Practical Guidance on Heart Failure Diagnosis and Management in Primary Care

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Table of contents

Abstract

Timely and accurate diagnosis of heart failure (HF) is important since treatments can alter prognosis as well as improve symptoms. HF is a common syndrome with a poor prognosis and high healthcare cost, but because symptoms are non-specific, early diagnosis is difficult. Primary care has a vital role in identifying persons with HF and in providing holistic, person-centred care from the first symptoms to end of life. During the European Primary Care Cardiovascular Society (EPCCS) Clinical Masterclass 2015, updated evidence based strategies to diagnose and manage HF were discussed, challenges identified, and suggestions formulated based on new scientific insights. This document summarises the discussion and aims to guide European primary care physicians towards improved diagnosis and management of HF patients in primary care. It considers the diagnostic work-up and treatment of both HF with preserved ejection fraction (HFpEF) and with reduced EF (HFrEF), indicating where management approaches may overlap and where the syndromes require distinct strategies. The new HFmrEF (mid-range: EF: 40-49%) category, introduced in the ESC 2016 guidelines, is also considered. This document gives practical guidance on lifestyle interventions, and which pharmacological therapy may provide benefit in various clinical presentations of HF. It thereby aims to facilitate the crucial role of the general practitioner in overseeing the overall health status of a patient, including monitoring comorbid conditions.

Introduction

Heart failure (HF) is a common and costly clinical syndrome. Timely diagnosis is important to optimise treatment opportunities but recognising the early stages of HF can be difficult. Primary care has a vital role in providing holistic, person-centred care from first symptoms to end of life.

During the 8th annual European Primary Care Cardiovascular Society (EPCCS) Clinical Masterclass, held in Prague, Czech Republic in late 2015, current strategies to diagnose and manage HF were discussed, challenges identified, and suggestions formulated based on new scientific insights. This document summarises the presented evidence as well as the discussion, in an attempt to guide European primary care physicians towards improved diagnosis and management of HF patients in primary care.

Recognising heart failure and active case-finding

The European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic HF 2016 defined the syndrome as “a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress” [1]. Clinically, HF used to

be classified according to ejection fraction - HF with reduced ejection fraction (HFrEF: a left ventricular ejection fraction (LVEF) <40-45%) and HF with preserved ejection fraction (HFpEF: LVEF >45-50%) [2].

The recently updated ESC HF Guidelines 2016 [1] have slightly amended the classifications, into: HFrEF where LVEF is below 40% and where treatments are well defined; a new HFmrEF (mid-range EF) where LVEF is from 40-49% plus either evidence of heart structural changes (such as left ventricular hypertrophy) or diastolic dysfunction (complicated echo criteria in the guideline) and treatments are less clearly evidence based; and HFpEF where LVEF is at or above 50% plus evidence of cardiac structural changes or diastolic dysfunction and treatments have not been shown clearly to be prognostically effective.

The definition of HF as stated in the 2016 guidelines restricts itself to stages at which clinical symptoms are apparent. As indicated, the diagnosis is determined by the presence of symptoms and/or signs of HF plus objective evidence of a structural or functional abnormality of the heart at rest [1]. Symptoms suggestive of HF include breathlessness, ankle swelling and fatigue. Signs are mostly related to fluid overload and include elevated jugular venous pressure, pulmonary crackles, and ankle oedema as well as displaced or broadened/sustained apex beat [2].

Early diagnosis of HF is difficult because symptoms are non-specific. Patients may be identified by presenting to medical care and undergoing further investigation based on their signs and symptoms, or via a more active case-finding approach where those at highest risk are screened for the condition. The latter approach can identify a large number of patients who may otherwise remain undiagnosed [3]. This includes both individuals with HF symptoms but without a diagnostic label, and a larger group of people with asymptomatic ventricular dysfunction [3].

