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Type D Personality and Mortality in Peripheral Arterial Disease

A Pilot Study

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Background: Type D personality refers to the tendency to experience negative emotions and to inhibit self-expression in social interaction and has been shown to be an independent predictor of mortality in cardiac disease. Information about the effects of psychological traits on prognosis is lacking in cases of peripheral arterial disease (PAD).

Objective: To examine whether type D personality predicts all-cause mortality in PAD.

Design: Pilot follow-up study.

Setting: Vascular surgery department of a teaching hospital.

Patients: A total of 184 patients with symptomatic PAD (mean [SD] age, 64.8 [9.8] years) were followed up for 4 years (interquartile range, 3.5-4.5 years).

Main Outcome Measures: Patients completed the type D Scale-14 measure of type D personality at baseline. Information about all-cause mortality was obtained from patient medical files.

Results: During 4-year follow-up, 16 patients (8.7%) died. Adjusting for age and sex, type D personality was predictive of mortality ($P = .03$). Ankle-brachial index ($P = .05$), age ($P = .009$), diabetes mellitus ($P = .02$), pulmonary disease ($P = .09$), and renal disease ($P = .02$) were also predictive of mortality. Multivariable logistic regression revealed that age, diabetes, and renal disease were independent predictors of all-cause mortality (odds ratios, 1.1-2.3). After adjustment for these clinical predictors, patients with type D personality still had a more than 3-fold increased risk of death (odds ratio, 3.5; 95% confidence interval, 1.1-11.1; $P = .04$).

Conclusions: Type D personality predicts an increased risk of all-cause mortality in PAD, above and beyond traditional risk factors. Further research is needed to confirm these findings, but this pilot study suggests that the assessment of type D personality may be useful for detecting high-risk patients with PAD.

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PERIPHERAL ARTERIAL DISEASE (PAD), a manifestation of generalized atherosclerosis, is a relatively underdiagnosed and undertreated disease.^{1,2}

However, patients with PAD are at a significantly increased risk of major secondary events, such as stroke, fatal myocardial infarction, and cardiovascular mortality, compared with patients who have other forms of vascular disease.³ In addition to this increased cardiovascular risk,⁴⁻⁶ these patients often experience impaired quality of life (QOL).⁷⁻⁹

See Invited Critique at end of article

Preliminary evidence suggests that personality traits such as hostility may also be associated with the severity and progres-

sion of atherosclerosis in patients with PAD.^{10,11} Another potential individual risk factor in this context is the distressed personality type (type D). Type D refers to the joint tendency to experience negative emotions and to inhibit self-expression in social interaction.¹² The distressed personality type is independently associated with morbidity, mortality, and poor QOL in cardiac patients.^{13,14} Previous findings in patients with PAD and controls indicate that type D personality is associated with impaired QOL, in addition to the impairment already related to having PAD.⁸ However, prospective research on the relationship between type D personality and mortality in patients with PAD is still lacking. Therefore, the aim of the present follow-up study is to evaluate the impact of disease severity, comorbidity, and type D personality on mortality in patients with PAD.

METHOD

PATIENTS

One hundred eighty-four patients with PAD (mean [SD] age, 64.8 [9.8] years) were followed up for 4 years (interquartile range, 3.5-4.5 years) to study the factors associated with subsequent all-cause mortality. These patients were selected from a sample that originally consisted of 241 patients with suspected intermittent claudication enrolled at the Vascular Outpatient Clinic, Department of Surgery, St Elisabeth Hospital, between September 1, 2001, and March 31, 2004. Patients were asked to complete the personality questionnaire before PAD diagnosis was established by a vascular surgeon based on the clinical examination and the ankle-brachial index (ABI). Exclusion criteria were cognitive impairment, the presence of severe psychopathologic (eg, psychosis and suicidal ideation) or invalidating somatic (eg, cancer) comorbidities, participation in another study, and insufficient knowledge of the Dutch language. Patients who did not have an abnormal resting ABI (<0.90) or a postexercise ABI decrease of 20% were also excluded ($n=15$). Six patients (2.5%) were excluded owing to cognitive impairment ($n=2$), recent myocardial infarction ($n=1$), visual problems ($n=1$), influenza ($n=1$), and participation in another study ($n=1$). Hereafter, 188 of 220 eligible patients (85.5%) agreed to participate. Of the remaining patients, 3 (1.6%) did not complete the baseline measurement of the type D personality questionnaire and were excluded from the analyses. Patients who died of an unnatural cause were excluded from the present study ($n=1$). This study was designed to conform to the Helsinki Declaration and was approved by the local ethics committee of the St. Elisabeth Hospital, Tilburg. All of the patients gave informed consent.

