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Impaired health status in Type D patients following PCI in the drug-eluting stent era

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Abstract

Background: Drug-eluting stenting reduces restenosis post-percutaneous coronary intervention (PCI), but subgroups of patients may not benefit optimally from this procedure. We examined the impact of Type D personality on health status over time and the clinical relevance of Type D as a predictor of impaired health status at 12 months in unselected post-PCI patients.

Methods: Consecutive patients ($n = 692$) participating in the *Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital* (RESEARCH) registry completed the Type D Scale at 6 months and the Short Form Health Survey 36 (SF-36) at 6 and 12 months post-PCI.

Results: Although there was a significant improvement in health status over time ($p < 0.001$), Type D patients reported a substantially lower score on all health status domains of the SF-36 compared with non-Type D patients ($p < 0.001$). Type D personality was an independent predictor of impaired health status on all SF-36 sub domains at 12 months except for physical functioning, adjusting for baseline demographic and clinical variables and health status at 6 months. In these adjusted analyses, Type D personality increased the likelihood of impaired health status at 12 months post-PCI from 60% (OR: 1.60; 95% CI: 1.04–2.46) to almost 300% (OR: 3.99; 95% CI: 2.52–6.32), varying among the parameters analyzed.

Conclusions: Type D personality was associated with impaired health status in post-PCI patients treated in the drug-eluting stent era. The role of personality factors as determinants of clinical outcome and health status should not be overlooked as these factors may have much explanatory power.

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Keywords: Coronary artery disease; Drug-eluting stent; Health status; Revascularization; Type D personality

1. Introduction

Despite a significant reduction in the incidence of restenosis and the need for revascularization following percutaneous coronary intervention (PCI) with drug-eluting stent implantation [1–3], subgroups of patients who have undergone a successful PCI may not benefit optimally from this invasive procedure in terms of improved health status. Health status has been identified as an important determinant of mortality [4,5], but health status is also increasingly receiving attention as an outcome measure in its own right. Advances in the treatment of cardiovascular disease has led to a shift from hard endpoints, such as mortality and myocardial infarction (MI), to include the patient's perspective and the value of these advances to society [6]; prolonged survival is no longer the "be all and end all" but also the quality of life of the patient has become important. With this shift in outcomes, identifica-

tion of subgroups at risk of impaired health status is gaining increasing importance, with knowledge of the determinants of impaired health status leading to a closing of the gap between research and clinical practice [6].

From the pre drug-eluting stent era, there is evidence to support the notion that subgroups of patients may benefit differentially from cardiac invasive procedures. In patients following PCI, vital exhaustion has been shown to predict the occurrence of new cardiac events including the need for revascularization [7]. Vital exhaustion is a mental state defined by unusual fatigue, irritability, and feelings of demoralization [7]. Prior history of depression [8] and smoking [9] also have been shown to impede the benefits of PCI on health status. Other factors associated with impaired health status include female gender [10,11], impaired left ventricular function [12], depression [13], and the *distressed* (Type D) personality [14], although the majority of these studies were conducted in patients with acute coronary syndromes rather than in patients following PCI.

In a recent study of this sample, we showed that Type D personality was associated with a 5-fold increased risk of death or MI adjusting for all other factors [15]. Type D defines those individuals who tend to experience increased negative emotions and who inhibit the self-expression of these emotions in social interactions [16]. A Type D patient typically worries, has a gloomy view of life, often feels unhappy, and is a closed kind of person who prefers to keep other people at a distance. In the pre drug-eluting stent era, Type D has been associated with adverse health status at 5-years' follow-up [14], major adverse cardiac events despite appropriate treatment [16–18], and has been found to exert a large and persisting effect on symptoms of vital exhaustion and fatigue pre- and post-intervention compared with that of gender [19]. It is important to note that the impact of Type D remained substantial when adjusting for demographic and clinical risk factors, with the associated risk being 4–8 fold for adverse prognosis [16]. However, to date no study has examined whether Type D personality has a persistent adverse impact on health status. It is also not known whether the impact of Type D on health status seen in the pre drug-eluting stent era still exists in the drug-eluting stent era. Although there is clear evidence to demonstrate that personality is an important explanatory factor of individual differences in outcome [16], paradoxically the inclusion of personality factors in psychosomatic research has become unfashionable since the controversy surrounding the Type A Behavior Pattern.