High-risk groups that may be suitable for case-finding include those with chronic obstructive pulmonary disease (COPD) or with type 2 diabetes, especially if of older age [4]. When these patients present to primary care, symptoms that could suggest HF may not be recognised as such, neither by the patients themselves, nor by their doctors. Symptoms may be interpreted as 'part of the ageing process', and not induce a doctor's visit. Moreover, atypical presentation or presentation with comorbidities can complicate identification of HF. For instance, in a patient diagnosed with COPD, it may be unclear whether progression of shortness of breath is due to COPD or HF.

A study performed by the Dutch Heart Failure Organisation (UHFO) examining the optimal HF diagnostic strategy in primary care showed that of 721 patients, with a mean age of 71 years old, suspected of having non-acute onset HF, only 207 (28.7%) had the condition. HFrEF and HFpEF were diagnosed in equal numbers [5]. In a study aimed at case-finding in older patients (>60 years old) not suspected of having HF but at risk due to type 2 diabetes, a similar percentage was found with 31% being diagnosed with HF, the majority - 83% - of which was HFpEF, and only 17% HFrEF [6]. Thus, case-finding strategies yield a higher proportion of patients with HFpEF in some high-risk groups, which is an issue important when it comes to treatment (see below).

A recent study confirmed that diagnosis of HF is difficult in primary care, especially without access to echocardiography. An expert panel evaluated 683 GP's diagnoses of HF, by verifying whether these diagnoses were in line with recommendations in the 2012 ESC HF guidelines [7]. Over one third of HF diagnoses made in primary care could not be confirmed by the expert panel, based on the ESC Guidelines. More specifically, 118 patients (17.3%) had no HF, 131 patients had possible HF (19.2%) and 434 patients had definite HF (63.5%) [7].

Diagnostic guidance in primary care

To diagnose HF, it is important to appreciate that in both HFrEF and HFpEF, the heart fails to pump adequately. As a consequence, signs or symptoms are similar in both types of patients, and so is the diagnostic work-up. Symptoms and signs may be divided in three major aspects; fluid overload (backward failure), compensation or adaptation, and lastly, reduced oxygen delivery to metabolising tissues (forward failure) which may be hard to recognise as a symptom, e.g. mild cognitive impairment, muscle fatigue, delayed recovery after exercise.

History taking: signs and symptoms to consider

The most common and important symptoms that should raise the suspicion of HF include breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, reduced exercise tolerance, fatigue/tiredness/increased time to recover after exercise, and ankle swelling. Since many symptoms are related to fluid overload, they may not be present when patients receive treatment for other conditions e.g. diuretics for hypertension. Signs may also be due to fluid overload; pulmonary crackles, ankle oedema, and elevated jugular venous pressure. A gallop rhythm is very specific for HF but uncommon in the primary care setting. Adaptation may be reflected by a laterally displaced apex impulse in the decubital position, a broadened or sustained apex beat in left lateral decubital position, or increased heart rate (tachycardia) [2]. Any clear symptom of forward failure may be lacking. Also, important possible causes (or consequences) of HF may be found on examination, e.g. cardiac murmur. It should be noted that, especially in early HF, symptoms may be transient rather than present all the time. Other important aspects in the patient's history include the presence of ischaemic heart disease, particularly prior myocardial infarction, and also type 2 diabetes and hypertension.

A less typical symptom, but one that deserves attention, is wheezing. Up to 35% of elderly patients with acute HF wheezed at initial presentation [8]. Wheezing can also be present in the more common non-acute HF presentation in primary care. Wheezing may be caused by fluid in the lungs that causes compression from outside the bronchioles. Although in the case of asthma and COPD, the pressure originates from inside the bronchioles, the symptomatology is the same. It is therefore important to consider that wheezing does not automatically imply a pulmonary disease, and that it can have a cardiac origin as well.

