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Effect of training general practitioners in drug treatment of newly detected heart failure patients with reduced or preserved ejection fraction: A cluster randomized trial

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ABSTRACT

Objective: To assess the effect of training general practitioners (GPs) in the optimization of drug treatment for newly detected heart failure (HF).
Design: Cluster randomized trial comparing the training programme to care as usual.
Participants: Community-dwelling older persons with a new HF diagnosis after diagnostic work-up.
Methods: Thirty GPs were randomized to care as usual or the training. Sixteen GPs of the latter group received a half-day training on optimizing HF medication in HF patients with a reduced (HFrEF), or with a preserved ejection fraction (HFpEF). At baseline and after six months of follow-up, the 46 HF patients in the intervention group and the 46 cases in the care as usual group were assessed on medication use, functionality, health status, and health care visits.
Results: After 6 months, uptake of HF medication and health status were similar in the two groups. Interestingly, patients in the intervention group had a longer walking distance with the six-minute walk test than those in the care as usual group (mean difference in all-type HF 28.0 (95% CI 2.9 to 53.1) meters; HFpEF patients 28.2 (95% CI 8.8 to 47.5) meters and HFrEF patients 55.9 (95% CI −16.3 to 128.1) meters). They also had more HF-related GP visits (RR 1.8, 95% CI 1.3 to 2.5) and fewer visits to the cardiologist (RR 0.6, 95% CI 0.3 to 1.1).
Conclusions: Training GPs in optimization of drug treatment of newly detected HFrEF and HFpEF did not clearly increase HF medication, but resulted in improvement in walking distance.

1. Introduction

Heart failure (HF) is a progressive chronic syndrome causing symptoms such as shortness of breath, fatigue and fluid retention. It is a common encountered health problem in older people in the population at large, with a prevalence rising from 0.8% in the group of 55–64 year olds to 20% among the age group of 85 years and older [1].

Heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) are the major phenotypes within the HF spectrum. Both are disabling conditions with high morbidity and mortality, and a substantial loss in functional capacity and health status [2]. The impact on health status is in general larger than for other chronic diseases such as osteo-arthritis, chronic obstructive pulmonary disease (COPD), and depression [3]. Reduced physical functioning seems to be a main driving force behind this.

Management of HF is complex. The European Society of Cardiology (ESC) provides guidance on patient counselling, including advices on lifestyle, how to optimize HF medication, monitor the individual clinical course of the disease and patient specific comorbidities, and when to consider devices [4]. For HFrEF the recommendations on initiation of drug treatment are clear: loop diuretics in case of volume overload, and mortality-reducing treatment with beta-blockers and angiotensin-converting enzyme inhibitors (ACE-inhibitors) (or when intolerated angiotensin receptor blockers (ARBs)), followed by mineralocorticoid

Abbreviations: HF, Heart failure; HFpEF, Heart failure with preserved ejection fraction; HFrEF, Heart failure with reduced ejection fraction; ESC, European Society of Cardiology; ACE, Angiotensin converting enzyme; MRA, mineralocorticoid receptor antagonists; GP, General practitioner; 6MWT, six-minute walk test; ECG, Electrocardiogram; NTproBNP, Amino-terminal pro-B-type natriuretic peptide; EQ-5D, EuroQol-5 Dimensions questionnaire; SF-36, Medical Outcomes Study 36-item Short Form Health Survey; PCS, physical component summary; MCS, mental component summary; MLHF, Minnesota Living with Heart Failure questionnaire; ICC, intra-cluster coefficient; GEE, generalized estimating equations; CI, confidence interval; RR, relative risk (for dichotomous outcomes) or rate ratio (for count outcomes); ARB, Angiotensin receptor blocker; NYHA, New York Heart Association.

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receptor antagonists (MRAs) if symptoms persist. ACE-inhibitors or ARBs and beta-blockers need to be up-titrated, 'starting low, going slow', targeting for recommended doses. For HFpEF the guidance on drug treatment is less clear, because clear evidence-based mortality-reducing treatment is lacking. Diuretics are useful for symptom relief in case of sodium and water retention in HFpEF patients, while blood pressure and comorbidities should be adequately managed [4].

The majority of patients with HF is primarily diagnosed and treated by their general practitioner (GP) [5], but treatment in the primary care setting seems suboptimal [6–8]. Physician-related barriers to guideline adherence include deficits in knowledge, skills, and lack of confidence to up-titrate medication [9–11]. Hence, education seems indicated to increase GPs' knowledge and competence on initiating HF drug therapy, and this could improve their patients' health status.

The aim of the present study was to evaluate whether a single half-day training of GPs in the practical application of a scheme to optimize HF drug treatment in newly detected patients with HFrEF and HFpEF results in improvements in uptake of HF medication, functional capacity, health status, and influences the number of health care visits.

2. Methods

2.1. Trial design

This cluster randomized trial was the second part of a combined diagnostic-therapeutic study conducted between December 2010 and December 2012 with the aim to improve both the diagnosis and treatment of HF in primary care. The diagnostic part included selective screening for HF of older persons who visited their GP with shortness of breath within the last 12 months. Among these patients, those with newly detected HF were eligible for this cluster randomized therapeutic study.

Random allocation to one of the treatment groups was executed at the level of the GP. As a result, patients with HF of one GP (a cluster) were all managed according to the same arm, hereby reducing the risk of contamination between patient groups. After a six month follow-up period outcomes were compared between groups, taking clustering into account. The study protocol was published previously [12].

2.2. Participants

General practices in the Zeist region in the center of the Netherlands, were invited to participate in this study. A total of thirty practices were recruited.

Persons aged 65 years or over who in the previous 12 months presented themselves to the GP with shortness of breath on exertion were selected from the electronic medical files of the participating GPs by a single physician (EvR). The selection was irrespective of whether persons were suspected of HF by the GP or not, or any prior non-HF diagnosis; thus, patients known with a pulmonary disease were also eligible. Those already known with an established diagnosis of HF, confirmed with echocardiography by the cardiologist, were excluded, as were patients with a life expectancy shorter than six months, and those unable to give informed consent. Informed consent was obtained from all participants and the study was performed according to the principles of the current version of the declaration of Helsinki.

Participants underwent a standardised diagnostic work-up conducted at the outpatient clinic of the Julius Center in Utrecht, or were visited at home if they were unable to travel to the study center. Diagnostic investigations included history taking, physical examination, electrocardiography (ECG), and a blood test for N-terminal pro B-type natriuretic peptide (NTproBNP) levels. Only participants with an abnormal ECG or NTproBNP levels above 125 pg/ml (15 pmol/l) underwent additional echocardiography, in accordance with the ESC HF guidelines [4], in the outpatient clinic of the Diakonessenhuis Hospital Zeist.

An expert panel consisting of two cardiologists (AL and ML) and a GP with special expertise in HF (FR) established or excluded HF following the latest criteria on HF of the ESC [4]. HF was further classified in HFrEF (defined as an ejection fraction ≤45%), HFpEF (defined as an ejection fraction >45% in combination with structural or functional abnormalities compatible with diastolic dysfunction) and 'isolated' right-sided HF. The study population of the trial consisted of the participants with newly detected HF according to the expert panel, except for those having a potentially treatable cause of their HF, who were directly referred to a cardiologist.

2.3. Interventions

The intervention consisted of a single half-day educational session. The GPs in this arm received training in the optimization of HF drug treatment for both HFrEF and HFpEF. They received detailed instructions on how and when to initiate diuretics and initiate and up-titrate ACE-inhibitors (or ARBs in case of intolerance to ACE-inhibitors), beta-blockers and possibly MRAs, in patients with HFrEF. For those with HFpEF, individualised titration of diuretic therapy was explained, and also the importance of optimal blood pressure control, and in those with atrial fibrillation, heart rate control [4]. See Fig. 1 for a simplified version of the initiation- and up-titration scheme, and the Additional file for the full content of the scheme. The protocol was designed to guide the GPs through the optimization steps to be fulfilled within three months after the new diagnosis of HF.

During the training session, special attention was given to potential barriers in HF drug treatment, such as fear of adverse effects and worries about ACE-inhibitors and beta-blockers in patients with comorbidities or polypharmacy [10].

The GPs randomly allocated to the care as usual group managed their newly detected cases of HF as they were used to, and did not receive the training. Both groups had access to the Dutch GPs' HF guideline ('NHG-standaard Hartfalen 2010') [13], a Dutch equivalent of the ESC Guideline on HF [4]. Referral to a cardiologist was possible at any stage in this pragmatic trial.

2.4. Outcomes

2.4.1. HF medication uptake

During the diagnostic work-up at baseline, patients were asked about their current drug use. In a preparatory letter, they were asked to bring their medication containers or a list of prescribed medication. Six months after the diagnosis of HF, the electronic medical files of GPs were scrutinized for medication changes. Changes within groups and differences between the two groups regarding use of diuretics, ACE-inhibitors or ARBs and beta-blockers after six months of follow-up were assessed.

2.4.2. Functional capacity

Especially for older persons exercise tolerance is of major clinical importance. Of the several modalities available, the six-minute walk test (6MWT) was used for the objective evaluation of functional capacity because the exercise level is consistent with daily physical activities [14]. The 6MWT is considered a valid, well-tolerated, and inexpensive test for functional capacity, that measures the distance that a patient can walk on a flat, hard surface during 6 min [15]. The test was executed according to the guidelines of the American Thoracic Society, at baseline (at the time of diagnosis) and after six months follow-up [14]. In general, an increase of 50 m in walking distance is considered a 'substantial improvement', and an increase of 20 m a 'small meaningful change' [16,17].

2.4.3. Health status

The EuroQol-5 Dimensions (EQ-5D) and the Short Form-36 (SF-36) were chosen as instruments to measure general health status. Both questionnaires have been extensively validated and are widely used [18–21].