The objective of the current study was two-fold: (1) To establish the stability of Type D personality as a modulator of health status at 6 and 12 months in post-PCI patients receiving a sirolimus-eluting stent (SES) or bare metal stent (BMS) implantation; (2) To investigate the clinical relevance of Type D personality as a predictor of health status at 12 months.

2. Materials and methods

2.1. Study design and participants

The study population comprised a series of consecutive patients ($n = 875$; 71% response rate) treated with PCI with either SES or BMS implantation at the Erasmus Medical Center Rotterdam between October 16, 2001, and October 15, 2002, as part of the *Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital* (RESEARCH) registry. The design of the RESEARCH registry [20] and the psychological sub study has been published previously [15]. In brief, the purpose of the RESEARCH registry was to evaluate the efficacy and the safety of the SES in the 'real world' of interventional cardiology. For this reason, no exclusion criteria were applied, and all patients were considered for enrolment regardless of anatomical or clinical presentation. Of note, the majority of patients (68%) enrolled in the RESEARCH registry would not have qualified for inclusion in randomized controlled trials due to their more complex profile [21].

At 6 and 12 months post-procedure, letters were sent to the civil registries requesting information on the survival status of each patient. Subsequently, all surviving patients were contacted by mail and asked to fill in a set of self-report questionnaires. Assessment at 6 months was chosen so as to represent patients in a stable condition, as the risk of restenosis is enhanced in the 0–6 months period post-PCI. Other studies have adopted a similar approach [22]. Clinical variables were also obtained at 6 months.

For the current sub study, only patients ($n = 692$) who had a score on the Short Form Health Survey 36 (SF-36) at 6 and 12 months post-PCI qualified for inclusion (Fig. 1). Responders on the SF-36 were less likely to have undergone a previous PCI compared with non-responders (23% vs. 32%; OR: 0.67; 95% CI: 0.47–0.96; $p = 0.03$). No other
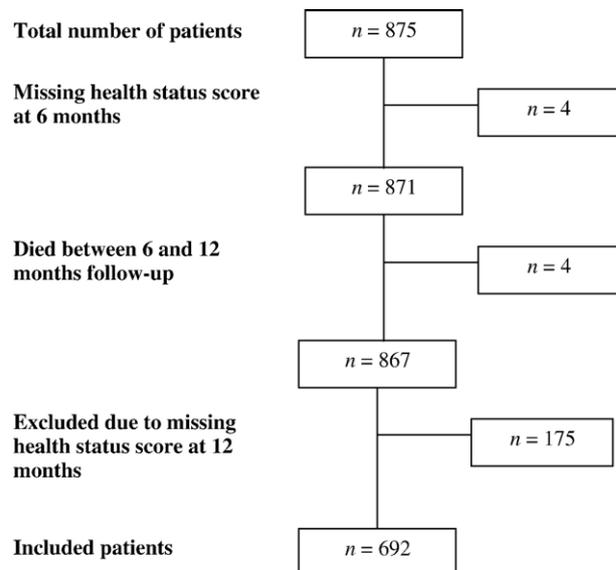
Fig. 1. Flow chart of patient selection.

differences on demographic and clinical baseline characteristics (as shown in Table 1) were found between the two groups.

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

2.2. Materials

2.2.1. Socio-demographic and clinical variables

Socio-demographic variables included gender and age. Information on clinical variables (SES or BMS implantation, previous MI, previous coronary artery bypass graft (CABG) surgery, previous PCI, recent cardiac event (defined as a MI, CABG or PCI 0–6 months post-PCI), multi-vessel disease, hypertension, dyslipidemia, diabetes mellitus, renal impairment, and smoking) was prospectively collected at the time of procedure and recorded in the institutional database.

2.2.2. Type D personality

Type D personality was assessed with the 14-item Type D Scale (DS14) [23]. The questionnaire measures negative affectivity (e.g. "I often feel unhappy") and social inhibition (e.g. "I am a 'closed' person"). Only patients who score

high on both components–as determined by a pre-defined cut-off ≥ 10–are classified as Type D. Although Type D is often mistaken for a measure of depression or negative affect, it is more than negative affect since it also includes how patients deal with these negative emotions [23]. Items are answered on a five-point Likert scale (0–4) with a score range of 0 to 28 for each subscale. The psychometric properties of the DS14 are good with Cronbach's alpha = 88/.86 and test–retest reliability $r = .72/.82$ for the negative affectivity and social inhibition subscales, respectively [23]. The DS14 was administered 6 months post-PCI.