ASSESSMENT OF TYPE D PERSONALITY

The Type D Scale-14 (DS14) was used to assess the presence of a type D personality before PAD diagnosis.¹² This 14-item questionnaire consists of two 7-item subscales, Negative Affectivity and Social Inhibition. The Negative Affectivity subscale evaluates the tendency to experience negative emotions (eg, "I often find myself worrying about something"), and the Social Inhibition subscale assesses the tendency to inhibit self-expression in social interaction (eg, "I would rather keep people at a distance"). Items are rated on a 5-point Likert scale from 0 (false) to 4 (true). A cutoff value of 10 or greater on both subscales is indicative of a type D personality. The DS14 is internally consistent, with Cronbach α values of .88 and .86, and has good factorial validity, with factor loadings ranging from 0.62 to 0.82.¹²

CARDIOVASCULAR RISK FACTORS AND COMORBIDITY

In the present study, diabetes mellitus, smoking, hypertension, hyperlipidemia, and cardiac, carotid, renal, and pulmonary status were measured at baseline in all patients according to the Society for Vascular Surgery/North American Chapter of the International Society for Cardiovascular Surgery recommended standards.¹⁵ Information was obtained from patient medical files.

ABI MEASUREMENT

A handheld Doppler device (Imexlab 9000; Imex Medical Systems Inc, Golden, Colorado) was used to obtain systolic pressures in the right and left brachial and posterior tibial and dorsalis pedis arteries. The ABI was calculated by dividing the

highest of the posterior tibial and dorsalis pedis ankle pressures in each leg by the highest brachial pressure. The ABI at rest was measured with the patient in the supine position. The lowest resting leg ABI was used in the analysis.

END POINT

The end point in this study was death from all causes. Deaths and causes of death were determined by the ward physician. When deaths were ascribed to cancer, there were always histologic results available that confirmed malignancies. Causes of death were, therefore, extracted from patient medical records. For patients who died at home, cause of death was verified by consultation with their general practitioner. Mean follow-up was 4.0 years (interquartile range, 3.5-4.5 years).

STATISTICS

Baseline characteristics were studied for the total sample and stratified by type D personality. χ^2 Tests were used for dichotomous variables, and unpaired t tests were applied for continuous variables. The risk for the association between type D and mortality was evaluated using sex- and age-adjusted Cox proportional hazards regression analysis. Multivariable logistic regression analysis (enter model) was used to determine the independent predictors of all-cause mortality. The criteria for entry and removal were $P \leq .10$ and $P > .10$, respectively. All statistical tests were 2-tailed. A statistical software program (SPSS for Windows, version 14.0.1; SPSS Inc, Chicago, Illinois) was used for all analyses.

RESULTS

No patients were lost at follow-up. All deaths were attributable to natural causes except for 1 (homicide). This participant was excluded from the analysis. Baseline characteristics of the total sample, and stratified by the presence of type D personality, are given in **Table 1**. There were no significant differences in risk factors as a function of type D personality.

During 4-year follow-up, 16 patients (8.7%) died. Most deaths (7 [43.8%]) were due to cancer, and 6 (37.5%) were due to cardiovascular death. The other 3 causes of death were pneumonia, acute pancreatitis, and terminal emphysema complicated by corticosteroid-induced diabetes.

Adjusting for age and sex, type D personality was predictive of all-cause mortality ($P=.03$). Age- and sex-adjusted estimates are commonly presented in mortality analyses and in observational studies, where groups could be biased by a differential in the sex ratio or average age.¹⁶ Survival percentages for type D and non-type D personality across time are presented in **Figure 1**. To test for differences between the resulting curves, age- and sex-adjusted Cox proportional hazards regression analysis was used (type D personality for all-cause mortality hazard ratio, 3.2; 95% confidence interval, 1.2-8.6; $P=.02$). Lower resting ABI ($P=.05$), older age ($P=.006$), and the presence of diabetes, renal disease ($P=.03$), and pulmonary disease ($P=.09$) were also predictive of mortality (**Table 2**). Risk estimates of dichotomous variables and their 95% confidence intervals are presented in **Figure 2**.

