Validation of the heart failure diagnosis in Sahlgrenska University Hospital in 2000 - 2012 and an examination of co-morbidities present

Master thesis in Medicine

Ann Reimstad

Supervisor Maria Schaufelberger

Department of Molecular and Clinical Medicine

Institute of Medicine

The Sahlgrenska Academy

UNIVERSITY OF GOTHENBURG

Programme in Medicine

Gothenburg, Sweden 2014

Table of Contents

Abstract

Master thesis for the programme in Medicine, "Validation of the heart failure diagnosis in Sahlgrenska University Hospital in 2000 - 2012 and an examination of co-morbidities present" by Ann Reimstad, Institute of Medicine; Gothenburg, Sweden. Supervisor Maria Schaufelberger.

Background: Heart failure (HF) is a complex clinical syndrome, characterized by a variety of symptoms. Patients with HF are often old and have several co-morbidities. HF is a common disease with high mortality and morbidity, and with a large impact on quality of life. Therefore, diagnostic accuracy is important.

Aim: To validate the HF diagnosis in patients hospitalized in Sahlgrenska University Hospital in Gothenburg under 2000- 2012, and also to examine whether co-morbidities may affect the validity of the diagnosis.

Method: All patients hospitalized with the diagnosis of HF in Sahlgrenska University Hospital in 2000- 2012 were identified (27 517 patients). 1 100 patients were randomly selected and studied. Their diagnosis was validated according to the European Society of Cardiology (ESC) diagnostic guidelines. The co-morbidities studied were ischemic heart disease (IHD), diabetes mellitus (DM), hypertension, hyper- and hypothyreosis, asthmatic or chronic obstructive pulmonary disease (COPD), kidney failure, cardiomyopathy, atrial flutter-/ defibrillation, systemic inflammatory disease and drug-/ alcohol abuse.

Results: Finally, 136 patients were excluded, mainly due to incomplete information or missing records. The validation of the HF diagnosis in the population studied (964 patients) were definite in 62.1 %, probable in 32.3 % and miscoded in 5.6 % of cases. No significant difference was found in the validity of the diagnosis when comparing the subgroups of co-morbidities to the whole study population.

Conclusions: The overall validity of the HF diagnosis was 94.4 % which is quite high, and in line with earlier validation studies.

Keywords: *Heart failure, validation, diagnosis, co-morbidities*

Introduction

The prevalence of heart failure (HF) in Sweden is approximately 2 - 3 % (1-3). The diagnosis causes high costs for society, estimated to be around 2 % of the total healthcare budget, with 75 % related to hospital care (1, 2). The 5- year mortality rate of HF exceeds many common types of cancer (4, 5). From time of diagnosis 50 % of the patients will die within 4 years, and for patients diagnosed with severe HF more than 50 % will die within one year (6). Chronic HF causes a large impact on the function and quality of life for the individuals who are suffering from the disease (7, 8).

Clinical presentation and pathophysiology

HF is a clinical syndrome which is caused by an underlying structural abnormality or function of the heart. This leads to an insufficient ability to deliver oxygen to the tissues of the body and results in a variety of symptoms. The most typical symptom of HF is exercise-induced dyspnea or dyspnea at rest, including ortopnea. Other common symptoms are fatigue, weight gain and ankle swelling, as well as palpitations. Weight gain and edema are caused by excessive fluid in the body due to a failed ability of the heart to maintain a proper blood flow. Severe, acute HF can due to fluid retention also cause pulmonary edema which leads to serious and sometimes fatal respiratory distress. HF is characterized by altered hemodynamics as well as an imbalance in other parts of the body, e.g. kidneys and the endocrine system (9, 10). The severity of symptoms and function in a patient can be classified according to the New York Heart Association (NYHA) classification scale (fig. 1). HF can preferably be divided into systolic and diastolic HF. In recent years, it has been established how to diagnose diastolic dysfunction.

Class	Functional Capacity: How a patient with cardiac disease feels during physical activity
I	Patients with cardiac disease but resulting in no limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

Figure 1. New York Heart Association (NYHA) classification of functional capacity in patients with cardiac disease. Source: http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp

Co-morbidities

There is always an underlying cause of HF and most common are ischemic heart disease (IHD) and long-term hypertension. Other causes are damage of the heart valves, cardiomyopathy, myocarditis, diabetes mellitus (DM), amyloidosis, endocrine or inflammatory diseases or arrhythmia of the heart, e.g. atrial fibrillation. Many of these diseases may not just be the cause of but can also co-exist with HF, i.e. co-morbidities, and it is often difficult to confirm exactly what is the underlying cause of HF and what is just a co-morbidity.

Hypertension, IHD, DM, hyper- and hypothyreosis, asthmatic or chronic obstructive pulmonary disease (COPD), kidney failure, cardiomyopathy, atrial flutter-/ defibrillation, systemic inflammatory disease and drug-/ alcohol abuse are common co-morbidities to HF. Earlier studies has shown that these co-morbidities may affect the prognosis and as we hypothesized, how to set the diagnosis (11-15). Therefore it is important to validate the HF diagnosis in the aspect of co-morbidities. For example, symptoms in lung disease such as

COPD may be similar to those of HF. This might affect how the diagnosis of HF is set. These different conditions requires substantially different treatment, and therefore it is important that the diagnosis is correct, in order to avoid inadequate treatment strategies. DM may also affect how to set the HF diagnosis, since HF patients with DM has been shown to have diastolic HF in a higher extent than others (11), and diagnostic criteria for diastolic HF has been very complicated until recently. Regarding the validation of the HF diagnosis according to co-morbidities, there are very few earlier studies.

Diagnostic methods

When a patient shows symptoms consistent with HF the patient is usually investigated with an electrocardiogram (ECG) which is easily accessed and associated with a low cost. Also the possibility to measure the natriuretic peptide BNP/ NT-proBNP in blood has made it easier to investigate the diagnosis as well, mainly as a tool to rule out HF in the early stages of investigation (16).

Echocardiography (ECHO) is the most specific tool for diagnosing HF and should be performed in the next step of investigation. The ECHO may also give information about the etiology. Ejection fraction (EF) is the most used tool when assessing left ventricle, and heart function (17). The EF is the amount of blood that leaves the left ventricle in each contraction in relation to the total amount of blood in the left ventricle during diastole (18). An EF more than 50 % is considered to be normal (6). As mentioned, HF can be divided into systolic and diastolic HF. In systolic HF or HF-REF (HF with reduced ejection fraction) systolic dysfunction can be measured when performing ECHO (usually defined as an EF below 40-45 %). In diastolic HF or HF-PEF (HF with preserved ejection fraction) the EF may be normal or slightly abnormal (45- 55 %) (6). HF-REF was defined already in the first European Society of Cardiology (ESC) HF guidelines from 1995. HF-PEF or diastolic HF is mentioned in the guidelines from 1995 and 2001 but were not defined until the 2005- update. The diagnosis of HF-PEF is more complex and difficult to set than HF-REF (19, 20). For the definition of HF-

REF and HF-PEF according to the current ESC guidelines see fig. 2. The guidelines published in 2012 states that patients with an EF 35- 50 % represents a "grey area" and could be diagnosed as HF-PEF but only after exclusion of other causes (6).