2.2.3. Health status

The Short Form Health Survey (SF-36) is a generic measure that assesses eight health status or health-related quality of life domains, i.e. physical functioning, role physical functioning, role emotional functioning, mental health, vitality, social functioning, bodily pain, and general health [24]. Scale scores are obtained by summing the items together within a domain, dividing this outcome by the range of scores and then transforming the raw scores to a scale from 0 to 100. A higher score on the SF-36 sub domains represents a better functioning with a high score on the bodily pain scale indicating freedom from pain. The scale has good reliability with Cronbach's alpha ranging from .65 to .96 for all subscales [25]. The SF-36 was administered at 6 and 12 months following PCI.

2.3. Statistical analyses

Discrete variables were compared with the chi-square test and are presented as percentages. Continuous variables were compared with the Student's t-test and are presented as means ± standard deviations (S.D.). Analysis of variance (ANOVA) for repeated measures was used to compare between group differences (Type D vs. non-Type D) over time on the eight health status domains of the SF-36. In a subsequent analysis, we adjusted for all baseline characteristics using an analysis of covariance (ANCOVA) for repeated measures. Prior to running logistic regression analyses, the eight subscales of the SF-36 were recoded into discrete variables, with the lowest tertile on the SF-36 indicating poor health status compared with the other two tertiles indicating good health status. Dichotomization was undertaken to enhance clinical interpretability, as proposed by others [26,27]. Subsequently, we performed multivariable logistic regression analyses to delineate predictors of the eight health status domains at 12 months. In the multivariable analyses, we adjusted for all baseline characteristics and health status at 6 months. For all multivariable analyses, adjustment for all baseline characteristics refers to those listed in Table 1. All tests were two-tailed. A p-value < 0.05 was considered to be statistically significant. Odds ratios (OR) with 95% confidence intervals are reported. All analyses were performed using SPSS 12.0.1 for Windows.

Table 1
Baseline characteristics (6 months post-PCI) stratified by Type D personality

	Type D (n = 190)	Non-Type D (n = 502)	p
Demographics			
Females (%)	31	27	0.38
Age, mean (S.D.)	62 (±11)	63 (±10)	0.30
Stent type			
SES (%)	42	41	0.83
Clinical variables			
Previous MI (%)	36	37	0.88
Previous CABG (%)	11	13	0.68
Previous PCI (%)	25	23	0.58
Recent event (%)	15	6	<0.001‡
Multi-vessel disease (%)	51	52	0.87
Hypertension[a] (%)	42	36	0.17
Dyslipidemia[b] (%)	84	79	0.13
Diabetes mellitus[a] (%)	16	13	0.36
Renal impairment[c] (%)	36	30	0.17
Current smoking[d] (%)	40	29	<0.01†

SES = sirolimus-eluting stent.
Previous MI = myocardial infarction prior to the index event.
Previous CABG = coronary artery bypass surgery prior to the index event.
Previous PCI = percutaneous coronary intervention prior to the index event.
Recent event = MI, CABG or PCI between 0 and 6 months post-PCI.
†$p < 0.01$; ‡$p < 0.001$.
[a] Present if being treated for the condition.
[b] Total cholesterol levels >240 mg/dl or on lipid lowering medication.
[c] Indicated by creatinine clearance <60 ml/min.
[d] Based on self-report.

3. Results

3.1. Patient characteristics

Patient characteristics stratified by Type D personality at 6 months are listed in Table 1. Type D patients were more likely to have had a recent cardiac event ($p < 0.001$) and to smoke compared with non-Type D patients ($p < 0.01$). No other significant differences were found between the two personality types on characteristics at 6 months.

3.2. Changes in health status between 6 and 12 months post-PCI

The ANOVA for repeated measures showed a general significant improvement in health status ($F(1, 690) = 20.418$; $p < 0.001$) between 6 and 12 months. Although the interaction effect Type D personality by time was significant ($F(1, 690) = 3.979$; $p = 0.046$), Type D patients experienced a significantly adverse health status compared with non-Type D patients at both 6 and 12 months ($F(1, 690) = 113.616$; $p < 0.001$) (Fig. 2). These differences were substantial ranging from 10 to 23 points dependent on the health status domain in question and the time point (6 or 12 months). Since the two personality taxonomies differed on baseline characteristics, we investigated whether the main effect of Type D remained significant in multivariable analyses using an ANCOVA for repeated measures. Type D patients were still found to report poorer health status after adjusting for all baseline characteristics ($F(1, 660) = 101.883$; $p < 0.001$).

3.3. Predictors of impaired health status at 12 months

Table 2 shows the variables associated with impaired health status at 12 months adjusting for stent type, clinical and demographic variables, and health status at 6 months. Only significant predictors are shown. Type D personality was a significant independent predictor of impaired health status for all domains of the SF-36, except for physical functioning (Table 2). In these corrected analyses, the
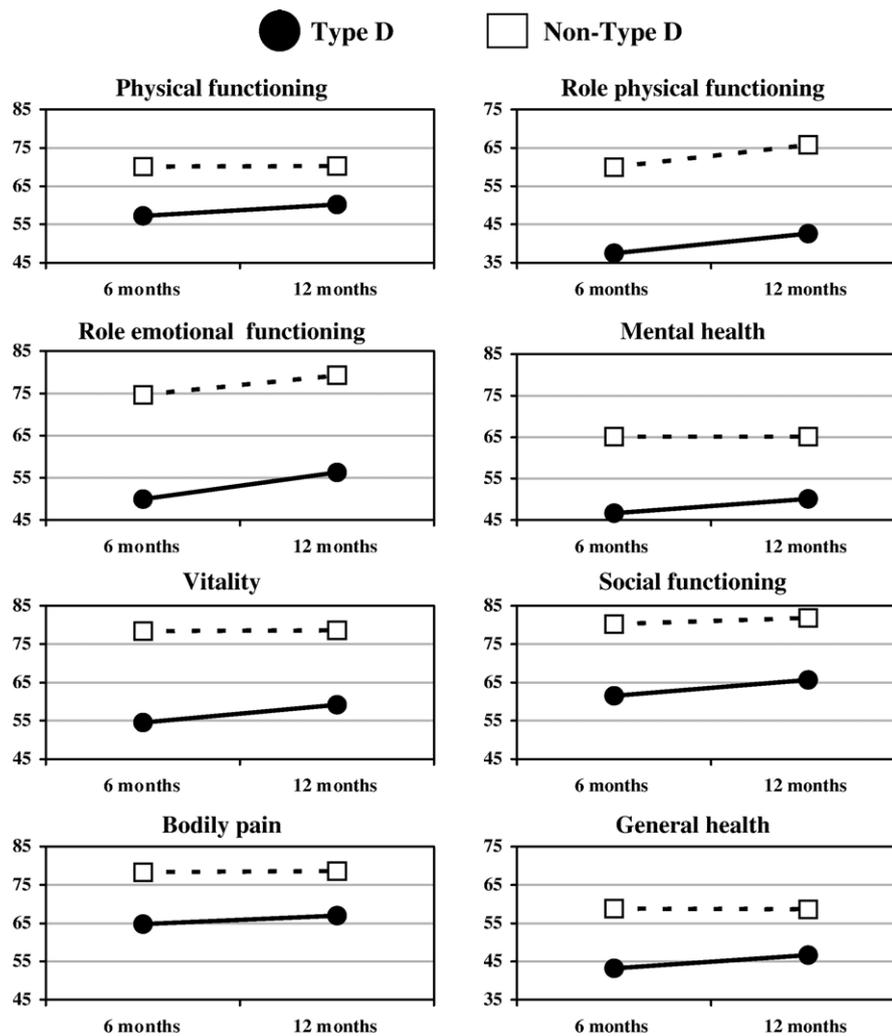

Fig. 2. Health status at 6 and 12 months stratified by Type D personality (ANOVA for repeated measures (univariable analyses); effect of personality for all subdomains of health status at 6 and 12 months ($p < 0.001$). A high score indicates better health status with a high score on bodily pain representing the absence of pain).

Table 2
Predictors of impaired health status at 12 months (multivariable analyses)

SF-36 subscales	Impaired PF OR (95% CI)	Impaired RPF OR (95% CI)	Impaired REF OR (95% CI)	Impaired MH OR (95% CI)	Impaired VI OR (95% CI)	Impaired SF OR (95% CI)	Enhanced BP OR (95% CI)	Impaired GH OR (95% CI)
Type D personality	ns	2.26 (1.50−3.38)‡	2.50 (1.60−3.90)‡	1.87 (1.19−2.93)†	3.99 (2.52−6.32)‡	2.64 (1.73−4.02)‡	1.60 (1.04−2.46)*	1.98 (1.32−2.97)†
Female gender	2.14 (1.31−3.48)†	2.39 (1.58−3.62)‡	ns	2.46 (1.57−3.85)‡	1.92 (1.21−3.04)‡	1.63 (1.06−2.52)*	ns	1.92 (1.27−2.90)†
Age ≥ 60	ns	ns	ns	0.63 (0.40−0.99)*	ns	ns	ns	0.54 (0.36−0.81)†
SES	1.73 (1.09−2.75)*	ns	ns	ns	ns	ns	ns	ns
Previous MI	ns	ns	ns	ns	ns	ns	0.57 (0.37−0.87)*	ns
Previous CABG	ns	1.82 (1.01−3.29)*	ns	2.35 (1.21−4.55)*	ns	ns	2.02 (1.09−3.74)*	2.09 (1.16−3.76)*
Previous PCI	ns	ns	ns	1.64 (1.01−2.66)*	ns	ns	ns	ns
Recent event	ns	ns	ns	ns	ns	ns	ns	ns
Multi-vessel disease	ns	ns	ns	0.53 (0.34−0.84)†	ns	ns	ns	ns
Hypertension	ns	ns	ns	ns	ns	ns	ns	ns
Dyslipidemia	0.56 (0.32−0.96)*	ns	ns	ns	ns	ns	ns	ns
Diabetes mellitus	ns	ns	ns	ns	ns	ns	ns	ns
Renal impairment	ns	ns	ns	ns	ns	ns	ns	ns
Current smoking	ns	ns	ns	ns	ns	ns	ns	ns
6 months health status	26.32 (15.94−43.46)‡	5.95 (4.03−8.77)‡	9.87 (6.41−15.19)‡	9.30 (5.98−14.46)‡	8.41 (5.41−13.09)‡	9.18 (5.86−14.39)‡	7.95 (5.27−12.00)‡	6.44 (4.36−9.51)‡

PF=Physical Functioning; RPF=Role Physical Functioning; REF=Role Emotional Functioning; MH=Mental Health; VI=Vitality; SF=Social Functioning; BP=Bodily Pain; GH=General Health.
SES=sirolimus-eluting stent.
*$p<0.05$; †$p<0.01$; ‡$p<0.001$.

presence of Type D personality increased the likelihood of impaired health status at 12 months post-PCI from 60% (OR: 1.60; 95% CI: 1.04–2.46) to almost 300% (OR: 3.99; 95% CI: 2.52–6.32), varying among the parameters analyzed.

4. Discussion

This is the first study to examine the impact of Type D personality on health status at 6 and 12 months in patients treated with PCI in the drug-eluting stent era. Although there was a general improvement in health status between 6 and 12 months, Type D patients had significantly lower scores on all health status domains as measured by the SF-36 at both time points. In addition, Type D personality was shown to be an independent predictor of impaired health status at 12 months post-PCI on all sub domains of the SF-36, except for physical functioning after adjusting for clinical and demographic characteristics and health status at 6 months. The reason for the lack of association between Type D and physical functioning may be that for this sub domain, baseline health status had a considerably larger impact (26-fold) than for any of the other sub domains (ranging from 5- to 9-fold).