A similar pitfall should be acknowledged with respect to spirometry, when a patient has shortness of breath. If a patient is stable and without clinical signs of fluid in the lungs, both forced expiratory volume (FEV1) and forced vital capacity (FVC) are decreased by around 20% in those with (unrecognised) HF, and thus the ratio FEV1/FVC is not affected. In the presence of clinically detectable pulmonary fluid overload in patients with (unrecognised) HF, FEV1 is more strongly reduced than FVC. Since a diagnosis of COPD is based on 'obstruction' with spirometry (operationalised as FEV1/FVC <70%), this could lead to overdiagnosis of COPD at the cost of missing HF. A better test in this situation would be bodyplethysmography. As residual volume (RV) and total lung capacity (TLC) are informative, even in the case of fluid overload [9].

Additional tests: natriuretic peptides and imaging

When HF is suspected on the basis of signs and symptoms, additional diagnostic measurements are required to exclude HF or select those who need further testing. Echocardiography can either be performed right away, or based on the result of natriuretic peptide assays (see also figure 1) [1].

In primary care, low exclusionary cut-off values for natriuretic peptide levels are used. These are set so that the likelihood of HF is very low if values are below the cut-off point [10-16]. Exclusionary cut-off values of less than 125 pg/mL for NT-proBNP and BNP less than 35 pg/mL in primary care are recommended in the ESC guidelines [1], while the National Institute for Health and Care Excellence (NICE) in England recommends 400 pg/mL and 100 pg/mL, respectively. Using low cut-off points for non-acute patients suspected of HF is useful in light of the lower a priori chance of disease and most importantly, because of the milder severity of disease in patients presenting in primary care [10-16]. Different negative and positive predictive values apply to more severe disease in the acute hospital setting, and higher cut-off values may be applied that still adequately exclude patients, but yielding much better positive predictive values. It should be noted that in the case of slow onset dyspnoea, other causes may underlie elevated

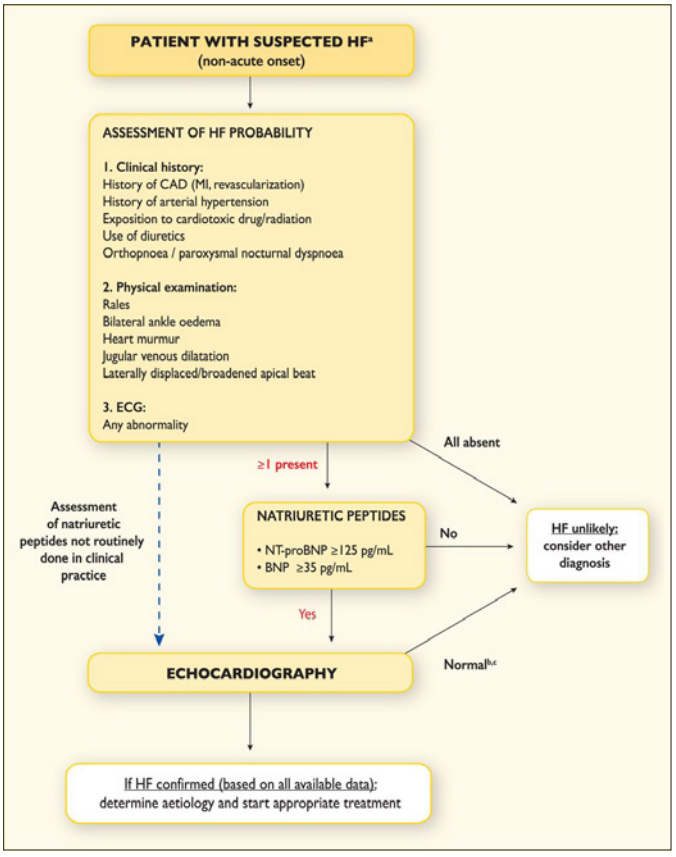

Figure 1: ***Diagnostic algorithm for a diagnosis of heart failure of non-acute onset***

BNP = B-type natriuretic peptide; CAD = coronary artery disease; HF = heart failure; MI = myocardial infarction; NT-proBNP = N-terminal pro-B type natriuretic peptide. aPatient reporting symptoms typical of HF.bNormal ventricular and atrial volumes and function. cConsider other causes of elevated natriuretic peptides. Reproduced from (1).

