary evidence suggests that psychological assessment at the time of PCI may be less optimal than 1 month post-procedure [28].

Given that we used a prospective design, analyses are based on 419 patients, who had a score on the relevant psychological questionnaires both at baseline and at follow-up. See Fig. 1 for a flowchart of the patient selection for the current study.

The study was approved by the local medical ethics committee and conducted in accordance with the Helsinki Declaration. Written informed consent was provided by all patients.

### Materials

#### Socio-demographic and clinical variables

Socio-demographic variables included gender and age. Information on clinical variables, that is, indication for PCI (stable or unstable angina), stent type (PES, sirolimus-eluting stent, or other), multivessel disease, previous cardiac history (i.e., MI, PCI, or CABG prior to the index PCI), hypertension, dyslipidemia, diabetes mellitus, smoking, and cardiac medication (aspirin, beta-blockers, diuretics, ACE inhibitors, and statins), was obtained from the patients' medical records.

### Type-D personality

We used the Type-D Scale (DS14) to assess the distressed (type-D) personality [21]. The scale consists of 14 items that are answered on a five-point Likert scale from 0 (*false*) to 4 (*true*). Seven items tap negative affectivity, and seven items tap social inhibition (score range, 0–28 for each subscale). Type-D caseness is defined by a high score on both subscales, as determined by a standardized cut-off score  $\geq 10$  [21]. The DS14 is a valid and reliable scale with Cronbach's  $\alpha = .88/.86$  and 3-month test-retest reliability ( $r = .72/.82$ ) for the negative affectivity and social inhibition subscales, respectively [21]. Type-D personality is more than negative affect, as it also takes into account how patients deal with this affect through the inclusion of the social inhibition component [21,22]. The DS14 was administered at baseline.

### Vital exhaustion

The Maastricht Questionnaire (MQ) was used to assess symptoms of exhaustion [1]. The questionnaire consists of 21 items that are answered on a three-point scale (0=*no*; 1=?; 2=*yes*), with a score range of 0–42. We used a standardized cutoff score  $\geq 14$  to identify patients who were exhausted [18,29]. The reliability of the scale, as measured by Cronbach's  $\alpha$ , is .89 [1]. The MQ was administered both at baseline and at 1 year post-PCI. Patients were asked to complete the MQ items with regard to how they felt at the time of completing the questionnaire; hence, answers were not prone to recall bias.

### Statistical analyses

Discrete variables were compared with the chi-square test (Fisher's exact test when appropriate), whereas continuous variables were compared with Student's *t* test for independent samples. Analysis of variance (ANOVA) for repeated measures was used to examine whether the impact of type-D was stable over time. Univariable and multivariable logistic regression analyses were used to examine the impact of type-D personality on exhaustion at 1 year. Prior to analyses, we dichotomized vital exhaustion using a standardized cutoff, with a score  $\geq 14$  indicating those who are exhausted [18,28]. Exhaustion scores were dichotomized to be able to compare results with previous research and to enhance clinical interpretability, as advocated by others [30,31]. In multivariable analyses, we entered type-D personality, baseline exhaustion, gender, age, indication for PCI, stent type, multivessel disease, previous cardiac history (defined as MI, PCI, or CABG prior to the index PCI), hypertension, dyslipidemia, diabetes, and smoking. Cohen's effect size index was used to evaluate the clinical significance of type-D personality compared with gender and age as predictors of exhaustion [32]. An effect size of 0.20, 0.50, and  $\geq 0.80$  is considered small, moderate, and large, respectively. We used a *P* value  $< .05$  to indicate statistical significance. Odds ratios (ORs) with 95% confidence intervals (CIs) are reported.

All statistical analyses were performed using SPSS 12.0.1 for Windows (SPSS, Chicago, IL, USA).

## Results

### Differences between responders and non-responders on baseline characteristics

Excluded patients and non-responders on psychological questionnaires were more likely to smoke (22% vs. 14%;  $P = .003$ ) but less likely to suffer from dyslipidemia (63% vs. 74%;  $P = .001$ ) than responders. No other differences were found between excluded patients/non-responders and responders on baseline characteristics, including cardiac medication.

### Patient baseline characteristics stratified by personality

Of the 419 patients, 104 (25%) had a type-D personality. Baseline characteristics stratified by personality type are shown in Table 1. Except for type-D patients being more likely to be prescribed diuretics compared with non type-D patients (5% vs. 1%;  $P = .02$ ), no differences were found on baseline characteristics between the two personality types.

