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Association between Type D personality and outcomes in patients with non-ischemic heart failure

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Abstract

Purpose The "distressed" (Type D) personality trait has been reported to be over-represented in patients with heart failure (HF) compared to the background population and may provide prognostic information for mortality. We examined the association between Type D personality and outcomes in the DANISH trial (The Danish Study to Assess the Efficacy of Implantable Cardioverter Defibrillators in Patients with Non-ischemic Systolic Heart Failure on Mortality).

Methods The DANISH trial included a total of 1116 patients with non-ischemic HF on guideline-recommended therapy. Type D personality was assessed with the Type D Scale (DS14) at baseline and investigated through follow-up accordingly. Multivariable Cox proportional hazard models were used to compare hazard ratios (HR) of cardiovascular and all-cause mortality.

Results Type D personality assessment was completed by 873 (78%) patients at baseline and Type D personality was found in 120 (14%) patients. The median follow-up was 67 months (interquartile range [IQR] 48–83). Among patients with versus without Type D personality, 22% versus 19% died from all-cause yielding similar incidence rates of 4.62 (95% CI 3.14–6.87) versus 3.95 (95% CI 3.37–4.66) per 100 person-years. The adjusted risk of all-cause mortality was not significantly different in patients with versus without Type D personality with an adjusted HR of 1.31 (95% CI 0.84–2.03, $p = 0.23$) with similar results for cardiovascular death (HR 1.46 (95% CI 0.88–2.44, $p = 0.15$).

Conclusion Type D personality was not significantly associated with increased risk of all-cause mortality or cardiovascular death in patients with non-ischemic HF.

Keywords Personality · Type D personality · Heart failure · Implantable cardioverter defibrillator

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Introduction

Studies examining the prognostic impact of the "distressed" Type D personality have flourished in the last decade, since the first proposed association was published in 1995, with particular focus on its impact on hard endpoint clinical outcomes as all-cause mortality, cardiovascular mortality, and myocardial infarction, in patients with cardiovascular diseases [1, 2]. Type D personality is classified as a distressed personality type and refers to the simultaneous occurrence of a stable joint trait constituted by a high level of social inhibition (SI) and negative affectivity (NA). The SI subdimension represents facets of social discomfort, reticence, and lack of social poise, whereas the NA subdimension covers characteristics such as irritability, anxiety, and dysphoria [3]. Depression is common in patients with HF and has also been associated with risk of mortality, but despite a relation, conceptual differences between depression and Type D personality exist as depression is episodic and Type D personality is a stable trait characteristic [4–6].

Several studies investigating the association between Type D personality and mortality exists, however, with large heterogeneity, as some have confirmed an association [7–11] while others did not [4, 12–14]. A systematic review found that in patients with coronary artery disease (CAD), the Type D personality affects the prognosis negatively, however not in patients with heart failure (HF) [2]. Some of the previous studies on patients with HF included in the systematic review did not adjust for age or gender, and all had less than 4 years of follow-up. Thus, it remains to be established whether Type D personality contributes with prognostic information in patients with HF.

Conventional risk factors of mortality in HF are primarily based on demographic, clinical, and physiological variables. However, a plea inclusion of patient-reported outcomes in clinical research and practice has been expressed by patients and scientific societies [15, 16].

The presence of Type D personality was assessed at baseline in the recent Danish Study to Assess the Efficacy of Implantable Cardioverter Defibrillators (ICD) in Patients with Non-ischemic Systolic Heart Failure on Mortality (DANISH) trial. The trial identified that ICD implantation was not related to overall improved survival in patients with non-ischemic HF [17]. In this study, we investigated the association between Type D personality and mortality in patients with non-ischemic HF included in the DANISH trial.