The diagnosis of HF-REF requires three conditions to be satisfied:
1. Symptoms typical of HF
2. Signs typical of HF[a]
3. Reduced LVEF
The diagnosis of HF-PEF requires four conditions to be satisfied:
1. Symptoms typical of HF
2. Signs typical of HF[a]
3. Normal or only mildly reduced LVEF and LV not dilated
4. Relevant structural heart disease (LV hypertrophy/LA enlargement) and/or diastolic dysfunction (see Section 4.1.2)

Figure 2. Diagnosis of heart failure. HF = heart failure; HF-PEF = heart failure with 'preserved' ejection fraction; HF-REF = heart failure and a reduced ejection fraction; LA = left atrial; LV = left ventricular; LVEF = left ventricular ejection fraction. [a]Signs may not be present in the early stages of HF (especially in HF-PEF) and in patients treated with diuretics. Source: McMurray, J. J., et al. (2012). "ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC." Eur Heart J 2012; **33**(14): 1787-1847.

Diagnostic criteria

In Sweden it is established to use the diagnostic criteria set in the HF guidelines from the ESC. In a study made in 2008 93 % of the cardiologists in Sweden told they were aware of the ESC guidelines and 92 % of those reported they continually follow the guidelines (21). The guidelines have changed during the years, and there are four versions of the guidelines that have been used clinically during 2000-2012. The first ESC guidelines were published in 1995, and have been updated and re-published in 2001, 2005, 2008 and 2012. Other established criteria regarding how to diagnose HF are the Framingham criteria, the Boston criteria and the Carlson criteria. The Framingham criteria demand two major criteria or one major and two minor criteria fulfilled, where the criteria describes typical and more rare

symptoms of HF respectively (22). The Boston criteria classifies the diagnosis of HF definite or possible when over a certain amount of points, which are gathered from the medical history, chest X-ray and the physical examination (22). The Carlson criteria are a variation of the Boston criteria (23).

Description of the ESC guidelines

The ESC guidelines of 1995;

The first guidelines published in 1995 suggest that the diagnosis of HF requires typical symptoms of HF as well as objective evidence of cardiac dysfunction, preferably ECHO. If the diagnosis is questionable improved symptoms after treatment aimed at HF (e.g. a diuretic or an ACE inhibitor) strengthens the diagnosis. Characteristic symptoms are said to be breathlessness/ dyspnea, ankle swelling or fatigue. Typical signs are preferably peripheral edema, hepatomegaly and a raised venous pressure (e.g. jugular vein distension) but also tachycardia, a third heart sound and pulmonary rales. E.g. if a patient has typical symptoms and signs (peripheral edema, a raised venous pressure and in addition a displaced apex beat as well as a third heart sound), the diagnosis of HF could be made with some confidence, even without an ECHO. According to the guidelines ECHO is the golden standard, and should be executed whenever HF is suspected and EF should be assessed. A normal ECG strongly opposes the diagnosis. Chest X-ray should preferably be executed, primarily in order to exclude pulmonary disease as a cause of symptoms. Diastolic dysfunction is mentioned, but how to set the diagnosis of diastolic HF is not stated. In blood works, the natriuretic peptide ANP is mentioned and stated to support the diagnosis if elevated; or oppose the diagnosis if not in an untreated patient (24).

The ESC guidelines of 2001;

The guidelines published in 2001 are similar to those of 1995, and also claims that symptoms of HF as well as objective evidence (preferably ECHO) is necessary for diagnosis. Response to treatment for HF, like before, supports the diagnosis if present. Typical symptoms are, as in

previous guidelines, breathlessness, ankle swelling and fatigue. Typical signs mentioned are peripheral edema, a raised venous pressure and hepatomegaly, but also tachycardia, a third heart sound, pulmonary rales and cardiac murmur. If a patient has typical symptoms and multiple signs of HF (e.g. pitting edema, a raised venous pressure, a displaced apex beat and a third heart sound), the diagnosis of HF could be made with some confidence. As before, a normal ECG strongly opposes the diagnosis. Chest X-ray should be part of the investigation when suspecting HF, primarily for excluding pulmonary causes of symptoms.

ECHO is still considered the golden standard to demonstrate cardiac dysfunction in an objective manner. Diastolic dysfunction is again mentioned, and diagnostic criteria have been proposed by the European Study Group on Diastolic Heart Failure (25). However, though no universally accepted criterion for diastolic HF existed at that time, no further criteria are mentioned in the guidelines (26).

The ESC guidelines of 2005;

As before, typical symptoms and objective evidence are required for the diagnosis of HF. Response to treatment aimed at HF strengthens the diagnosis. The method for showing objective evidence is still preferably a performed ECHO. Now it is clearly stated that cardiac dysfunction can be both systolic and diastolic. Diagnostic criteria for diastolic dysfunction (diastolic HF) are now established. To set the diagnosis appropriate signs or symptoms are required, as well as evidence of abnormal left ventricular relaxation, diastolic stiffness or diastolic distensibility, and a normal or mildly abnormal LVEF (left ventricular ejection fraction) of ≥45-50 %.

The natriuretic peptides BNP and NT- proBNP are first discussed in the 2005 guidelines. A normal concentration in an untreated patient makes HF unlikely and may determine whether to go further in investigations in a patient with symptoms, e.g. in primary care (27).

The ESC guidelines of 2008;

In the guidelines published in 2008, symptoms of HF and objective evidence of an abnormality of cardiac function and structure is required, as well as clinical signs. Clinical signs to look for are peripheral edema, pulmonary rales, tachycardia, tachypnoea, hepatomegaly, raised jugular venous pressure and pleural effusion. Symptoms required are dyspnea, fatigue, tiredness or ankle swelling. The objective evidence is specified as cardiomegaly on chest X-ray, a third heart sound, cardiac murmur, abnormality on ECHO or raised levels of natriuretic peptides in blood sample. Clinical response to treatment may help set the diagnosis in uncertain cases.

The part on diastolic HF (HF-PEF) is also extended. To recognize HF-PEF / diastolic dysfunction on an ECHO it is crucial to look for abnormal filling patterns. It is specified in the guidelines that there are three types of abnormal filling patterns; one pattern of "impaired" myocardial relaxation, one pattern of restrictive filling in the left ventricle (LV), and an intermediate pattern between the first two (impaired relaxation and restrictive filling). Hence, the diagnosis HF-PEF can be set under the circumstances that; apart from the fact that symptoms or signs of HF must be present, there is evidence of diastolic dysfunction and a normal or mildly abnormal LV systolic function on ECHO.

Natriuretic peptides can also be used as objective evidence when setting the diagnosis. An elevated NT-proBNP >2000 ng/L makes the HF diagnosis likely. On the contrary, a BNP <100 ng/L or NT-proBNP <400 ng/L makes the diagnosis of HF unlikely.

To summarize; in the new guidelines of 2008 in comparison to before, clinical signs are mandatory but the objective finding does not necessarily have to be a performed ECHO (28).

Validation

It is important to validate the diagnosis of HF in order to be able to decide whether trends in prevalence and incidence are true or not (2, 29). The trends may be influenced by praxis when

diagnosis is set, and this may of course affect the true figures. Earlier studies have shown low accuracy when diagnosing HF in elderly and obese and for patients with DM and atrial flutter (11, 30, 31). Many studies are old and few are made in Scandinavia, or made in an inpatient setting. Therefore, further studies are needed within the field.

Aim

The aim of this study was to validate the diagnosis of HF according to the ESC guidelines in patients hospitalized with HF in Sahlgrenska University Hospital in 2000-2012. In addition to this, the aim was also to examine whether co-morbidities may affect the validity of the HF diagnosis.

