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Health status of older patients with type 2 diabetes and screen-detected heart failure is significantly lower than those without☆,☆☆

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Heart disease is the major cause of death in patients with type 2 diabetes [1]. Existing disease management programs, however, mainly focus on glucose regulation, and pay little attention to early signs of structural or functional abnormalities of the heart [2]. The awareness of a strong relationship between type 2 diabetes and heart disease, including heart failure is growing [3,4]. We showed earlier that unknown heart failure (HF) is very prevalent in type 2 diabetes patients aged 60 years and over [5].

Cross-sectional studies showed that the health status of patients with type 2 diabetes and concurrent HF is significantly lower than in those without HF [6–8]. Whether the same is true for type 2 diabetes patients in whom HF is unmasked by screening is unknown.

We assessed the health status of patients with type 2 diabetes and compared those with screen-detected HF, to those already known with concurrent HF, and to those without HF.

From February 2009 to March 2010, patients with type 2 diabetes aged 60 years and older underwent a diagnostic assessment including echocardiography to unmask HF and left ventricular dysfunction. The study protocol was published previously [9].

In total, 605 persons participated. Twenty-four (4.0%) patients were already known with a cardiologist-confirmed diagnosis of HF, and the remaining 581 participants underwent a standardized one-day diagnostic work-up. Presence or absence of HF was determined by an expert-panel using all available diagnostic information, including echocardiography and following the definition of HF of the European Society of Cardiology; symptoms and/or signs suggestive of HF in combination with structural or functional abnormalities during echocardiography at rest [10].

All participants gave written informed consent, and the institutional review boards of the University Medical Center Utrecht and the Admiral de Ruyter Hospital in Goes, the Netherlands approved the study protocol.

At baseline, the duration of diabetes, smoking history, medical history, current medication use, and cardiovascular co-morbidities were registered [9]. All participants filled out the EuroQol (EQ-5D), Short Form 36 (SF-36) and Diabetes Health Profile (DHP-32) questionnaires during the assessment, and, at home, after 3 and 12 months (see Table 1). During follow-up, we also assessed medication use and hospital admissions. Research assistants phoned patients when questionnaires were not filled out or were incomplete, to reduce the number of missing data.

To compare groups, we used the chi-square test for differences in proportions, and ANOVA and Kruskal–Wallis for differences in means. To identify between which groups the differences were significant, post-hoc analyses were performed: Tukey for means and Bonferroni for proportions. Data with a skewed distribution were summarized as medians with interquartile ranges (IQR). We imputed 'zero' for the scores on the questionnaires at 3 and 12 months in nine (1.4%) patients who died during follow-up. We used generalized estimation equations (GEE) to compare the health status at baseline and over time between groups. This method applies a longitudinal regression analysis that considers variables at different time-points and uses all available data [11]. We adjusted in the GEE analysis for age, gender, and relevant comorbidities including ischaemic heart disease (IHD), stroke or transient

☆ **Registration:** The study is registered in the Dutch register of the Central Committee on Research Involving Human Subjects (CCMO), www.ccmo.nl, NL22717.041.08.
☆☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1
Health status questionnaires.

The EuroQol [12]	A generic questionnaire consisting of a classification system (EQ-5D) and a Visual Analogue Scale (EQ-VAS) measures preference-based utilities. It covers five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with three levels of functioning; no problems, some problems, and severe problems. The EQ-5D utility score was computed with the MVH-A1 algorithm yielding a score ranging from −0.594 (states worse than dead) to +1.00 (full health), where 0 means death [13]. The minimal clinical important change in the EQ-5D score was estimated at 0.074 [14]. The EQ-VAS is a graded vertical line anchored at 0 (worst imaginable health state) and ending at 100 (best imaginable health state). Participants were asked to mark a point on the EQ-VAS that best reflects his or her current health state [12].
Short Form 36 (SF-36) [15]	This questionnaire assessed generic health status. The Dutch translation of the SF-36 has been validated in both general and disease specific samples [16]. The SF-36 consists of 36 questions and generates a profile of scores on eight dimensions of health, namely physical functioning (PF), role limitation because of physical functioning (RP), bodily pain (BP), social functioning (SF), mental health (MH), role limitations due to emotional problems (RE), vitality (VT) and general health (GH). For all eight dimensions a score is calculated, with a range from 0 (least favorable health state) to 100 (most favorable health state). A physical component summary (PCS) and a mental component summary (MCS) can be calculated and compared with a standardized mean population value of 50 [17]. For physical functioning a score change of 10 to 15 points is generally considered as clinically relevant [18].
Diabetes Health Profile (DHP-32) [19]	This questionnaire was used to assess disease-specific health status. The DHP-32 contains 32 questions and generates a profile on three subscales; physical distress, barriers to activity, and disinhibited eating. The range is from 0 (severe dysfunction) to 100 (no dysfunction).

ischaemic attack (Stroke/TIA), asthma or chronic obstructive pulmonary disease, and renal failure (RF). Data were analyzed using SPSS Windows version 20.0 (SPSS, Chicago, IL, USA).

The mean age of the 605 participants was 71.8 (SD 7.5) years, and 54.2% were male. The median duration of diabetes was 5.5 (IQR 3.0–10.1) years, and the mean HbA1c 6.7% (SD 0.7) or 49.6 mmol/mol (SD 8.1). HF was detected in 161 patients during the baseline assessment, and the vast majority (83% of all screen-detected HF) had preserved ejection fraction (Table 2).

