In view of the high prevalence of unknown heart failure in type 2 diabetes, some have advocated screening strategies [1,2]. The prognosis of screen-detected heart failure in patients with type 2 diabetes, however, is unknown. We compared all-cause mortality and cardiac hospitalization rates between patients with and without screen-detected heart failure and also distinguished between those with screen-detected heart failure with reduced (HFrEF) and preserved ejection fraction (HFpEF).

Between 2009 and 2010, 581 patients with type 2 diabetes aged 60 years or over and not previously diagnosed with heart failure underwent a diagnostic work-up, including standardized echocardiography. Presence or absence of heart failure was determined by an expert panel using all available diagnostic information and applying the diagnostic criteria on heart failure of the European Society of Cardiology [3]. Follow-up data was obtained from October 2013 until March 2014 by scrutinizing the electronic medical files of the participating general practitioners, including letters from hospital specialists.

All participants gave written informed consent, and the institutional review boards of the University Medical Center Utrecht and the Admiraal de Ruyter Hospital in Goes, The Netherlands approved the study. The study is registered in the Central Committee on Research Involving Human Subjects (CCMO) register of The Netherlands; www.ccno.nl, NL22717.041.08.

We calculated incidence rates for mortality and cardiac hospitalization rates per 100 person-years. For analysis of differences between groups we used chi-square or Fisher exact tests for proportions, and the t-test and Kruskal Wallis tests for means. We performed survival analyses with time to death, time to first cardiac hospitalization, and the composite of both endpoints, whatever came first, using Cox regression analysis after adjustment for age and gender. We constructed Kaplan–Meier curves to compare survival of patients with screen-detected HFrEF, HFpEF, and without heart failure.

The mean age of the 581 participating patients with type 2 diabetes at baseline was 71.6 (SD 7.4) years, and 53.4% was male. The median duration of diabetes was 5.5 (interquartile range 3.0–10.1) years, and the mean HbA1c 49.5 (standard deviation 7.9) mmol/mol (Table 1). In 161 (27.7%) a screen-detected diagnosis of heart failure was established by the panel; 133 (82.6%) with HFpEF, and 28 (17.4%) with HFrEF.

The mean follow-up period was 4.4 (range 3.8–5.0) years. The vital status could be determined in 579 (99.7%) participants. The cumulative incidence of mortality and the first cardiac hospitalization are shown in Table 2. Those with screen-detected heart failure had a higher mortality rate than those without (3.31 versus 1.51 per 100 person-years). The mortality rate of those with HFrEF and HFpEF was 9.95 and 2.13 per 100 person-years, respectively. The incidence rate of first cardiac hospitalization was higher in those with screen-detected heart failure than patients without such a new diagnosis (7.79 versus 3.18 per 100 person-years). The corresponding incidence rate for those with HFrEF was 12.37 and for HFpEF 7.05 per 100 person-years, respectively.
The adjusted hazard ratios for all-cause mortality, and the risk of cardiac hospitalizations associated with concurrent screen-detected heart failure in patients with diabetes were 2.2 (95% CI 1.2–3.8) and 2.4 (95% CI 1.6–3.6), respectively. The HR of the composite outcome was 2.2 (95% CI 1.6–3.1). After adjustment for age and gender, the HR in screen-detected HF patients versus those without HF was 1.5 (95% CI 0.8–2.7) for all-cause mortality, 2.2 (95% CI 1.5–3.3) for cardiac hospitalizations and 1.8 (95% CI 1.3–2.6) for the composite of both endpoints. The adjusted hazard ratios for all-cause mortality, cardiac hospitalization and the composite endpoint were more pronounced for screen-detected HFrEF (HR 4.5, 3.4 and 3.7, respectively) than for screen-detected HfPEF (HR 1.0, 2.0, 1.5, respectively) (Table 3).

This is the first study that shows that heart failure unmasked with screening in older community-dwelling patients with type 2 diabetes carries a poor prognosis in terms of a higher risk of mortality and cardiac hospitalizations, a result driven by screen-detected HFrEF.

### Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

### Acknowledgments

We thank the participating patients and general practitioners, and the research assistants Carla Bakx, Jolette Bossers and Annelies van der Smissen.

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**Table 1**

Baseline characteristics and referrals to the cardiologist of 581 patients with type 2 diabetes aged 60 years and over, divided in those with screen-detected heart failure, and those without heart failure. Screen-detected heart failure divided in reduced (HFrEF) and preserved ejection fraction (HfPEF).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All screen-detected HF cases (n = 161)</th>
<th>Screen-detected HFrEF (n = 28)</th>
<th>Screen-detected HfPEF (n = 133)</th>
<th>No HF with screening (n = 420)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>74.6 (7.7)</td>
<td>75.2 (8.3)</td>
<td>74.4 (7.4)</td>
<td>70.5 (7.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>77 (47.8)</td>
<td>20 (71.4)</td>
<td>57 (42.9)</td>
<td>233 (55.5)</td>
<td>0.10</td>
</tr>
<tr>
<td>Duration of diabetes in years, median (IQR)</td>
<td>6.2 (3.2, 10.2)</td>
<td>7.4 (2.9, 13.2)</td>
<td>6.2 (3.3, 10.1)</td>
<td>5.1 (3.0, 10.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>HbA1c in %, mean (SD)</td>
<td>6.7 (0.7)</td>
<td>6.7 (0.6)</td>
<td>6.7 (0.7)</td>
<td>6.7 (0.7)</td>
<td>0.46</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>24 (14.9)</td>
<td>5 (17.9)</td>
<td>19 (14.3)</td>
<td>56 (13.3)</td>
<td>0.62</td>
</tr>
<tr>
<td>BMI in kg/m², mean (SD)</td>
<td>29.7 (6.0)</td>
<td>30.1 (10.1)</td>
<td>29.6 (4.7)</td>
<td>27.6 (4.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular and diabetic medication, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>69 (42.9)</td>
<td>12 (42.9)</td>
<td>57 (42.9)</td>
<td>130 (31.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>ACE-inhibitors or ARBs</td>
<td>102 (63.4)</td>
<td>18 (64.3)</td>
<td>84 (63.2)</td>
<td>204 (48.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>84 (52.2)</td>
<td>9 (32.1)</td>
<td>75 (56.4)</td>
<td>125 (29.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statins</td>
<td>117 (73.9)</td>
<td>15 (53.6)</td>
<td>104 (78.2)</td>
<td>202 (46.4)</td>
<td>0.009</td>
</tr>
<tr>
<td>Oral anti-diabetics</td>
<td>110 (68.3)</td>
<td>21 (75.0)</td>
<td>89 (66.9)</td>
<td>208 (48.6)</td>
<td>0.31</td>
</tr>
<tr>
<td>Insulin therapy</td>
<td>23 (14.3)</td>
<td>5 (17.9)</td>
<td>18 (13.5)</td>
<td>50 (11.9)</td>
<td>0.44</td>
</tr>
<tr>
<td>Referral to cardiologist within one year after the assessment, n (%)</td>
<td>34 (25.2)</td>
<td>5 (22.7)</td>
<td>29 (25.7)</td>
<td>17 (4.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 2**

Cumulative incidence of mortality and cause of death, and cardiac hospitalizations during a mean follow-up of 4.4 years in 581 patients with type 2 diabetes aged 60 years and over.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All screen-detected HF (n = 161)</th>
<th>Screen-detected HFrEF (n = 28)</th>
<th>Screen-detected HfPEF (n = 133)</th>
<th>No HF with screening (n = 420)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortalitya</td>
<td>22 (13.7)</td>
<td>10 (35.7)</td>
<td>12 (9.0)</td>
<td>27 (6.5)</td>
</tr>
<tr>
<td>Cardiovascular deathb</td>
<td>8 (5.0)</td>
<td>4 (14.3)</td>
<td>4 (3.0)</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td>Progressive heart failure</td>
<td>6 (3.7)</td>
<td>3 (10.7)</td>
<td>3 (2.3)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Other causes of deathc</td>
<td>5 (3.1)</td>
<td>2 (7.1)</td>
<td>3 (2.3)</td>
<td>19 (4.5)</td>
</tr>
<tr>
<td>Unknown cause of death</td>
<td>9 (5.6)</td>
<td>4 (14.3)</td>
<td>5 (3.8)</td>
<td>5 (1.2)</td>
</tr>
<tr>
<td>Cardiac hospitalizationsd</td>
<td>45 (28.0)</td>
<td>10 (35.7)</td>
<td>35 (26.2)</td>
<td>53 (12.6)</td>
</tr>
<tr>
<td>Heart failure hospitalizations</td>
<td>10 (6.2)</td>
<td>5 (14.9)</td>
<td>5 (3.8)</td>
<td>3 (0.7)</td>
</tr>
</tbody>
</table>

Values are numbers (percentages).

| a 2 missing on vital status because these participants moved to another city. |
| b Cardiovascular death includes myocardial infarction, heart failure. |
| c Other causes of death include malignancies, accidents, and other diseases than cardiovascular. |
| d Cardiac hospitalizations include hospitalizations on cardiology unit or on other units for cardiac interventions. |
References


Table 3
Crude and adjusted hazard ratios for all-cause mortality, cardiac hospitalizations, and the composite endpoint in relation to the presence of screen-detected HFrEF or HFpEF in patients with type 2 diabetes.

<table>
<thead>
<tr>
<th></th>
<th>Crude HR HFrEF</th>
<th>95% CI</th>
<th>Adjusted HR HFrEF(^a)</th>
<th>95% CI</th>
<th>Crude HR HFpEF</th>
<th>95% CI</th>
<th>Adjusted HR HFpEF(^a)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>6.7</td>
<td>3.3–13.9</td>
<td>4.5</td>
<td>2.1–9.4</td>
<td>1.4</td>
<td>0.7–2.8</td>
<td>1.0</td>
<td>0.5–1.9</td>
</tr>
<tr>
<td>Cardiac hospitalizations</td>
<td>3.8</td>
<td>1.9–7.5</td>
<td>3.4</td>
<td>1.7–6.7</td>
<td>2.2</td>
<td>1.4–3.4</td>
<td>2.0</td>
<td>1.3–3.1</td>
</tr>
<tr>
<td>Combined endpoint</td>
<td>4.6</td>
<td>2.7–7.7</td>
<td>3.7</td>
<td>2.2–6.3</td>
<td>1.8</td>
<td>1.3–2.7</td>
<td>1.5</td>
<td>1.0–2.2</td>
</tr>
</tbody>
</table>

\(^a\) Adjusted for age and gender.