Both at baseline and at 1 year post-PCI, 53% of the patients were exhausted according to the predetermined cut-off score  $\geq 14$ . Of the 419 patients, 173 (41%) experienced chronic symptoms, that is, a score  $\geq 14$  on the MQ both at baseline and at 1 year. Exhaustion at 1 year could not be

Table 1  
Baseline characteristics stratified by personality type

	Type-D ( <i>n</i> =104)	Non type-D ( <i>n</i> =315)	<i>P</i>
Demographics			
Males	79 (76)	235 (75)	.88
Age, mean (S.D.)	62 (10)	63 (11)	.30
Indication for PCI			
Unstable angina	55 (53)	137 (44)	.12
Stent type			
PES	91 (88)	284 (90)	.56
Clinical variables			
Multivessel disease	58 (56)	193 (61)	.38
Previous cardiac history <sup>a</sup>	55 (53)	174 (55)	.76
Hypertension	51 (49)	151 (48)	.94
Dyslipidemia	82 (79)	237 (75)	.54
Diabetes mellitus	23 (22)	57 (18)	.45
Current smoking	12 (12)	39 (12)	.96
Cardiac medication			
Aspirin	100 (96)	302 (96)	1.00
Beta-blockers	23 (22)	71 (23)	1.00
Diuretics	5 (5)	2 (1)	.02*
ACE inhibitors	13 (13)	25 (8)	.23
Statins	74 (71)	239 (76)	.41

Values are expressed as *n* (%) unless otherwise specified.

<sup>a</sup> MI, PCI, or CABG prior to the index PCI.

\*  $P < .05$ .

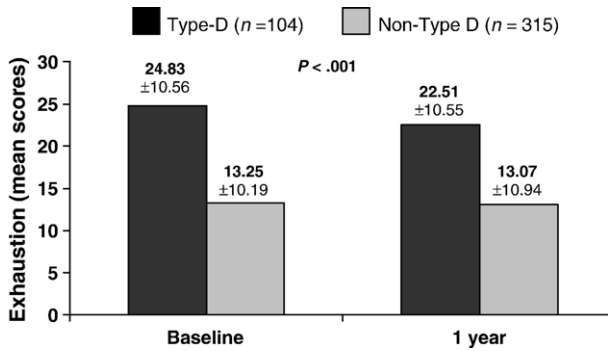


Fig. 2. Exhaustion (mean scores) stratified by type-D personality at baseline and at 1 year post-PCI. Mean scores ( $\pm$  standard deviations) are presented on top of bars.

attributed to a cardiac event (i.e., MI, PCI, or CABG) during follow-up (12% vs. 7%;  $P=.07$ ).

*Impact of type-D personality on exhaustion*

As indicated in Fig. 2, ANOVA for repeated measures showed that type-D patients [ $F(1, 417)=98.688$ ;  $P<.001$ ] had significantly higher mean exhaustion scores compared with non type-D patients both at the time of the index PCI and at 1 year. The within-subjects effect for time was also significant [ $F(1, 417)=5.005$ ;  $P=.03$ ], indicating a general decline in symptoms of exhaustion over time. The type-D $\times$ time interaction effect was not significant [ $F(1, 417)=3.702$ ;  $P=.06$ ], showing that type-D exerted a stable effect on exhaustion over time.

Patients with chronic exhaustion, defined as exhaustion both at baseline and at 1 year, were more likely to have a type-D personality compared with patients with exhaustion at either baseline or follow-up alone or exhaustion at neither time points, with patients in the no-exhaustion group having the lowest prevalence of type-D [ $\chi^2(3, N=419)=58.822$ ;  $P<.001$ ] (Fig. 3).

In univariable analyses, type-D was associated with a five-fold increased risk of exhaustion at 1 year post-PCI (OR=5.53; 95% CI=3.23–9.45;  $P<.001$ ).

*Independent predictors of exhaustion at 1 year*

In multivariable analysis, type-D (OR=3.53; 95% CI=1.88–6.64;  $P<.001$ ) remained an independent predictor of

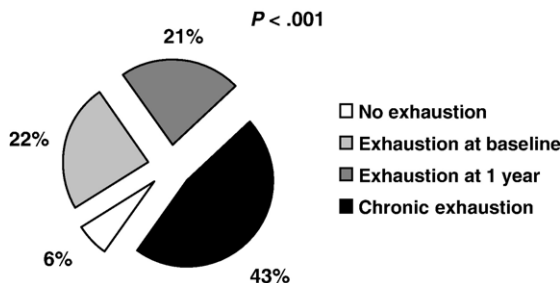


Fig. 3. Prevalence of type-D personality stratified by chronicity of exhaustion.