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NT-proBNP levels, including age over 75 years, atrial fibrillation, renal impairment, left ventricular hypertrophy and severe COPD.

If a patient has natriuretic peptide levels above cut-off values, echocardiography is usually indicated as the next step of the diagnostic process. Open access echocardiography is still not available to most primary care physicians. This could be a useful means to bring diagnosis of HF to primary care. With echocardiography, HFrEF can be distinguished from HFpEF. In patients with HFpEF the LVEF is 'preserved', but there are abnormalities in parameters related to impaired relaxation and inadequate filling, which in turn are related to a different pumping impairment mainly effecting the 'suction' of the heart and not so much the contractility (a stiff, insufficiently relaxing left ventricle).

Other investigations, such as electrocardiogram (ECG), chest x-ray, spirometry and other blood tests than natriuretic peptides might also be considered in the diagnostic work-up of a patient with possible HF. ECGs are useful to detect possible causes, and consequences, of HF, such as atrial fibrillation. Chest X ray is not very helpful, unless in the case of clear fluid overload. In that situation, however, signs and symptoms generally already point in the same direction. Spirometry should only be performed in stable and euvolemic patients, to prevent overdiagnosis of COPD in patients with ankle oedema and pulmonary crackles. Blood tests can also be useful to rule out precipitating factors such as thyroid disease or anaemia, measure modifiable cardiovascular risk factors such as cholesterol and assess baseline liver and renal function prior to initiating treatment.

Overall, history taking and investigation of signs and symptoms is very important in primary care. Of additional tests, natriuretic peptides are most informative and valuable [5, 10-12]. High-risk patients (e.g. type 2 diabetes, COPD) may benefit from case-finding. If these patients present with shortness of breath, measuring natriuretic peptide is a simple tool to identify possible cardiac origins. The suggested diagnostic algorithm is summarised in figure 1.

When to refer a patient

The decision to refer a patient will depend on the individual expertise of the GP and the organisation of the healthcare system. Most guidelines advocate an initial specialist assessment to make the formal diagnosis of HF. Once a definitive diagnosis is reached, specialists may initiate HF medication or this may be done by the GP. Consideration of device therapy is usually done at the specialist level based on parameters including ejection and widening of the QRS. Referral for rehabilitation may also be via specialist or GP teams.

Prevention

The 2013 European Society of Hypertension/ESC guidelines for the management of arterial hypertension [17] state that hypertension is the most important attributable risk factor for developing HF [18]. Preventing HF is the largest benefit associated with blood pressure-lowering drugs. This was seen in treatment with diuretics, beta-blockers, ACE inhibitors (ACEi) and angiotensin receptor blockers (ARBs) [19]. The very elderly are no exception [20]. Thus, adequately addressing high blood pressure in primary care is important to prevent development of HF. Optimal treatment of other cardiovascular risk factors such as hypercholesterolaemia and type 2 diabetes through pharmacological and lifestyle interventions is also important to prevent HF. Timely management of myocardial infarction to reduce muscle loss may also help to reduce the number of patients developing left ventricular dysfunction in the longer term.

Management and pharmacotherapy

The 2016 ESC guideline recommends both lifestyle interventions and pharmacological therapies (figure 2 shows a therapeutic algorithm proposed in the 2016 guidelines, for a patient with symptomatic HFrEF) [2]. The aim of pharmacological treatment is to relieve symptoms, improve prognosis and optimise quality of life [21]. From a healthcare systems viewpoint, it is also important to manage costs, particularly by preventing hospital admissions where possible [22].