Methods

Study design and subjects

The study design and primary results of the DANISH trial have been reported previously [17, 18]. Briefly, the DANISH trial was a randomized multicenter study that assessed the efficacy of prophylactic ICD implantation in patients with symptomatic non-ischemic systolic HF. The DANISH trial enrolled 1116 patients, recruited from the five ICD implanting centers in Denmark from 2008 to 2014 and randomized to either ICD group or control group with usual clinical care [17]. All patients received contemporary guideline-specified therapy with inclusion of medical therapy with beta-blockers (BB), angiotensin-converting enzyme (ACE) or angiotensin-receptor blockers (ARB) and mineralocorticoid-receptor antagonists. Inclusion criteria were New York Heart Association (NYHA) functional class II or III, (or IV if cardiac resynchronization (CRT) was decided), a left ventricular ejection fraction (LVEF) $\leq 35\%$, and an elevated level (>200 pg. per milliliter) of N-terminal pro-brain natriuretic peptide (NT-proBNP). The decision to implant a CRT device was required to be conducted prior to randomization and patients randomized to the ICD group underwent the implantation within 1 month. The study design of this investigation was an observational cohort study. Patients were enrolled only after providing informed consent. The DANISH trial is registered at ClinicalTrials.gov with the identifier NCT00542945. The study was approved by the regional scientific ethics committee for the capital region in Denmark, *De videnskabsetisk komitéer for Region Hovestaden* (H-D-2007-0101).

Type D personality

Type D personality was assessed with the Type D Scale (DS14), a 14-item self-administered questionnaire rated on a five-point Likert scale (0–4) [3]. The scale assesses two subdimensions, social inhibition (SI, 7-items) and negative affectivity (NA, 7-items), with a score range of 0–28 for each subdimension [3]. Patients are classified as Type D personality if they score ≥ 10 on both SI and NA, with all other patients classified as non-Type D. The cut-off of ≥ 10 has been identified by Item Response Theory as the most optimal [19].

The DS14 questionnaire is the current standard of assessing Type D personality, has high internal consistency, and is not confounded by mood status or disease severity [3].

In a sensitivity analysis, missing data in the DS14 questionnaire were imputed with the personal mean score

method [20, 21] if more than half questions had been answered. Thus, patients were excluded if they had completed less than half of the questions (the half-rule) [22, 23].

Statistical analysis

Baseline characteristics are presented as frequency (percentages) for categorical variables and median (interquartile range (IQR)) for continuous variables. Differences according to presence of Type D personality were assessed by *t* test or Mann–Whitney U test for continuous variables and χ^2-test for categorical variables. Patients excluded from the present study due to missing DS14 completion at baseline were compared with included patients using similar statistics.

The primary outcome in this study was all-cause mortality and the secondary outcomes were cardiovascular death and sudden death. All endpoints in the DANISH trial were adjudicated by a clinical endpoint committee. Crude incidence rates for each outcome are presented as events per 100 person-years (PY) with 95% confidence intervals. Event rates of each outcome according to Type D personality were plotted as cumulative incidence functions and compared using log rank or Grays test as appropriate. Hazard ratios (HR) of the outcomes according to Type D personality at baseline were compared using Cox proportional hazard regression models. Multivariable models were adjusted for demographic variables (age and sex), disease-related variables (systolic blood pressure, NYHA class, LVEF, log transformed N-terminal pro B-type natriuretic peptide (NT-proBNP), estimated glomerular filtration rate (eGFR) and HF duration), devices (ICD and CRT), HF medication, and comorbidities (diabetes, chronic obstructive pulmonary disease, cancer, and stroke or transient ischemic attack). In the DANISH trial, there was a significant interaction between age at randomization and the effect of ICD versus control on mortality [24]. Therefore, we conducted a subgroup analysis to investigate potential interactions in this study.

Separate analyses for each subdimension of DS14 were conducted by a dichotomization at the same cut-off at 10 as for the Type D personality assessment, as no other validated approach has been suggested. Furthermore, separate questions of the DS14 were investigated for their prognostic value. Two-sided *p* values < 0.05 were considered significant. All statistical analyses were completed in SAS 9.4 (Cary, NC, USA).