All (100%) participants filled out the health status questionnaires at baseline. The response rate during follow-up was 92% for the DHP, 94% for the SF-36 and 95% for the EuroQol.

Table 2 lower section shows the reported health status at baseline of patients with screen-detected HF, known HF, and without HF, as measured with the EuroQol, SF-36 and DHP questionnaires. At baseline, differences were found for the Euroqol and SF-36 physical component summary between type 2 diabetes patients with screen-detected HF, with known HF and those without HF (Table 2 lower section). We

Table 2
Baseline characteristics of 605 patients with type 2 diabetes divided in no heart failure, screen-detected heart failure, and already known with heart failure.

Characteristics	No heart failure (n = 420) Group 0	Screen-detected heart failure (n = 161) Group 1	Known heart failure (n = 24) Group 2	*P* value[a]
Age in years, mean (SD)	70.5 (7.0)^{1,2}	74.6 (7.7)^{0}	75.5 (8.8)^{0}	<0.001
Male gender (%)	233 (55.5)	77 (47.8)^{2}	18 (75.0)^{1}	0.03
Duration of diabetes in years, median (IQR)	5.1 (3.0, 10.0)	6.2 (3.2, 10.2)	5.0 (3.1, 8.5)	0.29
HbA_{1c} in %, mean (SD)	6.7 (0.7)	6.7 (0.7)	7.0 (1.1)	0.10
HbA_{1c} in mmol/mol, mean (SD)	49.4 (7.4)	49.9 (8.2)	53.0 (12.2)	0.10
Current smoker, n (%)	56 (13.3)	24 (14.9)	1(4.2)	0.35
BMI >30 kg/m^2, n %	100 (23.8)^{1}	63 (39.1)^{0}	5 (50.0)[c]	<0.001
NT-pro BNP, pmol/l, median (IQR)	8.0 (5,14)	16.0 (9,41)	Not available	<0.001
Comorbidities, n (%)				
Ischaemic heart disease[b]	59 (14.0)^{1,2}	50 (31.1)^{0,2}	20 (83.3)^{0,1}	<0.001
Atrial fibrillation	22(5.2)^{1,2}	20 (12.4)^{0,2}	10 (41.7)^{0,1}	<0.001
Hypertension	262 (62.4)^{1}	119 (73.9)^{0}	17 (70.8)	0.03
Stroke or TIA	32 (7.6)^{1,2}	23 (14.3)^{0}	5 (20.8)^{0}	0.01
Peripheral arterial disease	18 (4.3)^{1,2}	21 (13.0)^{0}	6 (25.0)^{0}	<0.001
Asthma or COPD	43 (10.2)^{1,2}	28 (17.4)^{0}	7 (29.2)^{0}	0.004
Renal failure	15 (3.6)^{2}	11 (6.8)	4 (16.7)^{0}	0.007
Thyroid disease	28 (6.7)	15 (9.3)	3 (12.5)	0.28
Medication, n (%)				
Diuretics	130 (31.0)^{1,2}	69 (42.9)^{0,2}	18 (75.0)^{0,1}	<0.001
ACE- inhibitors or ARB's	204 (48.6)^{1}	102 (63.4)^{0}	14 (58.3)	0.005
Beta-blockers	125 (29.8)^{1,2}	84 (52.2)^{0,2}	21 (87.5)^{0,1}	<0.001
Calcium channel blockers	55 (13.1)	39 (24.2)^{2}	1 (4.2)^{1}	0.001
Statins	291(69.3)	117 (72.7)	20 (83.3)	0.28
Oral anti-diabetics	268 (63.8)	110 (68.3)	19 (79.2)	0.21
Insulin	50 (11.9)	23(14.3)	2 (8.3)	0.61
Echo data, mean (SD)				
LVEF in %	61.4 (7.4)	56.9 (9.4)	Not available	<0.001
E/e'	8.8 (2.3)	11.4 (5.0)	Not available	<0.001
LA volume indexed in ml/m^2	25.9 (7.8)	32.6 (10.3)	Not available	<0.001
Health status, mean (SD)				
EQ-5D	0.85 (0.17)^{1,2}	0.73 (0.19)^{0}	0.66(0.21)^{0}	<0.001
EQ-VAS	80.0 (14.6)^{1,2}	70.9 (16.2)^{0}	67.7 (14.3)^{0}	<0.001
SF-36 physical component summary	46.7 (10.0)^{1,2}	38.3 (10.1)^{0}	35.0 (11.1)^{0}	<0.001
SF-36 mental component summary	53.8 (7.9)	53.8 (9.2)	53.0 (12.7)	0.90
Diabetes Health Profile	88.9 (7.2)^{1}	86.6 (8.7)^{0}	90.0 (8.5)	0.002

^{0,1,2}Indicate the groups whose proportion, mean or median differs significantly from this group at the 0.05 level (post-hoc analysis).

[a] Comparing three groups with Chi-square, ANOVA or Kruskal–Wallis.

[b] Myocardial infarction, angina pectoris, coronary bypass grafting or percutaneous intervention.

[c] BMI 14 missing in patients known with heart failure. Abbreviations: COPD, chronic obstructive pulmonary disease; TIA, transient ischaemic attack; ARB, angiotensin receptor blocker.