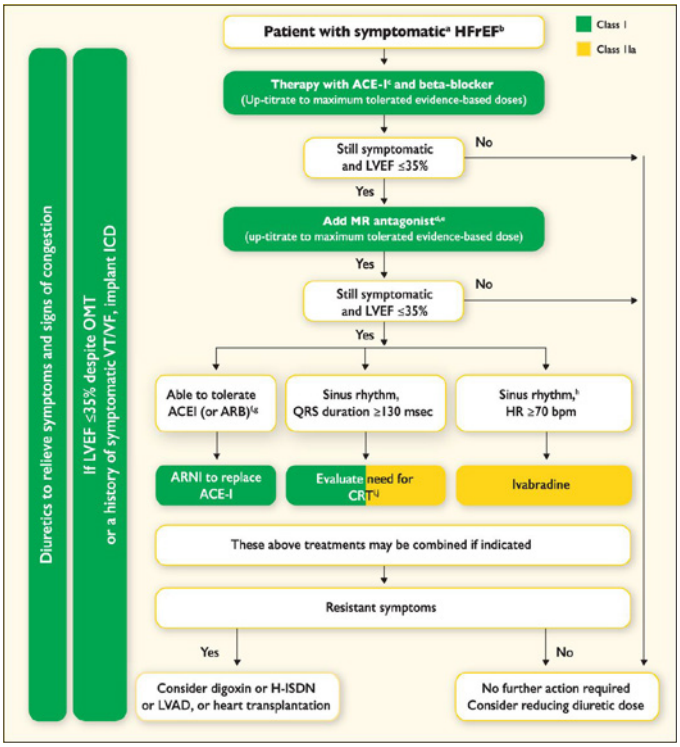

Figure 2: ***Therapeutic algorithm for a patient with symptomatic heart failure with reduced ejection fraction.***

Green indicates a class I recommendation according to ESC classification; yellow indicates a class IIa recommendation. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; BNP = B-type natriuretic peptide; CRT = cardiac resynchronisation therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; H-ISDN = hydralazine and isosorbide dinitrate; HR = heart rate; ICD = implantable cardioverter defibrillator; LBBB = left bundle branch block; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; MR = mineralocorticoid receptor; NT-proBNP = N-terminal pro-B type natriuretic peptide; NYHA = New York Heart Association; OMT = optimal medical therapy; VF = ventricular fibrillation; VT = ventricular tachycardia. aSymptomatic = NYHA Class II-IV. bHFrEF = LVEF <40%. cIf ACE inhibitor not tolerated/contra-indicated, use ARB. dIf MR antagonist not tolerated/contra-indicated, use ARB. eWith a hospital admission for HF within the last 6 months or with elevated natriuretic peptides (BNP > 250 pg/ml or NTproBNP > 500 pg/ml in men and 750 pg/ml in women). fWith an elevated plasma natriuretic peptide level (BNP ≥ 150 pg/mL or plasma NT-proBNP ≥ 600 pg/mL, or if HF hospitalisation within recent 12 months plasma BNP ≥ 100 pg/mL or plasma NT-proBNP ≥ 400 pg/mL). gIn doses equivalent to enalapril 10 mg b.i.d. hWith a hospital admission for HF within the previous year. iCRT is recommended if QRS ≥ 130 msec and LBBB (in sinus rhythm). jCRT should/may be considered if QRS ≥ 130 msec with non-LBBB (in a sinus rhythm) or for patients in AF provided a strategy to ensure bi-ventricular capture in place (individualised decision). Reproduced from (1).

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General management of heart failure

It is vital that patients with HF understand their condition and are actively involved in management decisions. It is also important to encourage aspects of self-care. Lifestyle interventions can improve patients' quality of life and prevent exacerbations. Patients should be made aware of the role salt and encouraged to avoid overuse, the importance of ensuring adequate hydration and a healthy diet, and the regular of exercise to increase functional capacity. For patients with more advanced HF, interventions such as daily weights and fluid restriction may be required and should be carried out under close supervision. Patients with HF benefit from formalised rehabilitation programmes which combine exercise with lifestyle and educational components as well as psychological support. Pharmacological therapies are the mainstay of treatment and considered below. For a proportion of patients with HFrEF device therapies such as cardiac resynchronisation therapy in patients with ejection fraction less than 35% and QRS duration >130ms might also improve cardiac function.