Results

Characteristics of the patients

A total of 873 (78%) patients of the 1116 enrolled in the DANISH trial completed the DS14 questionnaire at baseline (Supplement 1). Patients in the present study had a median age of 63 years (IQR 56–70), 28% were females, a median LVEF of 25% (IQR 20–30), and 56% were in NYHA class II. Patients included were well medicated with 97% of patients on ACE inhibitors or ARBs, 92% on beta-blockers, and 58% received mineralocorticoid-receptor blockers.

Patients with Type D personality, constituting 14% ($n = 120$), compared to patients without Type D personality, were younger (median age 60 vs. 63, $p = 0.0002$), received less ACE inhibitor or ARB medication (93% vs. 97%, $p = 0.01$), and fewer had an ICD (43% vs. 52%, $p = 0.04$) (Table 1). Patients with Type D compared to non-Type D personality had a median NA score of 13 (IQR 12–16) versus 6 (IQR 2–8) and a median SI score of 13 (IQR 12–16) versus 5 (IQR 2–8).

Patient characteristics for DS14 respondents compared with DS14 non-respondents differed on higher median systolic blood pressure, lower median NT-proBNP, higher median eGFR, lower NYHA class, shorter median duration of HF, and lower prevalence of CRT (Supplement 2).

Association between Type D personality and mortality

At the end of follow-up, after median 67 months (IQR 48–83), the primary outcome of death from any cause had occurred in 172 patients (20%), and of those, 113 (13%) were due to cardiovascular causes. Patients with Type D personality had a similar incidence of death from any cause compared to those with a non-Type D personality, respectively, 22% vs. 19% and incidence rates of 4.62 per 100 PY (95% CI 3.14–6.87) and 3.95 per 100 PY (95% CI 3.37–4.66) with a non-significant crude hazard ratio of 1.17 (95% CI 0.77–1.78, $p = 0.46$) (Table 2 and Fig. 1). In the multivariable adjusted model, type D personality was not associated with risk of all-cause mortality with a hazard ratio of 1.31 (95% CI 0.84–2.03, $p = 0.23$) compared to patients without Type D personality. Type D personality was not associated with significantly increased risk of all-cause mortality within any subgroup, and all subgroup interactions were insignificant including age interaction (Supplement 3).

The risk of cardiovascular death and sudden death were not significantly higher in patients with Type D personality versus those with a non-Type D personality (Table 2). The incidence rates of cardiovascular death were 3.55 per 100 PY (95% CI 2.29–5.50) for patients with Type D personality and 2.52 per 100 PY (95% CI 2.06–3.09) for those without Type D personality giving an adjusted HR of 1.46 (95% CI 0.88–2.44, $p = 0.15$). The incidence rates for sudden death in patients with Type D and non-Type D personalities were 1.60 per 100 PY (95% CI 0.83–3.07) and 1.03 per 100 PY (95% CI 0.75–1.42), respectively, with an adjusted HR of 1.51 (95% CI 0.72–3.20, $p = 0.28$).