Material and Methods

Study population

The Sahlgrenska University Hospital is located in Gothenburg and includes three different hospitals; the Östra hospital, the Mölndal hospital and the Sahlgrenska hospital. The city of Gothenburg has 500 000 inhabitants (32) but the Sahlgrenska University Hospital to some extent serves the population in the western part of southern Sweden (Västragötalandsregionen) with 1.6 million inhabitants (33). Between 2000 - 2012 27 517 patients were hospitalized with a HF diagnosis within the Sahlgrenska University Hospital. Of those, 1 100 hospitalizations (called index hospitalization dates) with unique patients were randomly selected, identified from the digital record system Melior by a statistician using the SAS version 9.3. All patients had been discharged with the diagnosis of HF; code I50 according to the WHO International Classification Diseases (ICD 10). Half of the patients (550) had HF as the primary diagnosis and the other half (550) had the diagnosis in any contributory position. After exclusions, 964 patients were finally included in the study. The most common reason for exclusions was missing data and errors in the selection process

(table 3). Missing data was either due to fractioned hospital care (part of admission on other hospitals outside of Gothenburg) or due to the fact that the records needed could not be found despite extensive search in the medical records archives. More patients with HF in contributory position were excluded than with HF as primary diagnosis, resulting in 534 patients included with HF as primary diagnosis and 430 included with HF as diagnosis in contributory position (table 2).

Collection of data

This was a retrospective study. Four medical students collected the material by going through medical records for symptoms and signs of HF and appropriate investigations (ECHO, blood samples, chest X-ray, ECG, magnetic resonance imaging (MRI) and radionuclide angiography) and whether symptomatic improvement after treatment occurred or not, using a specific composed form, see appendix. The form was made to associate to the content in the guidelines from the ESC. The data collection started in January 2013.

If the medical records could not be found in the digital system (Melior) it was searched for in the record- and microfilm archives. The reports on ECHO examinations were, if not available in Melior, searched for in the archives of the Clinical Physiology departments of the different hospitals. Symptoms, signs and investigations were collected from the emergency room notes throughout the whole hospitalization including the epicrisis. When collecting information about co-morbidities it could be sampled both from the admission notes and from the diagnostic codes in the epicrisis. The findings of the physical examination were collected primarily from the admission date, and were not noted as a clinical sign if only mentioned, e.g. in history-taking in the admission note.

For the patients with HF as primary diagnosis all data was collected from the index hospitalization. For patients with HF in contributory position information about signs, symptoms and investigations were sampled from the first hospitalization or other first

mentioning in the records for HF. Chest X-ray was collected up to a year before this hospitalization. The age of the patient were always noted from the index hospitalization date.

Diagnostic methods

Chest X-ray/ Computer tomography of the thorax;

From the radiology report of the chest X-ray / computer tomography of the thorax (CT-thorax) signs of HF were registered. Redistribution, pulmonary congestion, pulmonary edema and pleural fluid were noted as signs of HF as well as if the radiologist clearly reported that HF was present. In patients hospitalized in 2009-2012, the presence of cardiomegaly on chest X-ray was also noted as this was considered objective evidence when validating the diagnosis according to the guidelines of 2008.

Echocardiography (ECHO);

The ECHO report with the lowest EF before or during the index hospitalization was used for validation of the diagnosis. In this study, we considered an ECHO with an EF $\leq$45% as pathological. In all cases where ECHO had pathological findings but an EF >45 %, the case was reviewed by an experienced cardiologist. If the ECHO report stated "diastolic dysfunction" HF-PEF was considered present, if "diastolic dysfunction" was not mentioned but there were still abnormal findings that can be present in diastolic dysfunction; e.g. left ventricular hypertrophy, enlarged left atrium or high diastolic filling pressure, the case was judged by two experienced cardiologists on whether diastolic dysfunction was present or not. Also, if a patient had an earlier pathological ECHO performed (e.g. reduced EF or dilation of the heart) but during the index hospitalization the ECHO was normal, it was assessed by two experienced cardiologists for definite validation.

Electrocardiogram (ECG);

If more than one ECG was performed during the index hospitalization the first one was used for validation. For patients with HF in contributory positions, the first ECG taken in the hospitalization when HF was first diagnosed was used.

The ECG was assessed pathologic or non-pathologic considering the rhythm, QRS-width, presence of Q-waves, ST/T-changes or left bundle branch block. An ECG with none of the above abnormalities, and with sinus-rhythm, was considered non-pathologic. All ECG that appeared non- pathologic was assessed by one, and in case of doubt two experienced cardiologists before assessed as normal.

Natriuretic peptides;

For the patients with the HF diagnosis in contributory position the blood sample with the highest value of BNP or NT-proBNP before or during the index hospitalization was collected. This also applies to patients with HF as primary diagnosis, but not to all. For the first 400 patients studied, the latest value before the index hospitalization was collected, and for the rest of the patients with HF as primary diagnosis the highest value was collected.

Validation

After collecting the data the diagnosis was validated according to ESC guidelines in clinical use at time of index hospitalization by four medical students and an experienced cardiologist and defined as definite, probable or miscoded. If they could not make a final decision another two experienced cardiologists were consulted.

During the years studied, the ESC guidelines were updated four times. The first guidelines were published in 1995, with updates in 2001, 2005, 2008 and 2012. We anticipated that it takes up to a year before an updated version of the guidelines is in clinical use. For example, if the index hospitalization date was in 2005, the guidelines used were the ones from 2001; and if the hospitalization date was in 2006 the guidelines used were the ones from 2005.

The diagnosis was sorted into groups as definite, probable or miscoded for each patient validated. An EF of ≤45 % was assessed as pathological. To be defined as definite, the patient had to report symptoms, show findings during physical examination and objective finding of cardiac dysfunction (preferably ECHO). There are some differences between the ESC

guidelines of the different years. The guidelines of 1995, 2001 and 2005 require symptoms (dyspnea, peripheral edema and/ or fatigue) in the medical history, an objective finding (preferably an ECHO) and, in uncertain cases response to treatment directed towards HF support the diagnosis. In the guidelines from 2008, symptoms and an objective finding of cardiac dysfunction (abnormality on the ECHO, cardiomegaly, third heart sound, cardiac murmurs or raised level of natriuretic peptides) as well as clinical signs of HF are mandatory. Thus, the objective finding of cardiac dysfunction does not have to be a performed ECHO, according the guidelines of 2008. For a summary of the guidelines used in this study, see table 1.

In this study the validity of the HF diagnosis was also examined according to co-morbidities. The patients were divided into subgroups according to co-morbidity, and then the groups were compared to the whole study population to see if the validity was affected by the patient´s co-morbidities.

To ensure validation was made in a similar way by all four medical students involved in the project, 20 patients were picked from previous material and validated once again, in this part of the study. 10 patients with HF diagnosis in main and 10 patients with HF diagnosis in contributory position were randomly selected by a statistician and again validated to ensure inter-observer accuracy (table 7).

Table 1. Diagnostic assessment according to the European Society of Cardiology (ESC) guidelines.