Multivariable logistic regression revealed that age, diabetes, and renal disease were independent clinical predictors of all-cause mortality (odds ratios, 1.1-2.3). Af-

Table 1. Characteristics of the Total Sample and Stratified by Type D Personality

	Type D	Non-Type D	Total Sample (N=184)	P Value
Age, mean (SD), y	65.7 (9.4)	63.0 (10.1)	64.8 (9.8)	.08
Male sex, No. (%)	43 (67.2)	74 (61.7)	117 (63.6)	.46
ABI, mean (SD)	59.9 (14.9)	62.3 (13.8)	60.7 (14.5)	.28
Diabetes mellitus, No. (%)				
Mild	9 (14.1)	8 (6.7)	17 (9.2)	.36
Moderate	6 (9.4)	12 (10.0)	18 (9.8)	
Severe	0	1 (0.8)	1 (0.5)	
Tobacco use, No. (%)				
Mild	15 (23.4)	36 (30)	51 (27.7)	.40
Moderate	28 (43.8)	38 (31.7)	66 (35.9)	
Severe	11 (17.2)	21 (17.5)	32 (17.4)	
Hypertension, No. (%)				
Mild	14 (21.9)	16 (13.3)	30 (16.3)	.52
Moderate	12 (18.8)	26 (21.7)	38 (20.7)	
Severe	5 (7.8)	10 (8.3)	15 (8.2)	
Hyperlipidemia, No. (%)				
Mild	15 (23.4)	15 (12.5)	31 (16.8)	.11
Moderate	15 (23.4)	29 (24.2)	44 (23.9)	
Severe	3 (4.7)	16 (13.3)	18 (9.8)	
Cardiac status, No. (%)				
Mild	7 (10.9)	21 (17.5)	30 (16.3)	.30
Moderate	11 (17.2)	11 (9.2)	20 (10.9)	
Severe	1 (1.6)	1 (0.8)	2 (1.1)	
Carotid status, No. (%)				
Mild	4 (6.3)	4 (3.3)	8 (4.3)	.29
Moderate	5 (7.8)	4 (3.3)	9 (4.9)	
Severe	0	2 (1.7)	2 (1.1)	
Renal status, No. (%)				
Mild	1 (1.6)	2 (1.7)	3 (1.6)	.66
Moderate	2 (3.1)	1 (0.8)	3 (1.6)	
Severe	1 (1.6)	1 (0.8)	2 (1.1)	
Pulmonary status, No. (%)				
Mild	1 (1.6)	3 (2.5)	4 (2.2)	.84
Moderate	4 (6.3)	6 (5.0)	10 (5.4)	
Severe	0	1 (0.8)	1 (0.5)	

Abbreviation: ABI, ankle-brachial index.

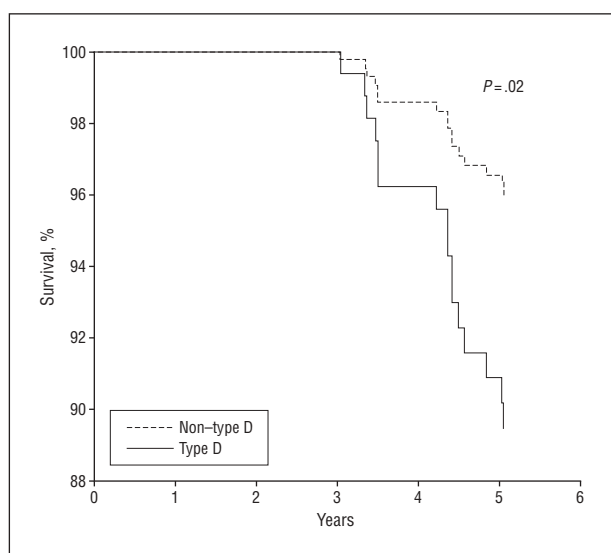


Figure 1. Cumulative survival across time stratified by type D personality.

ter adjustment for these clinical predictors, patients with type D personality still had a more than 3-fold risk of death ($P=.04$) (**Table 3**).

COMMENT

In this pilot study, we found that patients with a type D personality had a more than 3-fold risk of dying during follow-up. To our knowledge, no other psychological trait was ever studied in relation to the risk of mortality in PAD. Scarce evidence exists that personality traits, such as hostility and anger, are associated with PAD and atherosclerotic progression as measured by the ABI.^{10,11,17} Traditional risk factors, such as age, diabetes, and renal disease, were also independently associated with all-cause mortality; these findings are in line with recent literature.¹⁸ The ABI was not an independent predictor of mortality, but the ABI at baseline was relatively high in this sample, and previous research¹⁹ shows that higher ABIs have less specificity for the prediction of survival.

Although few deaths can be directly attributed to PAD, patients with PAD have generalized atherosclerosis and multiple risk factors that predispose them to an increased risk of fatal cardiovascular events.²⁰ Moreover, PAD is also a powerful predictor of all-cause mortality^{19,21,22}; cancer-related deaths, such as lung cancer, are especially more prevalent in PAD.²³ In the present study, most death causes were cancer related; pancreas and lung carcinoma were especially

Table 2. Characteristics of Participants According to Survival Status

	Survivors (n=168)	Nonsurvivors (n=16)	P Value
Age, mean (SD), y	64.2 (9.8)	71.1 (7.7)	.006
Male sex, No. (%)	106 (63.1)	4 (25.0)	.65
ABI, mean (SD)	61.4 (14.5)	54.0 (13.5)	.05
Diabetes mellitus, No. (%)			
Mild	16 (9.5)	1 (6.3)	.03
Moderate	13 (7.7)	5 (31.3)	
Severe	1 (0.6)	0	
Tobacco use, No. (%)			
Mild	45 (26.8)	6 (37.5)	.47
Moderate	59 (35.1)	7 (43.8)	
Severe	31 (18.5)	1 (6.3)	
Hypertension, No. (%)			
Mild	26 (15.5)	4 (25.0)	.70
Moderate	34 (20.2)	4 (25.0)	
Severe	14 (8.3)	1 (6.3)	
Hyperlipidemia, No. (%)			
Mild	28 (16.7)	2 (12.5)	.89
Moderate	40 (23.8)	4 (25.0)	
Severe	18 (10.7)	1 (6.3)	
Cardiac status, No. (%)			
Mild	25 (14.9)	3 (18.8)	.33
Moderate	18 (10.7)	4 (25.0)	
Severe	2 (1.2)	0	
Carotid status, No. (%)			
Mild	8 (4.8)	0	.79
Moderate	8 (4.8)	1 (6.3)	
Severe	2 (1.2)	0	
Renal status, No. (%)			
Mild	2 (1.2)	1 (6.3)	.03
Moderate	2 (1.2)	1 (6.3)	
Severe	1 (0.6)	1 (6.3)	
Pulmonary status, No. (%)			
Mild	4 (2.4)	0	.09
Moderate	7 (4.2)	3 (18.8)	
Severe	1 (0.6)	0	
Type D personality, No. (%)	55 (32.7)	9 (56.3)	.03 ^a

Abbreviation: ABI, ankle-brachial index.

^aAdjusting for age and sex.

common. Cardiovascular deaths accounted for 38% of the nonsurvivors. Lifestyle factors that are involved in the incidence of cardiovascular disease and cancer, such as smoking and obesity, may explain to a large extent the strong link between PAD and all-cause mortality.²⁴

New in the present study is the finding that a psychological trait was an independent predictor of all-cause mortality in patients diagnosed as having intermittent claudication. Psychological factors, such as chronic psychological distress, depression, and social avoidance, are extensively studied in other atherosclerotic diseases, such as coronary artery disease²⁵⁻²⁸ and cerebrovascular disease.²⁹ Chronic emotional stress and the inhibition of emotional and behavioral expression can be largely attributed to broad personality traits that refer to stable individual differences in emotions and behavior.³⁰ Moreover, the distressed personality type, or type D personality, is a strong predictor of impaired QOL and adverse prognosis in cardiac patients.^{8,13,31}

There are a variety of physiologic and behavioral pathways that may mediate the relationship between type D

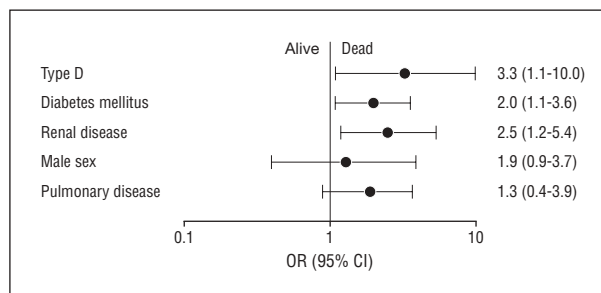


Figure 2. Univariate odds ratios (ORs) and 95% confidence intervals (CIs) of dichotomous predictors of all-cause mortality. Type D personality adjusted for age and sex.

Table 3. Independent Predictors of All-Cause Mortality in Patients With Peripheral Arterial Disease

Predictor	OR (95% CI)	P Value
Type D personality	3.5 (1.1-11.1)	.04
Age	1.1 (1.0-1.2)	.02
Male sex	2.3 (0.6-8.6)	.20
ABI	1.0 (0.9-1.0)	.34
Diabetes mellitus	2.3 (1.2-4.6)	.02
Renal disease	2.3 (1.0-5.3)	.04
Pulmonary disease	1.4 (0.7-3.2)	.37

Abbreviations: ABI, ankle-brachial index; CI, confidence interval; OR, odds ratio.

personality and adverse health outcomes in cardiovascular patients. Type D personality has been associated with increased immune activation in patients with chronic heart failure, as indicated by higher circulating plasma levels of the pro-inflammatory cytokine tumor necrosis factor (TNF) and its soluble receptors sTNFR1s and TNFR2.^{32,33} Type D personality has also been associated with disruption of the hypothalamic-pituitary-adrenocortical axis and increased cortisol reactivity in experimental³⁴ and clinical³⁵ research. Inadequate self-management of chronic disease is a potential behavioral mechanism that may explain the relation between type D personality and poor prognosis in cardiovascular disease.³⁶

Overall, attention for psychological factors, and personality in particular, will become increasingly important given the continuing epidemics of chronic cardiovascular disease, obesity, and diabetes.^{37,38} In addition to their adverse effect on cardiovascular prognosis, personality and chronic stress act as barriers to improvement of lifestyle factors in cardiovascular patients³⁹ and need to be addressed in clinical practice.⁴⁰ Although patients with PAD typically have multiple cardiovascular risk factors that put them at high risk for fatal cardiovascular events,¹ research shows that patients with PAD receive suboptimal secondary prevention.⁴¹ In addition to improving awareness of the traditional medical risk factors in PAD, attention should be given to psychological factors that may have an adverse effect on the clinical course of PAD. The present findings show that screening for type D personality may be especially important in this context.

These findings, however, need to be interpreted with caution because there were only a limited number of events in this pilot study. Nonetheless, the type D effect was dis-

cerned in the small sample. After controlling for important clinical risk factors, such as ABI, diabetes, and renal disease, the presence of the type D effect suggests that type D personality may have a significant adverse effect in patients with PAD. By analogy, initial observations on type D personality and mortality in a small sample of coronary patients⁴² were confirmed afterward in a larger patient sample.⁴³ Therefore, confirmatory research on the distressed personality and mortality in patients with PAD is warranted in multiple centers that are involved in PAD management. Although age tended to be higher in patients with type D personality (not statistically significant), controlling for age in multivariable analysis did not explain the association between personality and mortality. On the contrary, it suppressed the irrelevant variance in type D personality, and there are no indications that type D is associated with older age.^{13,14,31,41} Finally, the standard assessment of personality before diagnosis of PAD and the prospective design are major strengths of this study.

Hence, in light of the challenge of optimizing risk management in PAD, a personality-based approach may be useful. Previous research has already shown that type D personality predicts prognosis in cardiac patients^{13,14,31,41} and impaired QOL.^{8,25} This study suggests that attention on personality variables may also improve the detection of high-risk patients with PAD.

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Author Contributions: Drs Aquarius, Denollet, and Ms Smolderen had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Aquarius, Smolderen, Hamming, De Vries, Vriens, and Denollet. *Acquisition of data:* Aquarius, Smolderen, Hamming, and Vriens. *Analysis and interpretation of data:* Smolderen. *Drafting of the manuscript:* Aquarius, Smolderen, and Hamming. *Critical revision of the manuscript for important intellectual content:* Hamming, De Vries, Vriens, and Denollet. *Statistical analysis:* Smolderen. *Obtained funding:* Denollet. *Administrative, technical, and material support:* Aquarius, Smolderen, and Hamming. *Study supervision:* Aquarius, Hamming, De Vries, Vriens, and Denollet.

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INVITED CRITIQUE

We are all (hopefully) scientists, and we live our lives based on objective, repeatable data. Having said this, it also must be conceded that subjective, difficult-to-quantify psychological factors seem to affect clinical outcomes. We have all had the experience of looking at a patient who has “lost the will to live” and being sure, albeit without any hard data at all, that this patient will not do well.

Aquarius and colleagues, in this relatively straightforward study, provide us with a bit of objectivity regarding this concept. Even after controlling for age, diabetes mellitus, and renal and pulmonary disease, patients with vascular disease whose premorbid answers on a personality questionnaire put them into the type-D (“distressed”) category had a 3-fold higher risk of death when observed for 4 years.

Whether the specific pattern of answers really means that these patients are “distressed” or not, the fact that answers on a psychological questionnaire predict mortality 4 years later is very interesting. Correlation does not imply causation, but the implications are intriguing.

Perhaps these people have poorer health habits and their disease (although not measurable in this study) is, in fact, worse at presentation than that of controls, or perhaps their coping mechanisms regarding identification and treatment of ongoing problems and complications as time goes on are less effective. The former explanation implies that this is simply a predictive finding, but the latter implies that intervention to improve outcome is possible. Should we assess all our patients like this? Perhaps; obviously much more work is needed, but these findings are of interest and add a bit of objectivity to the concept that the personality of a patient can affect his or her health and well-being.

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