Table 1 Baseline patient characteristics stratified by type D personality

Characteristic	Type D personality ($N=120$)	Not Type D personality ($N=753$)	p Value
Median age (IQR)—years	60 (53–67)	63 (57–71)	0.002
Female sex—%	27 (23)	216 (29)	0.16
Median blood pressure—mm Hg			
Systolic	124 (107–139)	125 (111–140)	0.48
Diastolic	73 (67–83)	74 (66–82)	0.99
Median body-mass index (IQR)—kg/m^2	27 (23–30)	27 (24–30)	0.87
Median NT-proBNP level (IQR)—pg/ml	1020 (487–2141)	1147 (592–2165)	0.30
Median QRS duration (IQR)—ms	140 (112–168)	146 (110–166)	0.32
Median left ventricular ejection fraction (IQR)—%	25 (20–30)	25 (20–30)	0.98
Median eGFR (IQR)—ml/min/1.73 m^2	77 (61–94)	75 (59–92)	0.19
NYHA class—no. (%)			
II	62 (52)	424 (56)	0.57
III	56 (47)	321 (43)	
IV	2 (2)	8 (1)	
Median duration of heart failure (IQR)—months	13 (7–58)	16 (8–60)	0.51
Coexisting conditions—no. (%)			
Diabetes	25 (21)	134 (18)	0.42
Hypertension	35 (29)	233 (31)	0.74
Renal insufficiency	4 (3)	23 (3)	0.87
Cancer	5 (4)	68 (9)	0.07
Chronic obstructive pulmonary disease	12 (10)	89 (12)	0.56
Stroke	10 (8)	77 (10)	0.54
Medications—no. (%)			
ACE inhibitor or ARB	112 (93)	734 (97)	0.01
Beta-blocker	108 (90)	697 (93)	0.33
Mineralocorticoid-receptor antagonist	73 (61)	432 (57)	0.48
Amiodarone	6 (5)	44 (6)	0.71
CRT—no (%)	71 (59)	416 (55)	0.42
ICD—no (%)	51 (43)	395 (52)	0.04
Social variables			
Living alone (%)	36 (31)	207 (28)	0.49
Highest education			
Primary school—(%)	74 (62)	437 (58)	0.39
High school—(%)	14 (12)	75 (10)	
Higher education ≤ 4 years—(%)	11 (9)	118 (16)	
Higher education > 4 years—(%)	9 (8)	63 (8)	
NA	12 (10)	60 (8)	
Smoking (%)	28 (24)	134 (18)	0.14

ACE angiotensin-converting enzyme, *ARB* angiotensin-receptor blocker, *CRT* cardiac resynchronization therapy, *GFR* glomerular filtration rate, *ICD* implantable cardioverter defibrillator, *IQR* interquartile range, *NT-proBNP* N-terminal pro-brain natriuretic peptide, and *NYHA* New York Heart Association

As a sensitivity analysis, personal mean score method imputation increased the number of eligible patients by 57, representing 23% of the excluded 243 patients from the DANISH trial. The increase in patients from 873 (78%) to 930 (83%) did not alter the prevalence of Type D personality (120/837 (13.8%) and 132/930 (14.2%)) and the sensitivity analysis yielded similar results for all-cause mortality as complete case analysis with an insignificant crude HR of 1.12 (95% CI 0.75–1.66, $p=0.59$) and an adjusted HR of 1.20 (95% CI 0.79–1.81, $p=0.39$).

Table 2 Outcomes stratified by personality type

Outcome	Personality		Incidence rate		Hazard ratio			
	No. of events/total no. (%)		Events/100 person-years (95% CI)		Unadjusted		Adjusted*	
	Type D ($N=120$)	Not Type D ($N=753$)	Type D	Not Type D	Hazard ratio (95% CI)	*p* Value	Hazard ratio (95% CI)	*p* value
Death from any cause	26 (22)	146 (19)	4.62 (3.14–6.78)	3.95 (3.37–4.66)	1.17 (0.77–1.78)	0.46	1.31 (0.84–2.03)	0.23
Cardiovascular death	20 (17)	93 (12)	3.55 (2.29–5.50)	2.52 (2.06–3.09)	1.42 (0.88–2.30)	0.16	1.46 (0.88–2.44)	0.15
Sudden death	9 (8)	38 (5)	1.60 (0.83–3.07)	1.03 (0.75–1.42)	1.57 (0.76–3.25)	0.22	1.51 (0.72–3.20)	0.28

*The adjusted model includes demographic variables (sex and age), disease-related variables (NYHA class, log transformed NT-proBNP, LVEF, eGFR, ICD, CRT, HF medication, HF duration, and systolic blood pressure), and comorbidities (diabetes, chronic obstructive pulmonary disease, cancer, and stroke or transient ischemic attack)

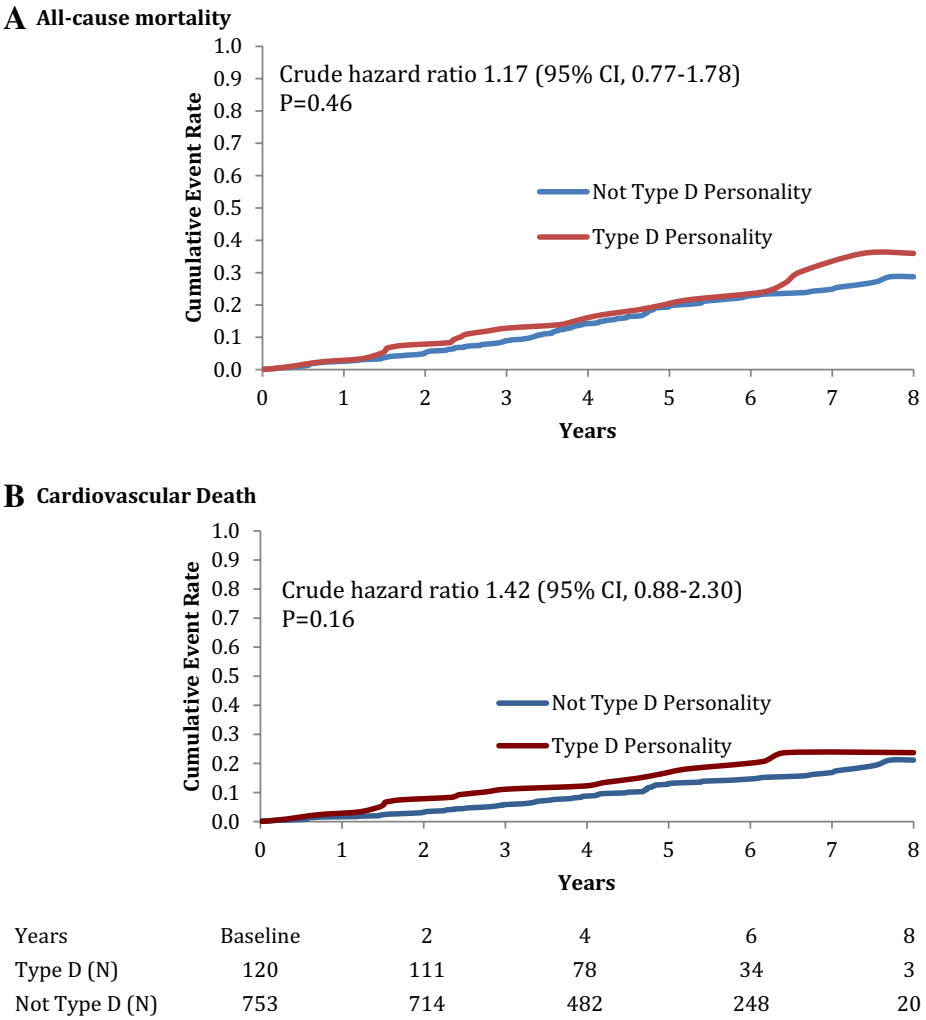

Fig. 1 Time-to-event curves according to Type D personality. The figure shows the cumulative incidence curve for patients divided by Type D personality versus non-Type D personality in DS14

Subdimension analyses

The subdimensions of the DS14, NA and SI, were not associated with all-cause mortality (Supplement 4). Patients scoring high on SI were, however, significantly more prone to cardiovascular death compared to those scoring low on SI with a crude HR of 1.49 (95% CI 1.01–2.20, $p=0.05$) (Fig. 2). However, this association between SI and