	1995	2001	2005	2008
	Supports if present/ Opposes if normal or absent	Supports if present/ Opposes if normal or absent	Supports if present/ Opposes if normal or absent	Supports if present/ Opposes if normal or absent
Appropriate symptoms	+++*/---	+++*/--	+++*/---	++*/--
Appropriate signs	+++/-	+++/-	+++/-	++*/-
Response to treatment	+++/---	+++/---	+++/---	+++/--
Pathological ECG	/---	/---	/---	++/--
Cardiac dysfunction on imaging	+++*/---	+++*/---	+++*/---	+++**/--
Chest X- ray	+/-	+/-	+/-	+++/-
Natriuretic peptides	n/a	+ (if elevated) /---	+ (if elevated) /---	+++ (if elevated) /---

Abbreviations: +/- of some importance; ++/-- of particular/ considerable importance; +++/--- of major importance. * Necessary for definite diagnosis. ** Considered an objective evidence of cardiac dysfunction. ECG = electrocardiogram; ESC = European society of cardiology. This assessment adapted from the heart failure diagnostic guidelines edited by the ESC in 1995, 2001, 2005 and 2008.

Co-morbidities

In the form it was noted if the patient apart from HF suffered from IHD, DM, hypertension, hyper- or hypothyroidism, pulmonary disease (asthmatic or obstructive/ COPD), kidney failure, cardiomyopathy, atrial flutter /-fibrillation, systemic inflammatory disease or drug- / alcohol abuse. Information about drug- / alcohol abuse was not sampled in the first 422 patients but was added in the last 542 patients. Lupus, rheumatic arthritis, polymyalgia rheumatica, temporal arteritis/ vasculitis and Morbus Bechterew were considered as systemic inflammatory diseases. Patients were considered to suffer from kidney failure if it was expressed in the admission note or as a diagnostic code in the epicrisis (as for all other co-morbidities). For patients with HF in contributory position the patient was also considered to suffer from kidney failure if an elevated serum-creatinine was present (>100 mmol/L). The first available serum-creatinine from the hospitalization was sampled.

For all the patients co-morbidities were collected from the index hospitalization.

Ethics

Revealing the identity of the patients involves a violation of integrity. Due to the retrospective design of this study, no approval from the patients was collected. However, each patient was given a code, which was continually used through the process of collecting data. The identity and social security number of the patient was strictly kept in a separate file, only able to be accessed by the few persons involved in the study. All material with personal information was kept within the hospital, in a locked compartment. Only patient data relevant for the study was viewed. Approval to access patient information and - data was collected from the manager of each clinic involved in the study. As knowledge about the epidemiology of HF is very important, e.g. for planning on how to use the health care budget in the most cost-effective way in the future, we believe that the violation of integrity of the patients involved in the study could be motivated. Also, all results in this report are presented as group data, and no individual patient can therefore be able to recognize him- or herself in hind-sight.

The study was approved by the Ethical review board of the University of Gothenburg with registration number: 2011-588/08/10.

Statistical methods

Descriptive statistics was used to present baseline characteristics and determine percentages, mean scores, standard deviations (SD) and range. Since the variables studied were normally distributed, comparisons between groups were assessed with t-test for continuous variables, or Pearson Chi-square test and Generalized Linear Models were used when comparing dichotomous variables. For comparing categorical values frequencies was used. Analyses were conducted using the SPSS Advanced Statistics for Windows statistical package, version 21 (SPSS Inc., Chicago, IL, USA). A two-sided p-value < 0.05 was considered statistically significant.

Results

Participants and exclusions

The total study population included 964 patients, 50.5 % women and 49.5 % men (table 2). Of the patients 55.4 % had the HF diagnosis in primary position and 44.6 % in any contributory position. The mean age of the study population was 78.7, and the median age was 81 years (at time of index hospitalization). The age ranged from 19 to 100 years. A total of 776 patients were hospitalized in an internal medicine clinic and another 188 in a cardiology clinic (80.5 % and 19.5 %, respectively).

Table 2. Study population.

Characteristic		Number of patients (% of total)
Age (years)		
- Mean (SD)	78.7 (11.1)	
- Median (range)	81 (19-100)	
Men		477 (49.5)
Women		487 (50.5)
Diagnostic position:		
- Primary position		534 (55.4)
- Contributory position		430 (44.6)
Sahlgrenska Hospital		354 (36.8)
Mölndal Hospital		192 (19.9)
Östra Hospital		418 (43.4)
Hospitalized in internal medicine clinic		776 (80.5)
Hospitalized in cardiology clinic		188 (19.5)
Validated according to:		
- ESC guidelines of 1995		210 (21.8)
- ESC guidelines of 2001		328 (34.0)
- ESC guidelines of 2005		179 (18.6)
- ESC guidelines of 2008		247 (25.6)
Total		**964 (100)**

Table 3. Exclusions. Exclusions according to category.

Reason for exclusion	Number of patients
Errors in selection process	**54**
- Diagnosis other than HF	11
- Clinic other than medicine or cardiology	35
- Missing digit in social security number	7
- Age < 16	1
Information missing	**60**
- Part of hospitalization in another hospital	12
- Medical record not found	37
*- Patient unable to leave history information**	11
Hospitalization due to elective procedure	**22**
Excluded, contributory position	**113**
Excluded, primary diagnosis	**23**
Total excluded	**136**

* dementia or other cognitive impairment, intoxication, unconsciousness, aphasia

Validity

The validity for the whole study population was definite in 62.1 % of cases (599 patients), probable in 32.3 % (311 patients) and miscoded in 5.6 % of cases (54 patients) (table 4). Thus, the diagnosis was definite or probable in 94.4 % of cases (fig. 3).

Co-morbidities

The most frequent co-morbidities in the study population were IHD, atrial defibrillation/ - flutter and hypertension (table 5). Drug - or alcohol abuse was present in 8.3 % of cases (out of 542 patients). The least common of the co-morbidities registered was hyperthyreosis, which was present in 0.6 % of the cases (6 patients). Cardiomyopathy was present in 4.7 % of the patients.

No significant difference was found when comparing the validity between the whole study population and the different subgroups of co-morbidities (p-value varied from 0.094 to 1.0). In this analysis age and sex were thought to be possible confounding factors. Therefore, when

analyses were made for the subgroups of co-morbidities they were included as confounding factors. This did not alter the results.

Investigations

ECHO was performed in 74 % of the whole study population. Out of the patients with cardiomyopathy, 44 out of 45 patients had an ECHO performed (98 %). For patients with pulmonary disease (obstructive and/ or asthmatic) ECHO was performed in 78 % of cases, for IHD in 79 %, for DM in 81 %, and for patients with inflammatory systemic diseases and drug/ alcohol abuse in 80 % and 89 %, respectively (table 6).

Of the whole study population 94 % had an ECG performed (907 patients). Of those, 791 patients had an assessment made in our study whether the ECG was pathological or not. Of those 95 % (752 patients) had a pathological ECG. An MRI or radionuclide angiography was performed in 0.2 % of patients, respectively.

In 93.5 % of patients a chest X-ray/ CT thorax had been performed. Of those, 66 % showed signs of HF on the examination. Another 20.2 % of patients had a BNP/ NT-proBNP taken. The mean value of NT-proBNP was 7003 ng/ L (SD 8511), with a range from 0 to >35 000 ng/ L.

Inter-observer validation

The result from the inter-observer validation, were 20 patients were re-validated in this part of the study, was 89.5 % (table 7).

Table 4. Result of validation. Results of validation separated according to each guideline year and in total. All numbers in n (%).