Table 2  
Predictors of exhaustion at 1 year (multivariable analysis)

	OR	95% CI	P
Type-D personality	3.53	1.88–6.64	<.001*
Exhaustion at baseline	9.33	5.73–15.19	<.001*
Males	0.81	0.45–1.43	.46
Age	1.01	0.99–1.04	.39
Unstable angina	0.96	0.59–1.56	.86
PES	2.12	0.94–4.76	.07
Multivessel disease	0.97	0.58–1.62	.92
Previous cardiac history <sup>a</sup>	1.48	0.90–2.43	.13
Hypertension	0.66	0.40–1.10	.11
Dyslipidemia	0.72	0.41–1.28	.26
Diabetes mellitus	1.64	0.87–3.11	.13
Current smoking	0.78	0.36–1.69	.53

<sup>a</sup> Previous MI, PCI, or CABG.

\*  $P<.001$ .

exhaustion at 1 year with a three-fold increased risk, adjusting for demographic (gender and age) and clinical risk factors (unstable angina, stent type, multi-vessel disease, cardiac history, hypertension, dyslipidemia, diabetes, and smoking) and exhaustion at baseline (Table 2). Exhaustion at baseline (OR=9.33; 95% CI=5.73–15.19;  $P<.001$ ) was also an independent predictor of exhaustion at follow-up.

*Clinical significance of type-D personality versus gender and age*

Given that gender and age are individual difference variables routinely included in CVD research, we wanted to evaluate the clinical significance of type-D compared with gender and age  $\geq 60$  in relation to exhaustion, using Cohen’s effect size index. We found that the effect of type-D on symptoms of exhaustion was large both at baseline and at 1 year, whereas the effect of gender was small and that of age was negligible at both time points (Fig. 4). In other words, although the effects of gender, age, and type-D on exhaustion were stable over the 1-year period, they had a significantly differential effect on exhaustion.

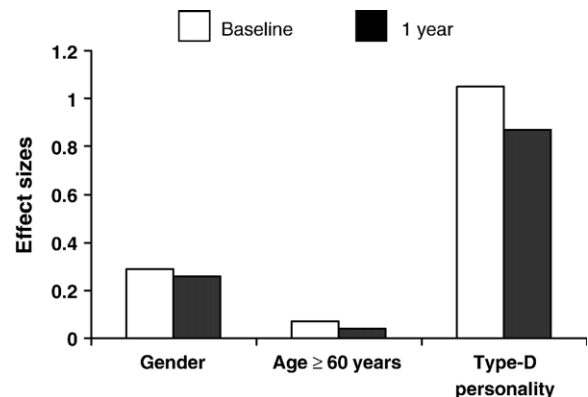


Fig. 4. Clinical relevance of type-D personality versus age and gender as determinants of exhaustion at baseline and at 1 year.

## Discussion

This is the first study to examine levels of exhaustion and the impact of personality on exhaustion in PCI patients treated in the drug-eluting stent era. The prevalence of exhaustion at the time of the index procedure and at 1 year was 53%, with 41% experiencing chronic symptoms. This indicates that exhaustion is also highly prevalent in the drug-eluting stent era. Patients with a type-D personality experienced significantly higher levels of exhaustion both at baseline and at 1 year, with type-D exerting a stable effect over time. Type-D was also an independent predictor of exhaustion 1 year post-PCI and was associated with a three-fold increased risk, adjusting for demographic and clinical baseline characteristics and exhaustion at baseline.

Despite treatment with PCI with drug-eluting stents, we found that exhaustion is still highly prevalent, with 41% being exhausted at both time points and, hence, experiencing chronic, persistent exhaustion. This suggests that, once present, exhaustion remains relatively stable and may not abate with time. Similar prevalence rates have been found in studies conducted in the pre-drug-eluting stent era in PCI patients [29] and mixed cardiac patients [20]. In the latter study, the prevalence of exhausted patients decreased from 75% at baseline to 59% following treatment [20]. However, it should be noted that the baseline assessment took place prior to PCI, CABG, or conservative treatment and that these prevalences were point prevalence rates and do not reflect levels of chronic symptoms.