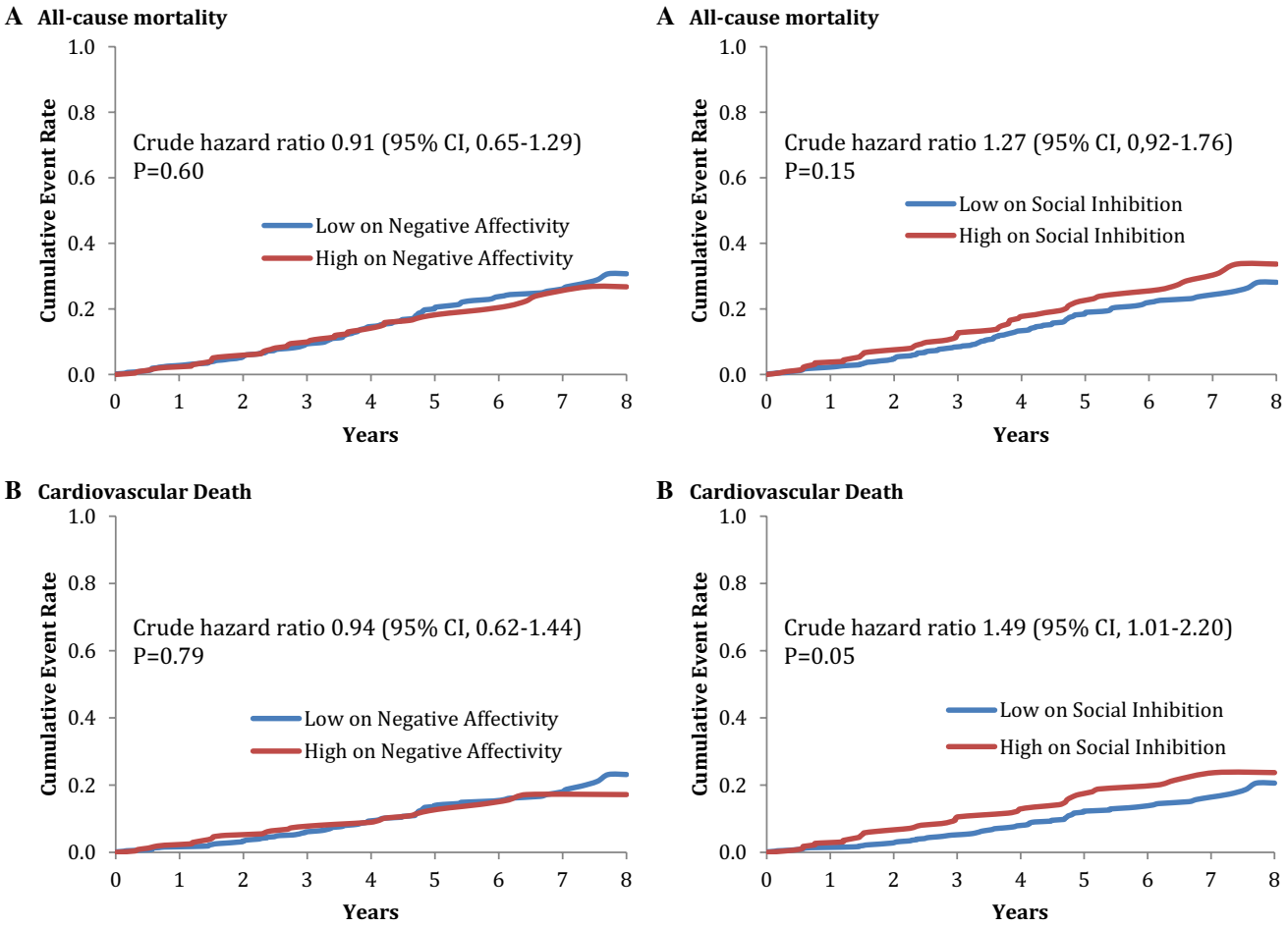

Fig. 2 Time-to-event curves according to Type D personality subdimensions. The figure shows the cumulative incidence curve for patients scoring ≥ 10 for negative affectivity and social inhibition, respectively, as subdimensions of the DS14

cardiovascular death was not significant in the multivariable adjusted model (hazard ratio 1.30 (95% CI 0.86–1.95, $p = 0.21$)).