ESC guidelines	Definite	Probable	Miscoded	Definite and probable	Total
1995	119 (56.7)	78 (37.1)	13 (6.2)	197 (93.8)	210 (21.8)
2001	178 (54.3)	123 (37.5)	27 (8.2)	301 (91.8)	328 (34.0)
2005	98 (54.8)	72 (40.2)	9 (5.0)	170 (95.0)	179 (18.6)
2008	204 (82.6)	38 (15.4)	5 (2.0)	242 (98.0)	247 (25.6)
Validity all years except 2008	395 (55.1)	273 (38.1)	49 (6.8)	668 (93.2)	717 (74.4)
Total validity	599 (62.1)	311 (32.3)	54 (5.6)	910 (94.4)	964 (100)

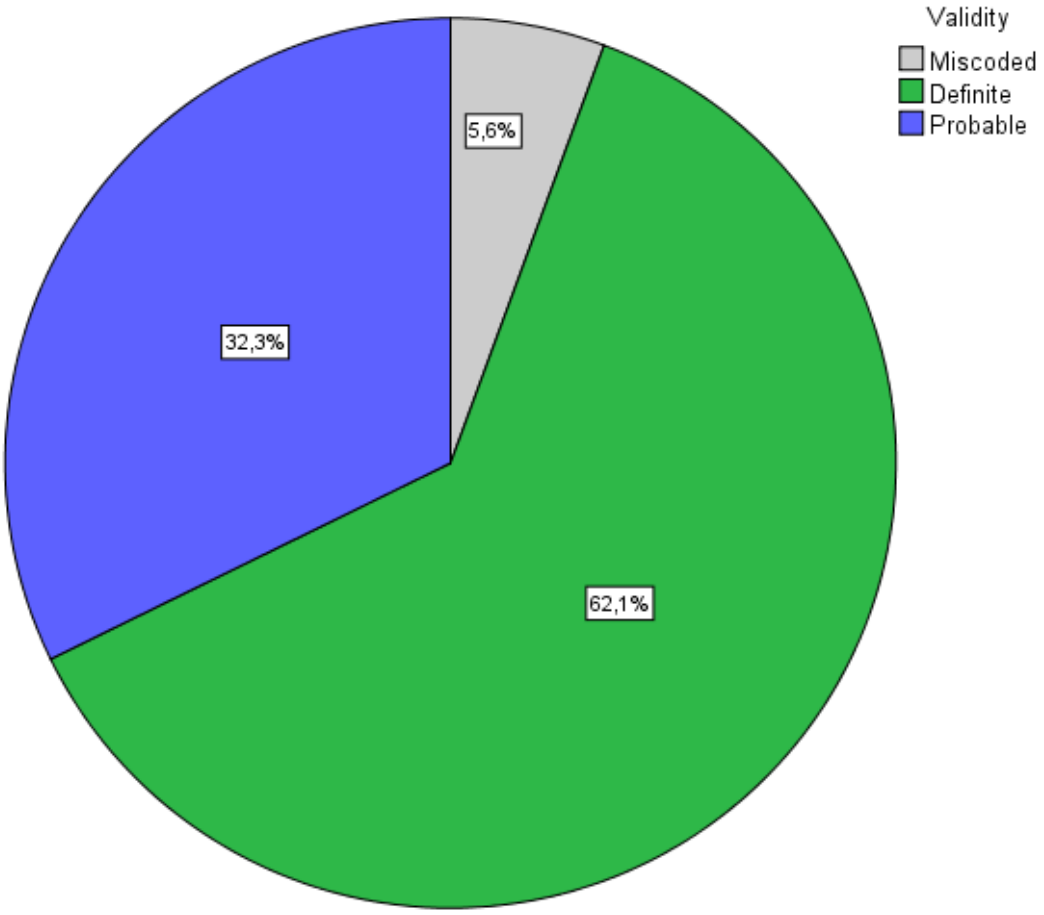

Figure 3. Total result of validation. The whole study population included.

Table 5. Co- morbidities in the study population.

Co- morbidities examined	Female sex (%)	Mean age (year)	Number of patients (%)
IHD	46.6	79.1	483 (50.1)
Diabetes mellitus	46.3	76.6	216 (22.4)
Hypertension	54.1	79.4	449 (46.6)
Hyperthyreosis	100	77.7	6 (0.6)
Hypothyreosis	81.0	81.7	79 (8.2)
Pulmonary disease (asthmatic/obstructive)	48.4	78.0	159 (16.5)
Kidney failure	41.8	78.8	153 (15.9)
Cardiomyopathy	44.4	65.7	45 (4.7)
Atrial defibrillation/ flutter	47.4	80.4	483 (50.1)
Inflammatory systemic disease	71.2	78.3	73 (7.6)
Drug or alcohol abuse (n=542)	28.9	62.4	45 (8.3)
Total patients	**50.5**	**78.7**	**964**

Abbreviations: IHD = ischemic heart disease.

Table 6. Performed echocardiogram (ECHO) in subgroups of co-morbidities in comparison to the whole study population.

Co- morbidity	ECHO performed (%)	P- value
IHD	78	0.002
Diabetes mellitus	81	0.021
Hypertension	75	0.768
Hypothyreosis	66	0.080
Pulmonary disease (asthmatic/ obstructive)	78	0.275
Kidney failure	83	0.008
Cardiomyopathy	98	<0.001
Atrial flutter/defibrillation	74	0.658
Inflammatory systemic disease	80	0.332
Drug- /alcohol abuse	89 [1]	0.030
Total study population	74	

Abbreviations: IHD = ischemic heart disease. [1] Only in 542 cases this co-morbidity was registered.

Table 7. Inter-observer accuracy. In numbers if not otherwise stated.

		Number of patients
Primary diagnosis	Total patients	527
Re-validated		10
Validated with same result		9
Different validation result		1 (probable instead of miscoded)
Contributory diagnosis	Total patients	437
Re-validated		10
Validated with same result		9
Different validation result		1 (probable instead of definite)
Total viewed		20
Different validation result		2
Total validation accuracy (%)		89.5

Discussion

Main findings in relation to consensus in the field

In this study the validity of the HF diagnosis was assessed as definite in 62.1 % and as probable in 32.3 %; overall a validity of 94.4 %. The patients assessed as probable had shown symptoms and/or objective findings typical for HF, and in several cases also had investigations performed supporting the diagnosis but did not fulfill all requirements for a definite diagnosis. Mostly, an ECHO was missing. Only 5.6 % were assessed as miscoded which is in line with earlier studies and is considered to show a high validity, i.e. a high diagnostic accuracy. In a study made by Ingelsson and co-workers in 2005 the diagnosis of HF was classified as definite in 82 %, as questionable in 16 % of cases, and only in 2 % as miscoded. All men, 50 years of age in year 1970 - 1974 in Uppsala County, Sweden, were invited to participate in a study. Of totally 2 322 men 321 were diagnosed with HF during a median follow-up time of 29 years. Only patients undergoing hospital care were included hence the patient data was collected from the Swedish hospital discharge register. Thus, the study population is both small and narrow, and does not include women. In the study by Ingelsson and co-workers the ESC diagnostic guidelines were used for validation, but were not strictly followed, thus other findings than ECHO could be used as objective evidence of HF, e.g. a pathological chest X- ray (34). In another study made by Khand and co-workers in Scotland in 2005, 791 patients discharged with HF or atrial fibrillation were included. The

patients were identified from the national hospital discharge register in the United Kingdom. They found that out of 330 patients diagnosed with HF, 87 % were jointly assessed as HF (definite, probable or possible) and 13 % were miscoded. They validated the diagnosis according to the ESC guidelines of 2005 (31). Thus, their result shows a lower level of validity than ours. Blackburn and co-workers made a validation study of HF from administrative hospital records in Saskatchewan, Canada, including 466 patients discharged with HF. They used the Framingham and Carlson criteria for validation. The result was that 74 % and 63.9 % of the patients met the criteria for the diagnosis of HF, respectively. This is line with the result in our study, as 62.1 % of the patients were assessed as definite HF, and we consider that equal fulfilled Framingham and Carlson criteria (23). Another validation study was made by Fonseca and co-workers in Portugal in 2008, where they looked at the validity in patients with HF as a discharge or death diagnosis. The patients were assessed as definite, possible or miscoded according to the ESC guidelines. It included 234 patients in total and shows a validity of 96 %. This is in line with our validation result (30).