Improvement in health status over time following revascularization is consistent with other studies post-CABG [10] and PCI [28] indicating the beneficial effects of revascularization on health status. However, in the current study we showed that subgroups of patients may not benefit from PCI on par with other patients, as Type D patients experienced significantly impaired health status compared with non-Type D patients. These differences were not only statistically significant but also clinically relevant with a mean difference of >10 points on the SF-36 even 12 months post-PCI. This finding is consistent with previous studies conducted in the pre drug-eluting stent era. In a 5-year prospective study of patients with ischemic heart disease, Type D patients were shown to be at a 2-fold increased risk of poor perceived health compared with non-Type D patients adjusting for clinical risk factors [14]. In the latter study, however, health status was only assessed at one time point. Type D has also been associated with more than a 4-fold increased risk of vital exhaustion in patients both pre- and post-intervention with CABG, PCI or pharmacotherapy [19]. In a recent study of patients with an implantable cardioverter defibrillator, patients and partners with a Type D personality experienced significantly increased levels of distress with the risk ranging from 4–8-fold after adjusting for other factors, including shocks in patients [29]. Taken together, these results indicate that Type D patients comprise a subgroup of patients that may not benefit from pharmacological and invasive treatment on par with non-Type D patients.

This does not imply, however, that Type D patients do not stand to gain considerably from treatment including cardiac invasive procedures, as they did experience some improvement in health status and reduction in distress between 6 and 12 months in the current study. In a previous study, Type D patients also reported vital exhaustion scores far exceeding those of non-Type D patients pre- and post-intervention, but Type D patients nevertheless experienced a decrease in symptoms of exhaustion following intervention, another psychosocial risk factor in coronary artery disease [19]. Similar findings have been reported in a recent study examining the impact of a prior history of depressive disorder on health status following PCI [8]. These results testify to the clinical benefits of cardiac invasive procedures for particular subgroups of patients, but more importantly they assert that these subgroups require further intervention, likely of a psychosocial nature, in order to experience benefits on par with the fellow patients.

However, is Type D at all amenable to change given the notion that it is a personality construct that exerts a stable influence on behavior? The results of the current study clearly show that their perceived health status can be changed, although the effect of any given intervention, medical or psychosocial, is likely to have a less beneficial effect on Type Ds compared with non-Type Ds. Clinical intervention trials of a psychosocial nature are warranted to establish whether a reduction of distress in Type D patients may lead to improved prognosis and gains in health status.

It is noteworthy that disease severity as measured by multi-vessel disease generally was not associated with health status in the current study. This finding concurs with two previous studies that identified depressive symptoms as a determinant of health status independent of clinical risk factors [13,30].

The results of the current study should be interpreted with some caution. Patients who died between 0 and 6 months post-PCI did not have the opportunity to fill in the psychological questionnaires. This may have biased our results, as the sickest patients were excluded. Nevertheless, there is some debate whether baseline assessment in PCI patients is the best time to assess psychological symptoms [31]. Moreover, assessment of health status after 6 months has been adopted in other studies in order to represent patients in a stable medical condition, since the risk of restenosis is increased the first 6 months post-procedure [22]. Second, Type D and non-Type D patients differed on particular baseline characteristics. However, we adjusted for these characteristics in multivariable analyses. Third, we had no information on the use of psychopharmaca and treatment by a psychiatrist or a psychologist, which may have had an influence on health status. Finally, the study cannot point to pathways that may be responsible for the link between Type D personality and adverse health status, however, the study was not designed to investigate this objective.

Despite these limitations, this study has several strengths. It is the first study to examine the impact of Type D personality on health status in unselected consecutive patients treated successfully with PCI in the drug-eluting

stent era. It is also the first study to investigate whether the effect of Type D on health status persists over time. In addition, the study included multiple assessments of health status, which has been advocated as a means by which to bridge the gap between research and clinical practice [32]. Finally, patients represented those seen in daily clinical practice, as no patients were excluded due to clinical or anatomical criteria [21].

In conclusion, Type D personality was found to modulate the effect of PCI in patients with ischemic heart disease and to be an independent predictor of impaired health status. Of note, the impact of Type D on health status was persisting over time. The role of personality factors as determinants of clinical outcome and health status should not be overlooked as they may have much explanatory power. Studies are now warranted that delineate which pathways are responsible for the adverse impact of Type D on prognosis and health status in patients with established heart disease. The first preliminary study in patients with heart failure points to the immune system as being one possible pathway [33]. Other potential pathways include disease-promoting behaviors, such as smoking, not adhering to treatment regimens, etc.

Acknowledgements

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