Type-D personality was shown to exert a stable effect on exhaustion during the 1-year follow-up period. In addition, type-D was an independent predictor of exhaustion at 1 year post-PCI, even when adjusting for demographic and clinical characteristics and exhaustion at baseline, with the risk being three-fold. This finding is at odds with a prospective study on personality predictors of chronic fatigue in a sample of working men and women, which found that the impact of personality is negligible when adjusting for baseline fatigue [33]. However, the latter study investigated the impact of single personality traits rather than the combination of traits, used fatigue as the outcome measure rather than the broader construct of exhaustion, and was conducted in a healthy population rather than in CVD patients. In a previous study of a mixed group of cardiac patients in the pre-drug-eluting stent era, we also found that type-D personality was an independent predictor of exhaustion at baseline and at follow-up, but in this study, we did not adjust for baseline scores of exhaustion [20].

The results of the current study have implications for research and clinical practice. Symptoms of exhaustion are still highly prevalent in the drug-eluting stent era, with future studies needing to investigate whether exhaustion is also related to adverse clinical outcome in this era. More importantly, these symptoms persisted over time, which has also been shown by others, both in CVD patients [18,20] and in a healthy sample [34]. Although the EXIT

trial demonstrated that a behavioral intervention can successfully alleviate symptoms of exhaustion leading to improved prognosis, this benefit was only seen in patients without a previous cardiac history [18]. In other words, we still have no means by which to reduce exhaustion in patients with a previous cardiac history and enhance their survival, although several suggestions have been put forward in a recent substudy of the EXIT trial that examined the impact of the intervention on quality of life and other secondary outcomes [35]. These suggestions comprise the targeting of inhibition and hostility in future intervention trials and to be aware of potential limiting factors, such as chronic, painful comorbidities (e.g., rheumatism).

Future studies also need to examine the potential interrelationship between exhaustion and depression. Exhaustion and depression conceptually share several features, and to date, results as to their independence have been conflicting [15,16]. This knowledge is important to reduce the burden to patients and for epidemiological research, given the limited number of questionnaires that can usually be included in a study design.

The current study pointed to type-D personality as an important predictor of exhaustion, with type-D exerting a stable and clinically significant effect compared with the effect of gender and age. Gender and age are routinely included in CVD research, whereas, to a large extent, a personality approach has been abandoned since inconsistent results in relation to the type-A Behavior Pattern were reported [36]. The findings of the current study and other studies [23–26] indicate that a personality approach may be advantageous in terms of identifying high-risk patients. However, the ensuing question is that if type-D personality is an all-important predictor of exhaustion, how do we modify its impact on exhaustion and other health outcomes? Undoubtedly, it will be important to teach type-D patients to cope with stress in a different way, which can be done by means of a combination of cognitive behavioral therapy, psychotherapy, and relaxation therapy. However, designing an intervention trial targeting type-D at this point in time is somewhat premature, as we know very little about the moderators and mechanisms that may relate type-D to adverse health outcome, be they physiological or behavioral or a combination thereof. In other words, attention should now be focused on research into these moderators and mechanisms, which may, on the long term, lead to the designing of more successful intervention trials.

The results of the current study should be interpreted with some caution. First, the response rate was 75%, with non-responders/excluded patients being more likely to smoke but less likely to suffer from dyslipidemia than responders. Second, we only included patients with stable or unstable angina, and the results may not generalize to patients, who had an acute MI as indication for PCI. Nevertheless, the studying of patients with angina is important since psychosocial factors have also been shown to predict mortality in these patients [37]. Third, we had no

information on participation in cardiac rehabilitation and the use of psychotropic medication, such as antidepressants, which could potentially influence levels of exhaustion. Fourth, there is evidence to suggest that the Maastricht Interview for Vital Exhaustion may have better predictive validity concerning future cardiac events than the self-report MQ [38], which was used in the current study. However, the MQ has also been shown to predict future adverse clinical events [3,5] and is a more feasible instrument to use in clinical research and practice. An advantage of the current study was its prospective design with the assessment of exhaustion at two time points.

In conclusion, the results of the current study show that exhaustion is still highly prevalent in PCI patients treated in the drug-eluting stent era and that symptoms remain relatively stable over a 1-year period. Type-D personality exerted a three-fold increased risk even when adjusting for baseline exhaustion in addition to demographic and clinical characteristics. When comparing the clinical relevance of type-D with gender and age, two characteristics that are routinely included in CVD research, a large effect was found for type-D, whereas small effects were found for gender and age. CVD research and clinical practice may benefit by adopting a personality approach in order to identify high-risk patients.

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