In addition, the study by Fonseca also investigated patients discharged with conditions associated to HF (e.g. coronary artery disease and atrial fibrillation among others). When viewing these patients, it was concluded that the HF diagnosis was underestimated in 21 % of cases (30). This suggests that HF is often under-diagnosed. Similar results were also found in the previously mentioned study by Khand. They found that the diagnosis of HF had incorrectly not been given in between 16 and 36 % the group discharged with atrial fibrillation (31). This study supports the results of Fonseca, that HF may often be under-diagnosed. This might be a problem in Swedish hospitals as well, although it has not been investigated in our study as we have only examined patients with a HF diagnosis. On the contrary, we investigated the validity of the HF diagnosis, and thus if a possible over-diagnosis was present.

In this study we wanted to investigate if co-morbidities affect the validity of the HF diagnosis. No significant differences were seen between the whole study population and the different co-morbidity groups, in relation to validity in this study. One hypothesis, mentioned in the introduction, was that the symptoms of pulmonary disease such as COPD could be similar to those of HF and affect the diagnostic precision. Our results did not support this hypothesis.

We also investigated to what extent ECHO was performed in the groups of co-morbidities (table 6). ECHO was performed to a significantly higher degree in patients with cardiomyopathy, kidney failure, IHD, DM and drug-/alcohol abuse. Patients with cardiomyopathy had ECHO performed to a high extent (98 %). This could be due to that cardiomyopathy is a diagnosis of exclusion and therefore an ECHO must have been performed before this diagnosis is set. Use of ECHO in the different groups might be due to other causes, e.g. the age or sex of the patient or which clinic the patient was admitted to. The unequal use of ECHO in the subgroups could have affected the validity of the HF diagnosis in the different subgroups of co-morbidities, as ECHO is an important tool of investigation. Therefore, the unequal use of ECHO could have shaded possible differences when comparing the validity of the subgroups to the validity of the whole study population. Interestingly, the patients with pulmonary disease, which we hypothesized would have had a ECHO performed to a higher extent due to differential diagnostic difficulties, did not have an ECHO performed to a higher extent compared to whole study population. Therefore our hypothesis could not be confirmed by our results.

In our study we found that the most common co-morbidities were IHD, hypertension and atrial fibrillation. In a recent study by Lund and co-workers hypertension and atrial fibrillation/-flutter as well as numerous non-cardiovascular co-morbidities were associated with HF-PEF (14). In another recent study Le Corvoisier and co-workers found high prevalence of co-morbidities in patients with acute decompensated HF in their study of 555 patients admitted to emergency departments in five French hospitals. The most frequent co-

morbidities were hypertension, atrial fibrillation/-flutter and DM (12). Another study was made by van Deursen and co-workers, and they also found that co-morbidities are highly prevalent in HF patients. Their study contained 3 226 patients within Europe, and the co-morbidities studied were DM, hyper- and hypothyroidism, stroke, COPD, sleep apnea, chronic kidney disease (CKD) and anemia. They found that 74 % of the patients had at least one co-morbidity; the most frequent were CKD, DM and anemia (15). The most frequently occurring co-morbidities associated with HF mentioned in the introduction were thus common both in our study as well as in these mentioned studies. This shows that our data is representable for HF in the general hospital population. Notably anemia mentioned in the last study was not examined in our study and could possibly have been interesting to examine.

To our knowledge there are no earlier studies made where the diagnosis of HF has been validated according to co-morbidities.

Methodological considerations

The validation process of this study is also important to discuss. ECHO is considered golden standard when setting the diagnosis of HF, but was not performed in all patients in this study. The diagnosis could still be considered definite, in cases validated according to the guidelines of 2008 and in two cases validated according to guidelines from 2005 and 2008 where EF was determined from MRI and radionuclide angiography instead of ECHO. A normal ECG makes the diagnosis of HF less likely according to the ESC guidelines of all years in this study (table 1). Of the patients, 95 % (791 was assessed in this matter) had a pathological ECG. Normal level of natriuretic peptides in blood sample makes HF unlikely in an untreated patient according to the guidelines of 2005 and 2008 (after the general introduction of the sampling of natriuretic peptides). However, only around 20 % of the patients in our study population had a BNP/NT-proBNP taken because it was not used routinely until the latest years of this study. All in all, when taking all these measurements in account, the HF diagnosis in our study was validated according to guidelines even in absence of an ECHO. This study includes

patients with HF as a primary diagnosis as well as patients with HF as a contributory diagnosis. When validating the patients with HF in contributory position we went back to the first available hospitalization when the diagnosis was set, to collect the data. Therefore it may be claimed that those patients were validated in the same way as patients with HF as primary diagnosis. Even so, the diagnosis was always validated in reference to the index hospitalization date for all patients and at that time the patients treating physician had all the old information, therefore we used all this information too in the validation.

The study population in this study is large in comparison to earlier validation studies (23, 30, 31, 34, 35) as it includes 964 patients, which is a major strength of this study. As mentioned, there are several guidelines available when validating the diagnosis of HF. The ESC guidelines are elaborated and updated by European expertise in cardiology according to current knowledge. Also, the awareness and use of the ESC guidelines in Sweden is proved high (21).

This study included patients admitted to three different hospitals in Gothenburg located in different areas. Two hospitals, Mölndal and Östra are primary hospitals whereas one, the Sahlgrenska hospital is both a primary hospital for about 250 000 citizens of Gothenburg and a tertiary hospital for the Västra Götaland region (1.6 million inhabitants). This, as well as the number of patients studied, makes it possible, to some extent to generalize our data to the whole of Sweden. However, patients with a primary diagnosis of HF are seldom referred to a tertiary hospital, just in case of need for left ventricular assist or heart transplant. In case of HF as secondary diagnosis the figures are more difficult to estimate. In cases where Sahlgrenska was used as a tertiary hospital 12 cases were excluded due to missing information in the records. This, as for all exclusion processes, may have caused a selection bias as we could not control or account for which patients were excluded due to missing data.

In this study 136 patients were excluded. A majority had HF as a contributory diagnosis (83 %). This could be explained by the difficulty to find the records from the first hospitalization

date for HF as a diagnosis which sometimes was several years back. Early records were harder to find as they were not digitalized which resulted in exclusion due to missing records (table 3). This resulted in a higher number of exclusions in this group than for the patients with HF as a main diagnosis. As mentioned above, this may have caused a selection bias.

Another limitation of this study is that the study population only consists of patients that were hospitalized and not patients diagnosed in primary care. According to Zarrinkoub and co-workers, 35 % of all HF patients in Stockholm are managed only in primary health care (2). Therefore the in-hospital population examined in this study can be assumed to have a more severe disease than the over-all HF population, which may have affected the validation.

Also, when analyzing the material in this study, the validity of the HF diagnosis in the groups of co-morbidities was compared to the validity of the whole study population. Another statistical analyze that could have been made would have been to compare the validity of the HF diagnosis in the subgroups of co-morbidities to each other. Even so, the analyze made for the most part does answer the aim of this study; to examine whether co-morbidities may affect the validity of the HF diagnosis.