A few words on diuretics

It has not been definitely established whether diuretics give a long term prognostic benefit but are essential to relieve symptoms, particularly in acute situations. Diuretics are the only drugs that can adequately remove fluid from the body in those overfilled. Generally, physicians act on both aspects: diuretics for immediate relieve of symptoms, irrespective of whether it is HFrEF, HFmrEF, or HFpEF. In those with HFmrEF or HFpEF there are no drugs with proven prognostic benefit, so treatment strategies are symptom focused and include titrating diuretics to the fluid status of the patient, adequate blood pressure control, and control of heart rate in atrial fibrillation. In those with HFrEF, up-titration of ACEi (or ARB when ACEi not tolerated; dry cough in up to 5% of cases) and beta-blockers should follow. Additionally, mineralocorticoid receptor antagonists (MRAs) are also beneficial in patients with more severe HF who remain symptomatic. At the end of the up-titration process a reduction in diuretics may be possible. If after this combination of therapies, patients still have symptoms, or have an LVEF <35% and a broad QRS complex on the ECG, and/or a LVEF<30%, further management should be done by the cardiologist (such as the fitting of a cardiac synchronisation devices).

Managing patients with HF requires careful monitoring and prescribing. In particular, balancing the use of (loop) diuretics and their adverse effect on kidney function can be challenging. To help safely manage these patients, prerenal dysfunction should be distinguished from postrenal dysfunction. In prerenal dysfunction, the patient is dehydrated, due to the use of too high a dosage of diuretics, which causes the blood pressure in the kidney to be too low to filtrate. In postrenal dysfunction, on the other hand, there is too much fluid (venous congestion) and consequently too much venous pressure on the kidney. Both situations lead to decreased kidney function. Practically, this means that patients who are overloaded should receive diuretics and this can have a beneficial effect on kidney function. Glomerular filtration rate (GFR) might even increase as a result. Caution is needed where the patient is already on diuretic treatment - giving too high a dose can lead to further deterioration in renal function. Urea and GFR can then be monitored to see if the dose of diuretics needs to be lowered.

Acute heart failure

When a patient presents with acute pulmonary oedema and acute shortness of breath, most primary care physicians will send the patient immediately to the hospital. In a case of suspected acute HF (AHF), the

following steps can be considered by the primary care physician before the ambulance arrives but only if they have the equipment, expertise and feel confident to do so [2]:

- furosemide 40 mg intravenously (iv), and those already on a loop diuretic even higher dosage, while calling the ambulance and the cardiologist (note that furosemide needs about 20 minutes to work)
- when oxygen saturation <92%: give 2 l/min oxygen, this can be vital for immediate survival, but should be provided to long (minutes, not hours), and stopped when saturation is >92%
- when severe dyspnoea/agitation: 5 mg morphine slowly iv
- when systolic blood pressure > 110 mmHg: nitroglycerine sublingual

Chronic HFrEF

The ESC guidelines on heart failure 2016 recommend a treatment algorithm for chronic HFrEF patients [2]. As already mentioned, almost all HFrEF patients will need diuretics, to relieve symptoms and signs of congestion. Diuretic use may be temporarily discontinued or reduced when the patient receives other medication, but eventually the majority of patients need to continue taking diuretics. Other treatment generally starts with an ACEi (if not tolerated ARB), after which a beta-blocker can be added. If symptoms persist (class II-IV based on the New York Heart Association (NYHA) functional classification), a MRA such as spironolactone or eplerenone can also be added.

If symptoms (NYHA class II-IV) still persist despite the use of these three drugs plus diuretics, some patients may benefit from ivabradine, if they are in sinus rhythm, LVEF<35% and their heart rate is >70 beats/min [23].

Chronic HFpEF

Little evidence-based therapy is available for patients with HFpEF. Adequate titration of diuretics can give important symptom relieve. Elevated blood pressure should also be managed well.
Drugs that yield good results in HFrEF, have not shown clear benefits in HFpEF (ACEi in PEP-CHF, ARB in I-PRESERVE, MRA in ALDO-DHF/TOPCAT [24], ARNI in PARAMOUNT). More specifically, the TOPCAT trial compared the MRA spironolactone with placebo. Overall, it did not reduce the incidence of the primary endpoint (HR: 0.89, 95%CI: 0.77-1.04, P=0.138), but it did lower the incidence of first and total number of HF hospitalisations. Also, an interaction by inclusion stratum and region was seen, with no favourable effects in Russia/Georgia (HR: 1,10, 95%CI: 0.79-1.51), but a favourable profile in the United States, Argentina and Brazil (HR: 0.82, 95%CI: 0.69-0.98) were most included patients had elevated natriuretic peptide levels at inclusion [25]. Thus, TOPCAT does not give conclusive evidence on the use of spironolactone in HFpEF, but it may hint at a benefit for these patients with elevated natriuretic peptide levels.

Novel treatment options

A new treatment strategy has been developed and tested recently. The so-called ARNI (angiotensin receptor neprilysin inhibitor) exerts dual action; it consists of an ARB (valsartan) and a neprilysin inhibitor. It acts to reduce sympathetic tone, aldosterone levels and sodium retention, through inhibition of the overactive renin angiotensin system while simultaneously potentiating protective vasoactive neuropeptides.

The first ARNI being developed is sacubitril-valsartan (formerly known as LCZ696), which was evaluated in the PARADIGM-HF trial, in comparison to enalapril 10 mg b.d. [25]. After 27 months of follow-up, the trial was stopped early due to positive interim results. In symptomatic patients with HFrEF (LVEF<40%, BNP>150 pg/mL, mean age 63.8 years) who were treated with ACEi or ARB, and other background HF therapy such as betablockers and MRAs, the absolute risk of the composite of cardiovascular mortality and hospitalisation for HF was reduced by 4.7% (21.8% vs. 26.5%, relative risk reduction [RRR]: 20%) with sacubitril-valsartan vs. enalapril in HFrEF patients on optimal HF background therapy. All-cause mortality was 17.0% with the ARNI as compared with 19.8% with enalapril, yielding a hazard ratio of 0.84 (95%CI: 0.72-1.31, P<0.001), and a number needed to treat of 32 [25].

It should be noted that relative to primary care practice, included patients were relatively young, and 21% were female. Moreover, as a consequence of a run-in phase in the trial design, only patients who could tolerate ACEi and ARB were enrolled. Indeed, not many adverse effects were reported.

Data from the PARAMOUNT trial comparing sacubitril-valsartan with valsartan in HFpEF, showed that ARNI reduced NT-proBNP levels, left atrial volume index and increased the eGFR, more so than with valsartan alone, independent of its systolic blood pressure-lowering effect [26]. The potential benefit of an ARNI in HFpEF is investigated further in the ongoing PARAGON trial.

The position of sacubitril-valsartan in primary care needs to established in ongoing discussions. It may not be prescribed by GPs in the next years, but this may change in the future.

Heart failure and comorbidities

GPs have a particularly important role in overseeing the overall health status of patients. They are the ones most aware of comorbid conditions. Treating comorbidities may improve HF symptoms. It should be noted, however, that effects of improving symptoms vs. improving prognosis may need to be carefully balanced. For instance, the SERVE-HF trial showed that addressing central sleep apnoea which is very common in HFrEF with mask ventilation improved symptoms, while prognosis was reduced [27]. Importantly, cardioselective beta-blockers may be prescribed in patients with comorbid COPD, and in those with comorbid type 2 diabetes metformin is the preferred drug. Very recently, the EMPA-REG OUTCOME showed that empagliflozin (an inhibitor of sodium glucose cotransporter (SGLT-2) in the kidney) added to metformin for glucose lowering had beneficial prognostic cardiovascular effects (CV mortality, non-fatal myocardial infarction, and non-fatal stroke) compared to placebo in patients with diabetes and cardiovascular disease [28]. Subgroup analysis has suggested the benefit was consistent for patients with and without HF [29].