Of the 14 questions constituting the DS14 scale, one single question (question 2) was significantly associated with all-cause mortality in the unadjusted analyses "I often make a fuss about unimportant things" (HR 0.83, 95% CI 0.71–0.97, $p = 0.02$). In the multivariable model, none of the questions were independent predictors of all-cause mortality (Supplement 4).

Discussion

The main finding of the present study was that Type D personality in subjects with non-ischemic HF was not associated with either increased risk of all-cause mortality or cardiovascular death. To the best of our knowledge, this study is the largest investigating the impact of Type D personality in a population with non-ischemic HF.

Type D personality has been associated with adverse outcomes in several former studies with the usage of DS14 as the main questionnaire for assessment [7–11, 25]. Proposed deleterious effects of Type D personality [26] include increased oxidative stress burden [27], endothelial dysfunction [28], higher levels of cortisol [29], and dysfunctional cytokine balance [30, 31]. However, more recent studies have not been able to confirm an association between Type D personality and adverse cardiovascular outcomes [4, 12–14, 32–35]. Kupper and Denollet [36] proposed that the heterogenic findings regarding outcomes in patients with Type D personality may be related to choice of endpoint and age of patients. Notably, we examined both all-cause mortality and cardiac death and found no significant association between Type D personality and any of the mortality outcomes. With regard to age, Kupper and Denollet found that Type D consistently predicted major adverse cardiac event (MACE) in lower age groups, however not in those above 70 years. We conducted interaction analysis with an age cut-off at 68 years

of age; however, we found no interaction with age and Type D personality for all-cause mortality, $p = 0.65$.

A review pooling various cardiovascular diseases identified that Type D personality was associated with a significantly higher rate of MACE [7]. Per contra, a large German cohort study similarly included patients with various cardiovascular diseases and did not find an association between Type D personality and all-cause mortality [33]. These contradictory findings indicate uncertainty with respect to the added prognostic information of Type D personality in a population with various cardiovascular diseases. The prognostic value of Type D personality may be related to the etiology of the cardiovascular disease according to a systematic review reporting that Type D personality affects prognosis in patients with CAD, but not in patients with HF [2]. One study reported an association between Type D personality and increased mortality in patients with HF [25], but this has not been confirmed in the majority of studies on patients with HF [32–35]. Our findings are consistent with reports of a lack of association between type D personality and outcomes in patients with heart failure.

The findings of the present study should be interpreted with some caution due to several limitations. First, the DANISH trial randomized 1116 patients, whereas due to missing data, this substudy excluded 22% of the study population. There were significantly fewer ICD implantations in patients with Type D personality; however, as the DANISH trial [17] identified that ICD implantation was not related to overall improvement in survival, these do not affect our results in patients with non-ischemic HF. Excluded patients—where the personality type was unknown—compared with included patients were more likely to have more severe HF. Additionally, patients who did not complete the DS14 had a higher mortality rate compared to those included in this study, respectively, 33% versus 20% ($p < 0.0001$). The prevalence of Type D personality in our population of patients with non-ischemic HF was 14%, which is in the lower range as Type D personality has been reported to be around 13–25% in former studies for patients with HF [33–35] and in the general population (16.6–38.5%) [37]. However, a sensitivity analysis with imputation of those originally excluded due to partially incomplete DS14 questionnaire data did not increase the proportion of Type D personalities nor alter the Cox proportional hazard model. Major strengths of the study are that data are derived from a large nationwide multicenter HF population with detailed clinical information (although not diagnosis of depression), patients included were on contemporary medical therapy, and there was a long follow-up with adjudicated endpoints.

In conclusion, patients with non-ischemic HF and Type D personality was not associated with an increased risk long-term all-cause mortality or cardiovascular death compared to patients without Type D personality.

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Compliance with ethical standards

Conflict of interest JCN is supported by a grant from the Novo Nordisk Foundation (NNF16OC0018658). CTP reports support for clinical studies from Bayer in the field of protection against thrombosis. LK receives personal fees from Novartis.

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