Yet another limitation of this study could be that there have been four medical students who collected the material. To ensure inter-observer accuracy regular meetings with the group of medical students and supervisor were held during the data collection process. During these meetings it was discussed how to interpret data when reading the patient medical records. In addition, 20 patients out of the total 964 were revalidated in this part of the study to ensure inter-observer accuracy. The result was 89.5 % accuracy (table 7). Only one patient was assessed probable instead of miscoded. The other patient was considered probable instead of definite (still considered having the diagnosis of HF).

Conclusions

In total, the validity of the HF diagnosis was high, thus only 5.6 % of the cases were assessed as miscoded. No significant difference in validity was found when comparing the groups of co-morbidities to the whole study population, thus indicating that the diagnostic accuracy is not affected by the patient´s co-morbidities. However, there was a significant difference in to what extent the groups of co-morbidities had a performed ECHO compared to the whole study population. This, as well as the fact that the study population had a performed ECHO in only 74 % of cases, may indicate that a wider use of ECHO may even further improve the validity of the HF diagnosis.

Populärvetenskaplig sammanfattning på svenska*

Hjärtsvikt är en allvarlig sjukdom som drabbar ca 2 % av Sveriges befolkning. Symtomen vid hjärtsvikt är bland andra andfåddhet, trötthet och bensvullnad. Dödligheten är jämförbar med några av de vanligaste cancersjukdomarna, med en dödlighet på 50 % inom fyra år. För patienter med svår hjärtsvikt är dödligheten 50 % inom ett år. Hjärtsvikt kan t.ex. uppstå efter genomgången hjärtinfarkt. Andra orsaker kan vara högt blodtryck, hjärtrytmrubbning eller diabetes. Ofta har hjärtsviktspatienter flera olika sjukdomar samtidigt, s.k. komorbiditeter. De komorbiditeter, d.v.s. sjukdomar, vi tittat på i den här studien är ischemisk hjärtsjukdom (d.v.s. hjärtinfarkt och kärlkramp), högt blodtryck, diabetes, sköldkörtelsjukdom, njursvikt, hjärtrytmrubbning, inflammatorisk systemsjukdom, lungsjukdom, hjärtmuskelsjukdom och alkohol- och drogberoende sjukdom. Syftet med studien var dels att titta på validiteten för hjärtsviktsdiagnosen för hela studiepopulationen, dels för grupper av patienter med olika komorbiditeter. Detta är viktigt för att kunna bedöma om uppgifter om sjukdomens förändring över tid är verklig, eller om diagnossättningen vid hjärtsvikt är påverkad t.ex. av lokal praxis.

Under 2000- 2012 vårdades 27 517 patienter på Sahlgrenska universitetssjukhuset i Göteborg med diagnosen hjärtsvikt. 1 100 patienter valdes slumpmässigt ut i den här studien och

slutligen granskades 964 patienter. Information om patientens symtom och utförda undersökningar såsom röntgenundersökningar, hjärtultraljud och laborationsprover samlades in. Sedan validerades hjärtsviktsdiagnosen utifrån Europeiska hjärtföreningens riktlinjer. Diagnosen bedömdes utifrån riktlinjerna som definitiv, trolig eller felaktig.

Resultatet blev att 94,4 % av patienterna i studien bedömdes ha en definitiv eller trolig hjärtsviktsdiagnos medan 5,6 % av patienterna bedömdes att felaktigt ha fått en hjärtsviktsdiagnos.

Vi fann också att det inte fanns några skillnader i diagnossättningen när vi jämförde grupperna av patienter med olika komorbiditeter med hela studiepopulationen. Däremot kunde man se att vissa grupper av patienter oftare var utredda med hjärtultraljud, jämfört med hela studiepopulationen. Detta gällde för patienter med ischemisk hjärtsjukdom, diabetes, njursvikt, hjärtmuskelsjukdom och med alkohol- eller drogberoendesjukdom. Hjärtultraljud underlättar diagnossättningen av hjärtsvikt, och varför vissa grupper i högre grad än andra har hjärtultraljud utfört skulle t.ex. kunna bero på patienternas ålder eller om patienten vårdats inom en hjärtklinik eller inte, något som skulle kunna utredas vidare i framtida forskningsstudier.

Acknowledgements

My appreciation goes to Associate Professor Maria Schaufelberger for her guidance during this research project. I would also like to thank Professor Annika Rosengren for her valuable input on study design and assessment of some challenging patient cases.

I would like to thank statistician Tatiana Zverkova Sandström for her time spent working on the randomization process of the patient database.

My appreciation also goes to medical students Sofia Ekestubbe, Mattias Schaufelberger and Simon Hultgren for their help in data collection and study design, and to medical student Josefin Henninger for help in proofreading this report.

References

1. Paren P, Schaufelberger M, Bjorck L, Lappas G, Fu M, Rosengren A. Trends in prevalence from 1990 to 2007 of patients hospitalized with heart failure in Sweden. European journal of heart failure. 2014;16(7):737-42.
2. Zarrinkoub R, Wettermark B, Wandell P, Mejhert M, Szulkin R, Ljunggren G, et al. The epidemiology of heart failure, based on data for 2.1 million inhabitants in Sweden. European journal of heart failure. 2013;15(9):995-1002.
3. Mejhert M, Persson H, Edner M, Kahan T. Epidemiology of heart failure in Sweden--a national survey. European journal of heart failure. 2001;3(1):97-103.
4. Stewart S, Ekman I, Ekman T, Oden A, Rosengren A. Population impact of heart failure and the most common forms of cancer: a study of 1 162 309 hospital cases in Sweden (1988 to 2004). Circulation Cardiovascular quality and outcomes. 2010;3(6):573-80.
5. Shafazand M, Schaufelberger M, Lappas G, Swedberg K, Rosengren A. Survival trends in men and women with heart failure of ischaemic and non-ischaemic origin: data for the period 1987-2003 from the Swedish Hospital Discharge Registry. European heart journal. 2009;30(6):671-8.
6. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. European heart journal. 2012;33(14):1787-847.
7. Falk H, Ekman I, Anderson R, Fu M, Granger B. Older patients' experiences of heart failure-an integrative literature review. Journal of nursing scholarship : an official publication of Sigma Theta Tau International Honor Society of Nursing / Sigma Theta Tau. 2013;45(3):247-55.
8. Falk K, Patel H, Swedberg K, Ekman I. Fatigue in patients with chronic heart failure - a burden associated with emotional and symptom distress. European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology. 2009;8(2):91-6.
9. Braunwald E. Heart failure: pathophysiology and treatment. American heart journal. 1981;102(3 Pt 2):486-90.
10. Braunwald E. Heart failure. JACC Heart failure. 2013;1(1):1-20.
11. Go YY, Allen JC, Chia SY, Sim LL, Jaufeerally FR, Yap J, et al. Predictors of mortality in acute heart failure: interaction between diabetes and impaired left ventricular ejection fraction. European journal of heart failure. 2014;16(11):1183-9.
12. Le Corvoisier P, Bastuji-Garin S, Renaud B, Mahe I, Bergmann JF, Perchet H, et al. Functional status and co-morbidities are associated with in-hospital mortality among older patients with acute decompensated heart failure: a multicentre prospective cohort study. Age and ageing. 2014.
13. Sankaranarayanan R, Kirkwood G, Visveswariah R, Fox DJ. How Does Chronic Atrial Fibrillation Influence Mortality In The Modern Treatment Era? Current cardiology reviews. 2014.
14. Lund LH, Donal E, Oger E, Hage C, Persson H, Haugen-Lofman I, et al. Association between cardiovascular vs. non-cardiovascular co-morbidities and outcomes in heart failure with preserved ejection fraction. European journal of heart failure. 2014;16(9):992-1001.