Organisation of care

Various examples of cooperative care have been developed across Europe. Often patients with HFrEF are managed in the hospital outpatient clinic for 3-6 months after diagnosis, to titrate medication to optimal doses. Hospital and community-based HF nurses can play an invaluable role in management and education of patients.

Although current guidelines recommend outpatient follow-up in specialised HF clinics, the optimal duration of these programmes has not been established, nor whether all or only high-risk patients would benefit. The randomised Danish Northstar trial compared extended follow-up of stable patients on optimal medical therapy in the HF clinic

with referral back to the GP [30]. After a median follow-up of 2.5 years, no differences were seen in time to death or hospital admission with a cardiovascular problem (HR: 1.17, 95%CI: 0.95-1.45, P=0.149 HF outpatient clinics vs. GPs), nor in any of the secondary outcomes of mortality, HF admission, quality of life, number of days admitted, and number of admissions. Also high-risk patients, as identified by NT-proBNP>1000 pg/mL did not benefit from follow-up in a HF clinic, as compared with referral to their GP [30].

The Dutch COACH-2 study also found no difference between follow-up in primary care vs. in a HF clinic in number of deaths and cardiovascular hospital admissions. Guideline adherence was assessed by the Guideline Adherence Indicator (GAI-3) as well as patient adherence (Medication Possession Ratio [MPR]), and no differences were observed after 12 months [31]. Both studies conclude that HFrEF patients can be referred back to primary care after initial management in hospital. The COACH-2 study group points out that, given the complexity of the HF syndrome and its comorbidities, close collaboration between health care providers is crucial in order to provide optimal, integrated care.

The role of the GP in end of life care

Special attention should be dedicated to the last phase of life of HF patients. In a Dutch study, most elderly patients (mean age 82.3 years) did not often visit the cardiology outpatient clinic (0.4 times) in their last year of life, which makes the home visits (12.1 visits in last year) by the GP more important [32]. Of note, in the Netherlands, most (55.9%) HF patients passed away at home or in a home for the elderly. Among those who died in hospital (32.6%), only a small part died on the cardiology ward (5.8% of total). Thus, most patients die with, not of HF. Causes of death in this study were sudden death (28%), progressive HF (23%), cancer (20%) or other (29%) [32].

It is important to realise that there is tremendous individual variation in the disease trajectory of HF. One cannot know when the palliative phase starts; patients generally do not follow a gradual downward path. Some feel and function quite well and die suddenly, while other may follow an upward path after a period of poor quality of life. Diverse and multiple comorbidities further complicate the disease trajectory, warranting regular monitoring. Thus, the GP plays a crucial role and should lead the end of life care of patients with HF.

Recommendations for further research

This document provides a summary of the key issues in diagnosis and management of patients with HF but there are gaps in the evidence base for primary care which require further research.

- HF is a prevalent condition in primary care but what is the best strategy for case finding? Which groups should be targeted and should there be a standardised approach across Europe?
- Can clinical decision rules help to identify patients most likely to have HF who would benefit from further investigation?
- What is the optimal cut-off point to use for natriuretic peptide testing?
- Currently there are large differences in guideline recommendations across Europe. Where do ESC and national guidelines vary, and where do they overlap?
- When to classify as HFrEF - different cut-offs are used in studies (earlier studies: 35%, then trials 40%, and epidemiological studies 45%) so what threshold should be used?
- In the treatment of HFrEF, what is the role of primary care in providing novel therapies such as ivabradine and ARNIs?
- Is there a treatment for HFpEF which has prognostic benefit?
- What is the best way to provide integrated care for HF patients? How can the organisation of care be improved?
- How can patients with HF who are reaching the end of their lives be identified more effectively and managed appropriately within primary care?

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