Overdiagnosis of heart failure in primary care: a cross-sectional study

Abstract

Background
Access to echocardiography in primary care is limited, but is necessary to accurately diagnose heart failure (HF).

Aim
To determine the proportion of patients with a GP’s diagnosis of HF who really have HF.

Design and setting
A cross-sectional study of patients in 30 general practices with a GP’s diagnosis of heart failure, based on the International Classification of Primary Care (ICPC) code K77, between June and November 2011.

Method
Electronic medical records of the patients’ GPs were scrutinised for information on the diagnosis. An expert panel consisting of two cardiologists and an experienced GP used all available diagnostic information, and established the presence or absence of HF according to the criteria of the European Society of Cardiology (ESC) HF guidelines.

Results
In total, 683 individuals had a GP’s diagnosis of HF. The mean age was 77.9 (SD 11.4) years, and 42.2% were male. Of these 683, 79.6% received cooperative care from a cardiologist. In 73.5% of cases, echocardiography was available for panel re-evaluation. Based on consensus opinion of the panel, 434 patients (63.5%, 95% CI 59.9 to 67.1) had definite HF, of which 222 (32.5%, 95% CI 30.9 to 34.1) had HF with preserved ejection fraction (HFpEF), 207 (30.3%, 95% CI 29.0 to 31.6) had HF with reduced ejection fraction (HFrEF), and five (0.7%, 95% CI 1.2 to 2.6) had isolated right-sided HF. In 17.3% of cases, echocardiography was available for panel re-evaluation. Based on consensus opinion of the panel, 434 patients (63.5%, 95% CI 59.9 to 67.1) had definite HF, of which 222 (32.5%, 95% CI 30.9 to 34.1) had HF with preserved ejection fraction (HFpEF), 207 (30.3%, 95% CI 29.0 to 31.6) had HF with reduced ejection fraction (HFrEF), and five (0.7%, 95% CI 1.2 to 2.6) had isolated right-sided HF. In 17.3% of cases, echocardiography was available for panel re-evaluation. Based on consensus opinion of the panel, 434 patients (63.5%, 95% CI 59.9 to 67.1) had definite HF, of which 222 (32.5%, 95% CI 30.9 to 34.1) had HF with preserved ejection fraction (HFpEF), 207 (30.3%, 95% CI 29.0 to 31.6) had HF with reduced ejection fraction (HFrEF), and five (0.7%, 95% CI 1.2 to 2.6) had isolated right-sided HF.

Conclusion
More than one-third of primary care patients labelled with HF may not have HF, and such overdiagnosis may result in inadequate patient management.

Keywords
cross-sectional studies; health professionals; heart failure; multiple deprivation; primary care; resilience; rurality.

INTRODUCTION
Heart failure (HF) is a chronic progressive disease mainly affecting older people. Pharmacological treatment, devices, and HF management programmes can reduce morbidity and mortality in patients who have HF with reduced ejection fraction (HFrEF). In this study the authors defined HFrEF as symptoms and/or signs suggestive of heart failure, and a left ventricular ejection fraction (LVEF) ≤45% with echocardiography. In patients who have HF with preserved ejection fraction (HFpEF) clear evidence-based disease-modifying treatment is still lacking, but, importantly, symptoms may be reduced with adequate titration of diuretics during periods of fluid retention. This study defined HFpEF as symptoms and/or signs suggestive of heart failure, and an LVEF ≤45% plus structural or functional abnormalities with echocardiography.

The diagnosis of non-acute HF is primarily initiated in primary care, but this diagnosis is notoriously difficult without echocardiography, especially in the early stages of the disease, in the obese, older people, and in patients with chronic obstructive lung disease. Additional investigations with natriuretic peptides and referrals for echocardiography are needed, and have increased in primary care over the past decade. GPs tend to follow the recommendations of existing guidelines that advocate considering referral for echocardiography of individuals with suggestive symptoms and signs who in addition have natriuretic peptide levels above the exclusionary threshold. Nevertheless, this strategy has not been completely implemented yet, resulting in the risk of over- and underdiagnosis of HF if GPs consider the clinical assessment only. Multiple studies have mentioned underdiagnosis of HF in primary care, but exact data on overdiagnosis in this setting are lacking.

The authors wanted to quantify overdiagnosis of HF in primary care, and therefore evaluated whether patients with a GP’s diagnosis of HF really had HF according to an expert panel that applied the criteria of the European Society of Cardiology (ESC) HF guidelines. Additionally, the study determined which patient characteristics were associated with referral for echocardiography.

METHOD
Design and study population
The authors performed a cross-sectional study in 30 general practices in and around Amersfoort, a town in the middle of the Netherlands. Around 70 000 individuals were enlisted in these practices in 2010. Notably, all citizens in the Netherlands are enlisted with a GP, irrespective of cooperative care by a specialist, except for those living in nursing homes. Those
eligible for inclusion in the study were community-dwelling individuals with a GP’s diagnosis of HF (International Classification of Primary Care [ICPC] code K77) registered during at least two encounters to prevent including those who had been accidentally misclassified.12 The GPs’ electronic medical records (EMRs) and specialists’ letters of patients were scrutinised for information on demographics, medical history, medication, comorbidities, laboratory tests, and results of echocardiography between June and October 2011. In November 2011, all participating GPs received a letter recommending completion of the diagnostic work-up of any of their patients labelled with HF who had not yet undergone echocardiography to confirm the diagnosis and to help discriminate heart failure with reduced ejection fraction from heart failure with preserved ejection fraction, as recommended in the Dutch general practice guidelines on HF.13 The current study is a cross-sectional analysis of the baseline characteristics of all 683 patients labelled with HF. Those with a definite HF diagnosis, established by an expert panel (n = 434), then participated in a cluster-randomised trial. In this cluster-randomised trial, the 30 GP practices were randomised either to a one-day training course on the diagnosis and drug management of HF, or to usual care. The GPs working in the 15 GP practices of the intervention arm received a second reminder on the relevance of echocardiography.14

Cooperative care of patients by both a GP and cardiologist was pragmatically defined as any contact with the cardiologist (outpatient clinic visit or cardiac hospitalisation) in the 18 months before the assessment.

**Definition of heart failure**

An expert panel composed of two cardiologists and a GP with expertise in HF determined the presence or absence of HF (definite HF, possible HF, or no HF) during consensus meetings using all available diagnostic information, including echocardiography. Available echocardiograms were re-evaluated. The panel based the diagnosis of HF on the criteria laid out in the ESC HF guidelines, that is, signs and symptoms suggestive of HF, and objective evidence of structural or functional cardiac abnormality related to ventricular dysfunction in rest with echocardiography.1 Disagreement between panel members was solved by discussion and a majority vote. In participants lacking information on natriuretic peptides and echocardiography the panel decided on the absence of heart failure, and in participants lacking information on echocardiography the panel decided between no HF and possible HF, apart from patients who had been hospitalised for an episode of acute HF — they were diagnosed as ‘definite HF’ by the panel. Patients with definite HF were further classified based on echocardiography as HFrEF, HFpEF, or isolated right-sided HF. For HFrEF the LVEF had to be ≤45%. For HFpEF, the LVEF had to be >45%, in the presence of a composite of echocardiographic indices of diastolic dysfunction or structural abnormalities (left ventricular hypertrophy or left atrial enlargement). For isolated right-sided HF, the LVEF had to be >45%, and the estimated systolic pulmonary artery pressure >40 mmHg, with the absence of evident left ventricular dysfunction or valvular disease.1

**Data analysis**

To compare groups the authors used Student’s t-tests or Mann–Whitney U tests for continuous variables, and the χ² test for categorical variables. The authors compared patients with definite, no, and possible HF. They also compared patients who received cooperative care from a cardiologist with those who had no cooperative care from a cardiologist, and patients who had HFpEF with those who had HFrEF. The association between patient characteristics and referral for echocardiography was assessed using multivariable logistic regression analysis to identify independent predictors for referral. All analyses were done with SPSS version 20.0.

**RESULTS**

Baseline characteristics of the 683 patients with a GP’s diagnosis of HF are presented in Table 1. The mean age was 77.9 (SD 11.4) years, 42.2% were male, and 79.6% received cooperative care from a cardiologist. A total of 77 (17.8%) patients had been hospitalised for acute HF. The expert panel was able to use the results of natriuretic peptide
measurements in 69.3% of the patients, and echocardiography in 73.5%.

In total, 118 (17.3%, 95% CI = 14.4 to 20.0) patients had no HF according to the panel, and 131 (19.2%, 95% CI = 16.3 to 22.2) patients had possible HF.

The 139 patients who received care from a GP only were significantly older (81.5 versus 76.9 years, \( P < 0.001 \)), had less prior myocardial infarction (10.8 versus 31.4%, \( P < 0.001 \)), had echocardiography less often (30.9 versus 84.4%, \( P < 0.001 \)), and were less often prescribed an angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) (43.9 versus 61.8%, \( P < 0.001 \)) and mineralocorticoid receptor antagonists (MRAs) (15.1 versus 25.6%, \( P = 0.009 \)) than the 544 patients who received cooperative care from a cardiologist (Table 2).

Multivariable analysis showed that younger age, prior myocardial infarction, and prescription of ACE-I/ARBs were independent predictors of referral for echocardiography (Table 3).

The 434 (63.5% of the 683 patients with a GP's label of HF, 95% CI = 59.9 to 67.1) patients with definite HF can be divided into 222 (32.5%, 95% CI = 30.9 to 34.1%) with HFpEF, 207 (30.3%, 95% CI = 29.0 to 31.6%) with HFpEF, and five (0.7%, 95% CI = 1.2 to 2.6%) with isolated right-sided HF. Considering the ejection fraction only, the 434 patients with definite HF can be divided as follows: 33.9% had an LVEF < 40%, 21.2% had an LVEF of 40–50%, 36.4% had an LVEF > 50%, and in 8.5% an LVEF had not been recorded.

Comparing the 222 patients with HFpEF with the 207 with HFpEF showed that those with HFpEF were younger (74.5 versus 79.9 years, \( P < 0.001 \)), more often male (57.2% versus 37.7%, \( P < 0.001 \)), and had more often a prior myocardial infarction (47.7% versus 16.4%, \( P < 0.001 \)). Those with HFpEF more often had a history of hypertension (64.7% versus 45.5%, \( P < 0.001 \)), atrial fibrillation (62.3% versus 35.6%, \( P < 0.001 \)), and stroke/TIA (17.9% versus 9.9%, \( P = 0.02 \)) than those with HFpEF (Table 4).

**DISCUSSION**

**Summary**

This study demonstrated that among 683 patients with a GP’s diagnosis of HF the
Table 2. Characteristics of 683 patients with a GP’s diagnosis of heart failure, divided into patients receiving GP care only, and patients who received cooperative care from a cardiologist

<table>
<thead>
<tr>
<th></th>
<th>GP care only, % (n = 139)</th>
<th>Cooperative care from cardiologist, % (n = 544)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No HF, according to the panel</td>
<td>21.6</td>
<td>16.2</td>
<td>0.13</td>
</tr>
<tr>
<td>Possible HF, according to the panel</td>
<td>52.5</td>
<td>10.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Definite HF, according to the panel</td>
<td>25.9</td>
<td>73.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>81.5 (12.4)</td>
<td>76.9 (11.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>36.7</td>
<td>43.6</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Comorbidities

- Angina pectoris: 10.8 vs. 19.5, P = 0.02
- Prior myocardial infarction: 10.8 vs. 31.4, P < 0.001
- Atrial fibrillation: 36.7 vs. 42.8, P = 0.19
- Stroke: 10.1 vs. 9.2, P = 0.75
- COPD: 20.1 vs. 19.5, P = 0.86
- Hypertension: 53.2 vs. 53.5, P = 0.96
- Diabetes mellitus: 25.2 vs. 30.3, P = 0.22
- eGFR < 60 mL/min/1.73 m²: 33.1 vs. 38.2, P = 0.25

Additional investigations

- Natriuretic peptides measurements: 70.5 vs. 68.9, P = 0.72
- Echocardiography: 30.9 vs. 84.4, P < 0.001

Drug prescriptions

- Diuretics: 71.2 vs. 72.8, P = 0.71
- ACE inhibitors or ARBs: 43.9 vs. 61.8, P < 0.001
- Beta-blockers: 38.1 vs. 54.6, P = 0.01
- MRAs: 15.1 vs. 25.6, P = 0.009
- Digoxin: 15.8 vs. 19.3, P = 0.35

Table 3. Multivariable association between patient characteristics and referral for echocardiography in 683 patients with a GP’s diagnosis of heart failure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per year</td>
<td>0.98 [0.96 to 0.99]</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.19 [1.05 to 1.65]</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.01 [0.74 to 1.39]</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>1.00 [0.66 to 1.52]</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>1.73 [1.19 to 2.49]</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.35 [0.98 to 1.86]</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.91 [0.64 to 1.29]</td>
</tr>
<tr>
<td>COPD</td>
<td>1.02 [0.69 to 1.52]</td>
</tr>
<tr>
<td>Renal insufficiency (eGFR &lt; 30 mL/min/1.73 m²)</td>
<td>1.23 [0.70 to 2.16]</td>
</tr>
<tr>
<td>Mild renal impairment (eGFR between 30 mL/min/1.73 m² and &lt;40 mL/min/1.73 m²)</td>
<td>1.04 [0.73 to 1.47]</td>
</tr>
<tr>
<td>Natriuretic measurements performed</td>
<td>1.29 [0.94 to 1.79]</td>
</tr>
<tr>
<td>Diuretic prescription</td>
<td>1.21 [0.84 to 1.73]</td>
</tr>
<tr>
<td>ACE inhibitor or ARB prescription</td>
<td>1.42 [1.03 to 1.96]</td>
</tr>
<tr>
<td>Beta-blocker prescription</td>
<td>1.04 [0.75 to 1.44]</td>
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</tbody>
</table>

Comparison with other literature

To the best of the authors’ knowledge, this is the first study to provide exact data on the overdiagnosis of HF in primary care. Moreover, among those with established HF it also provides the exact percentages of cases with preserved and reduced ejection fraction. When considering these results, one has to bear in mind that patients could receive cooperative care from a cardiologist for diagnoses other than HF (such as, rhythm disorders, valvular disease, and ischaemic heart disease). Moreover, some of these patients could have been referred by a GP under the suspicion of HF (and were already labelled with ICPC code K77) without being confirmed by the cardiologist, and thus may have remained incorrectly labelled as HF (ICPC code K77) in the EMR of the GP.

Previous studies have reported that HF could be established in 14 to 72% of patients referred to an open-access facility or cardiologist.14,19–21 However, patients in these studies could also have been referred for analysis of a heart murmur, or for other cardiac causes of breathlessness.

Other studies have reported how often GPs performed additional investigations in suspected cases of HF. Electrocardiography (36 to 53%) and chest X-ray (20 to 50%) were performed in a minority of cases.22 At the beginning of the 21st century, just 12% of the
patients labelled with HF and managed by a GP only had undergone echocardiography. In this study, 45.2% of 683 patients had undergone echocardiography at the start of the study, and this number increased to 73.5% after two reminders to consider referral for echocardiography. Irrespective of the past decade’s increase in referrals for echocardiography of cases suspected of HF, there is still ample room for improvement. Multiple studies show that certainty about the diagnosis and knowing the type of HF greatly helps to improve the management of these patients.11,23 Moreover, previous studies have shown that patients with HF with missing LVEF results are older, are prescribed less required HF medication, and show more comorbidity and worse prognosis.24 A strength of this study is that it is the first to evaluate whether HF really is present in a representative sample of community-dwelling individuals who have a GP’s diagnosis of HF. The authors used an expert panel to evaluate all available data for these people, and if an echocardiogram was available it was re-evaluated. An expert panel diagnosis such as this is considered superior to the diagnosis of a single cardiologist during everyday practice, and previous studies have shown high reproducibility of such a panel diagnosis of HF.37

To answer the research question the authors had to use routine care data. Such data, however, are renowned for missing or incomplete diagnostic work-ups. As a result, the panel had to classify 26.5% of the patients without access to echocardiographic results. The percentage of echocardiography performed may on the one hand have been underestimated in this study because in some cases it may not be adequately registered in the GP’s EMR. On the other hand, overestimation is possible because the authors stimulated GPs to perform echocardiography. Importantly, however, this procedure did not affect the validity of the estimate of those with a GP’s label of HF — those who really had heart failure — because this estimate was based on those with a GP’s diagnosis of heart failure when the data were extracted from the EMR.

In this study, the authors used the cut-off value of 45% for the LVEF to distinguish between HFrEF and HfP EF. Alternative thresholds exist to define HFP EF, and 50% has also been recommended.25

In 19% of the subjects, the panel could not make a definite diagnosis of HF, and this was merely due to the absence of echocardiography. Although heart failure essentially is a clinical diagnosis, structural and functional cardiac abnormalities should be established to relate the non-specific symptoms and signs suggestive of heart failure to a cardiac origin.

Implications for practice
To facilitate the diagnostic pathway for primary care patients suspected of HF, easy access to echocardiography should become more widely available. Furthermore, optimisation of cooperative care with a cardiologist and HF outpatient clinic could promote drug use and result in more intensive up-titration of drugs. Previous studies have shown that the substitution of care from the HF outpatient clinics to primary care is safe and feasible for patients with HFrEF. However, this must be after they have been carefully and adequately up-titrated with evidence-based treatment.26–28

Table 4. Comorbidity and drug prescription of 434 patients with panel-confirmed heart failure, divided into those with reduced and preserved ejection fractiona

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>HFrEF, % (n = 222)</th>
<th>HfP EF, % (n = 207)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>74.5 (11.3)</td>
<td>79.9 (8.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>57.2</td>
<td>37.7</td>
<td>&lt;0.001</td>
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<td>Angina pectoris</td>
<td>14.0</td>
<td>23.7</td>
<td>0.10</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>47.7</td>
<td>16.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>35.6</td>
<td>62.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>9.9</td>
<td>17.9</td>
<td>0.02</td>
</tr>
<tr>
<td>COPD</td>
<td>20.7</td>
<td>18.8</td>
<td>0.56</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>9.9</td>
<td>9.7</td>
<td>0.75</td>
</tr>
<tr>
<td>[eGFR &lt;30 mL/min/1.73 m²]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>45.5</td>
<td>64.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>33.3</td>
<td>31.4</td>
<td>0.67</td>
</tr>
</tbody>
</table>

*Five (1.2%) patients with isolated right-sided HF are not included in this table. ACE inhibitors = angiotensin-converting enzyme inhibitors. ARB = angiotensin receptor blocker. COPD= chronic obstructive pulmonary disease. LVEF = left ventricular ejection fraction. MRAs = mineralocorticoid receptor antagonists. SD = standard deviation. TIA = transient ischaemic attack.

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Ethical approval
The study complied with the Declaration of Helsinki and was approved by the Regional Medical Ethics Committee (Verenigde Commissies Mensgebonden Onderzoek — VCMO) of four hospitals in the Utrecht region, including the Meander Medical Center in Amersfoort in the Netherlands (NL29397.100.10).

Provenance
Freely submitted; externally peer reviewed.

Competing interests
The authors have declared no competing interests.

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