15. van Deursen VM, Urso R, Laroche C, Damman K, Dahlstrom U, Tavazzi L, et al. Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey. European journal of heart failure. 2014;16(1):103-11.
16. Kelder JC, Cowie MR, McDonagh TA, Hardman SM, Grobbee DE, Cost B, et al. Quantifying the added value of BNP in suspected heart failure in general practice: an individual patient data meta-analysis. Heart (British Cardiac Society). 2011;97(12):959-63.
17. Packer M. Pathophysiology of chronic heart failure. Lancet. 1992;340(8811):88-92.
18. Ejection Fraction Heart Failure Measurement. The American Heart Association http://www.heart.org/HEARTORG/Conditions/HeartFailure/SymptomsDiagnosisofHeartFailure/Ejection-Fraction-Heart-Failure-Measurement_UCM_306339_Article.jsp: American Heart Association; Aug 4,2014.
19. Argulian E, Messerli FH. Misconceptions and Facts about 'Diastolic' Heart Failure. The American journal of medicine. 2014.
20. Becher PM, Lindner D, Fluschnik N, Blankenberg S, Westermann D. Diagnosing heart failure with preserved ejection fraction. Expert opinion on medical diagnostics. 2013;7(5):463-74.
21. Erhardt L, Komajda M, Hobbs FD, Soler-Soler J. Cardiologists' awareness and perceptions of guidelines for chronic heart failure. The ADDress your Heart survey. European journal of heart failure. 2008;10(10):1020-5.
22. Marantz PR, Tobin JN, Wassertheil-Smoller S, Steingart RM, Wexler JP, Budner N, et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. Circulation. 1988;77(3):607-12.
23. Blackburn DF, Shnell G, Lamb DA, Tsuyuki RT, Stang MR, Wilson TW. Coding of heart failure diagnoses in Saskatchewan: a validation study of hospital discharge abstracts. Journal of population therapeutics and clinical pharmacology = Journal de la therapeutique des populations et de la pharamcologie clinique. 2011;18(3):e407-15.
24. Guidelines for the diagnosis of heart failure. The Task Force on Heart Failure of the European Society of Cardiology. European heart journal. 1995;16(6):741-51.
25. Paulus WJ, Tschope C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. European heart journal. 2007;28(20):2539-50.
26. Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. European heart journal. 2001;22(17):1527-60.
27. Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. European heart journal. 2005;26(11):1115-40.
28. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). European journal of heart failure. 2008;10(10):933-89.
29. Barasa A, Schaufelberger M, Lappas G, Swedberg K, Dellborg M, Rosengren A. Heart failure in young adults: 20-year trends in hospitalization, aetiology, and case fatality in Sweden. European heart journal. 2014;35(1):25-32.
30. Fonseca C, Sarmento PM, Marques F, Ceia F. Validity of a discharge diagnosis of heart failure: implications of misdiagnosing. Congestive heart failure (Greenwich, Conn). 2008;14(4):187-91.
31. Khand AU, Shaw M, Gemmel I, Cleland JG. Do discharge codes underestimate hospitalisation due to heart failure? Validation study of hospital discharge coding for heart failure. European journal of heart failure. 2005;7(5):792-7.
32. http://www4.goteborg.se/prod/G-info/statistik.nsf/34f4087fac810b1ac1256cdf003efa4b/2acd96ba76aa5dc6c1257b350045bf6c!OpenDocument Nov 19, 2014.

33. http://www.vgregion.se/sv/Vastra-Gotalandsregionen/startsida/Om-Vastra-Gotalandsregionen/Regionorganisationen/Regionkansliet/Ekonomi/Nyckeltal/ Nov 19, 2014.
34. Ingelsson E, Arnlov J, Sundstrom J, Lind L. The validity of a diagnosis of heart failure in a hospital discharge register. European journal of heart failure. 2005;7(5):787-91.
35. Mard S, Nielsen FE. Positive predictive value and impact of misdiagnosis of a heart failure diagnosis in administrative registers among patients admitted to a University Hospital cardiac care unit. Clinical epidemiology. 2010;2:235-9.

Appendix

Kod:

Sjukhus och klinik för epikris: Kön: M / K

☐ Huvuddiagnos: ☐ Bi-diagnos: Ålder vid validering:

Första diagnostillfälle, år:

Valideringsår: Vårdtid: Avliden (idag): Ja / Nej / Okänt

Anamnestiska uppgifter

Trötthet: Ja / Nej / Okänt Dyspné: Ja / Nej / Okänt

Viktuppgång: Ja / Nej /Okänt Hosta: Ja / Nej / Okänt

Bensvullnad: Ja / Nej /Okänt Ortopné: Ja / Nej /Okänt

Övriga diagnoser:

☐ Ischemisk hjärtsjukdom ☐ Diabetes mellitus ☐ Hypertoni

☐ Hyperthyreros ☐ Hypothyreos ☐ Astma/KOL

☐ Njurinsufficiens, inkomst-kreatinin…….

☐ Kardiomyopatier ☐ FF/FFL ☐ Inflammatorisk systemsjukdom
☐ Missbruk Övrigt……..

Statusfynd

☐ Halsvenstas ☐ Perkussionsdämpning ☐ Blåsljud

☐ Perifera ödem ☐ Lungrassel/krepitationer ☐ Takykardi >90

☐ Leverförstoring ☐ Takypnè > 20 ☐ Tredje ton

☐ Ascites ☐ Cyanos

Genomförda undersökningar och svar

UCG utfört: Ja / Nej Datum…….. Rytm:……

EF:…… % ☐ VK-dilatation (med ord), diameter…….. mm

☐ VK-hypertrofi (med ord) ☐ Lungvensreversering (med ord)

☐ Klaffel:.....

☐ Decelerationstid < 150 ms ☐ S/D kvot < 1 ☐ E/É 8-15 ☐ E/É >15

☐ Patologisk E/A-kvot (med ord) ☐ Pseudonormaliserad E/A-kvot (med ord)

E/A-kvot:…….

☐ Relaxationsstörning i vä kammare (med ord)

☐ Diastolisk dysfunktion (med ord)

Vä förmak: ☐ > 40 ml/m^2 ☐ Måttligt eller kraftigt förstorat (med ord)

Vä förmak yta…… cm^2

☐ Hö förmak dilatation ☐ Hö kammar dilatation

Hö förmak yta…… cm^2

BNP/NT-proBNP (ng/l): >2000 / >900 / 400-900 / <400 / Ej taget
BNP/NT-proBNP:…….. ng/l

Sviktbild vid lungröntgen/CT thorax: Ja / Nej / Ej utfört

EKG: Ja/Nej Rytm: SR/FF/PM-rytm/Övrigt QRS-bredd:……ms
☐ Patologiskt EKG

☐ LBBB ☐ RBBB ☐ Patologisk Q-våg ☐ VK-hypertrofi
☐ Pat. R-vågsprogression ☐ Förlängd QTC-tid ☐ ST-förändringar
☐ T-förändringar

Hjärtscintigrafi: Ja* / Nej MR-hjärta: Ja* / Nej

Positivt svar på behandling : Ja / Nej / Okänt

Övriga kommentarer:

*Om ”ja” ovan, ange vad undersökningen visade här: