

SYMPTOMS AND CLINICAL SIGNS ASSOCIATED WITH HOSPITAL ADMISSION AND MORTALITY FOR HEART FAILURE

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SUMMARY

Little information is available on the predicting factors for hospitalisation and mortality in heart failure. The aim of this study was to determine the symptoms and clinical signs at the time of the diagnosis of heart failure that predict hospitalisation within the first month after diagnosis and mortality within the first six months after diagnosis. Data were prospectively collected during a two-year period by a nationwide network of sentinel family practices. All adult patients for whom the first time the diagnosis of heart failure was clinically suspected were registered. One, six and twelve months after the initial diagnosis, the family physicians completed a follow-up form with questions about the final diagnosis, evolution and outcome. In total 557 patients with confirmed heart failure were recorded (median age = 78 years). Hospitalisation within the first month after the diagnosis was best predicted by peripheral oedema ($p=0.001$), nocturnal dyspnoea ($p=0.022$) and pleural effusion ($p=0.032$) at the time of the diagnosis. Six months after the initial diagnosis the mortality was 19% and after 12 months it was 26%. Mortality within the first six months after the diagnosis was best predicted by age ($p<0.001$) and pulmonary rales ($p=0.001$). Peripheral oedema appeared more among the survivors ($p=0.035$). Peripheral oedema, nocturnal dyspnoea and pleural effusion are highly associated with hospitalisation within the first month after diagnosis.

Key words: heart failure, mortality, hospital admission, primary health care

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INTRODUCTION

Heart failure is one of the leading causes of hospital admission and mortality in patients over the age of 65 in the western world (1). This high number of patients and hospital admissions generates high economic costs in almost all countries (1).

The prevalence of heart failure in the adult population is between 2 and 3% and rises spectacularly from the age of 75 years. In the age group between 70 and 79 years the prevalence is estimated 10 to 20% (2). From the Framingham Heart Study the incidence of heart failure has been estimated 0.2% (3). The incidence almost doubles every decade making heart failure predominantly a disease of the elderly (3). The risk of death in elderly increases more than threefold with heart failure (4). Five years after the diagnosis of heart failure, only 40% of patients survive (5).

Heart failure is a disease with many symptoms and clinical signs. The diagnosis is often based on these symptoms and clinical signs and in many cases confirmed by diagnostic procedures which try to evaluate the ventricular function.

Thereupon, the new-onset of heart failure is often acute, with symptoms and clinical signs related to fluid retention. The term “acute” is in this context an indicator of time rather than severity. However, new-onset heart failure may also start after myocardial infarction, and in that case acute may be an indicator of severity.

Only little reliable data from primary health care about the symptoms and clinical signs associated with hospital admission and mortality are available for heart failure. These data from primary health care are probably different from those of the patients with heart failure who present in the hospital emergency department because only the worst cases are seen in the hospitals and patients dying at their residence are not included in hospital figures.

The aim of this study is to determine from a registration in primary health care the symptoms and clinical signs at the time of the diagnosis of heart failure that predict hospital admission within the first month after diagnosis and mortality within the first six months after diagnosis.

MATERIALS AND METHODS

Sentinel Network

The data for this study were collected by the Belgian network of sentinel practices. This network has been functioning since 1979 and serves as a reliable source on the surveillance of morbidity in Belgium (6–9). Such a surveillance system has already been tested and proved effective (8–11) and is currently applied in a number of countries (12). It has been adequately proven that the Belgian sentinel practices form an important source of data over a wide range of diseases.

The network of sentinel practices consists of family physicians who, with respect to age and gender, are representative of family physicians in Belgium. The sentinel practices are distributed evenly over the territory (13).

Case Ascertainment

The recordings for this study were made by the 178 sentinel practices who regularly participated in the registrations during the period 2005–06. All adult patients for whom for the first time the clinical diagnosis of heart failure was suspected were recorded on the weekly registration form. An additional in-depth questionnaire was sent one month after the initial recording to the physician. The physician was asked to confirm or deny the initial clinical diagnosis of heart failure and to provide more detailed information on diagnostic criteria and complementary examinations. Patients with other causes than heart failure for the non-specific clinical symptoms were dropped out of the study. Six and twelve months after the initial diagnosis, the family physicians personally completed a follow-up form with questions about evolution and outcome. For the present study, hospital admission was evaluated after one month and mortality six months after the initial diagnosis of heart failure. Only hospital admission for heart failure was taken into account. All cases of mortality were taken into account, those related to heart failure as well as those not related to heart failure.

Data Management and Statistical Analysis

The data of the sentinel practices are entered weekly using a database-based software. Databases were stored with a central data manager at the Scientific Institute of Public Health. Several control measures ensured data quality and limited missing data. Data cleaning and data analyses for this study were performed using SPSS17.0 (SPSS Inc). Univariate association between hospitalisation and symptoms/clinical signs was tested by means of χ^2 tests. The Fisher exact test was used when less than 10 observations were concerned. Multivariate analyses were performed with backward stepwise logistic regression to look at the association between the symptoms and clinical signs with hospital admission and mortality.

RESULTS

Registrations and Age

In total 557 patients with confirmed heart failure were recorded. In total 56% of the patients with heart failure were women. The median age of the patients with heart failure was 77.7 years (SD=10.3; range 26–101). Hospital admission within the first month after diagnosis was necessary for 51% of these patients. The median age of the patients with hospital admission was 77.6 years (SD=10.2; range 26–94) and for those without hospital admission 77.9 years (SD=10.4; range 27–101) ($p=0.762$).

After six months, 19% of the patients with heart failure died. The median age of the patients not surviving heart failure was 82.7 years (SD=9.0; range 43–101) and of the survivors 76.5 years (SD=10.2; range 26–99) ($p<0.001$).

Symptoms and Clinical Examination

At the time of the diagnosis, patients complained of breathlessness on exercise in 67% of cases, limitations of physical activity in 60%, orthopnoea in 46%, tiredness on exercise also in 46% and nocturnal dyspnoea in 26%. Other complaints such as night cough, oedema and sweating were observed in 12%.

During the physical examination, peripheral oedema was observed in 68% of the cases, pulmonary rales in 62%, raised jugular venous pressure in 26%, pleural effusion in 23%, cardiac murmurs in 22%, hepatomegaly in 16% and a third heart sound in 10%. Other clinical signs such as gain of weight, tachycardia and atrial fibrillation were observed in 16%.

At the time of the diagnosis, only few patients were classified as NYHA I (3%). Most of the patients were classified as NYHA III (49%), 26% as NYHA IV and 20% as NYHA II.

Hospital Admission

A hospital admission was necessary for 51% of the patients with newly diagnosed heart failure (54% of men and 48% of women). The patients needing hospital admission within the first month after the diagnosis of heart failure complained significantly more of nocturnal dyspnoea ($p<0.001$), orthopnoea ($p<0.001$) and breathlessness on exercise ($p<0.048$) than those not needing hospital admission.

Patients needing hospital admission within the first month after diagnosis presented significantly more with pleural effusion ($p<0.001$), pulmonary rales ($p<0.001$), hepatomegaly ($p=0.004$), raised jugular venous pressure ($p=0.014$) and a third heart sound ($p=0.019$) than those not needing hospital admission.

To determine the symptoms and clinical signs with the highest association with hospital admission, we built a model on the

Table 1. Symptoms and clinical signs for patients with and without hospital admission within first six months after the diagnosis of heart failure

	Hospital admission (n=274) n (%)	No hospital admission (n=283) n (%)	p-value
Nocturnal dyspnoea	92 (34)	51 (18)	<0.001
Orthopnoea	154 (56)	104 (37)	<0.001
Limitations of physical activity	171 (62)	163 (58)	0.25
Breathlessness on exercise	194 (71)	178 (63)	0.048
Tiredness on exercise	134 (49)	124 (44)	0.23
Other symptoms	39 (14)	26 (9)	0.064
Third heart sound	37 (14)	21 (7)	0.019
Cardiac murmurs	59 (22)	64 (23)	0.76
Pleural effusion	84 (31)	44 (16)	<0.001
Pulmonary rales	195 (71)	149 (53)	<0.001
Raised jugular venous pressure	84 (31)	61 (22)	0.014
Hepatomegaly	55 (20)	32 (11)	0.004
Peripheral oedema	184 (67)	197 (70)	0.53
Other clinical signs	48 (18)	41 (15)	0.33

basis of patient characteristics using backward stepwise logistic regression, with hospital admission for heart failure as the dependent variable. Peripheral oedema, nocturnal dyspnoea and pleural effusion had the best association with hospital admission within the first month after diagnosis.

Patients needing hospital admission within the first month after diagnosis had a higher NYHA classification at the time of the diagnosis than those not needing hospital admission. NYHA IV was found in 39% of the hospitalized patients compared to 14% in those not hospitalized ($p<0.001$). The patients with NYHA IV were hospitalised in 73%, those with NYHA III in 50%, those with NYHA II in 25% and patients with NYHA I in 39%.

Mortality

Six months after the initial diagnosis of heart failure the mortality was 19% with no differences between men and women. After 12 months the mortality was 26% and not significantly higher among women (28%) than among men (23%).

The patients dying within six months after the initial diagnosis of heart failure didn't complain significantly more of any symptom

Table 2. Logistic regression stepwise backwards last step for hospital admission

					95% Confidence Interval for O.R.	
	B	Std. Error	p-value	O.R.	Lower Bound	Upper Bound
Nocturnal dyspnoea	0.45	0.20	0.022	1.57	1.07	2.32
Orthopnoea	0.30	0.17	0.084	1.35	0.96	1.89
Pleural effusion	0.43	0.20	0.032	1.53	1.04	2.26
Pulmonary rales	0.28	0.16	0.087	1.32	0.96	1.83
Peripheral oedema	-0.54	0.16	0.001	0.58	0.43	0.79

Logistic regression with in the first step gender, age, nocturnal dyspnoea, orthopnoea, limitations of physical activity, breathlessness on exercise, tiredness on exercise, others symptoms, third heart sound, cardiac murmurs, pleural effusion, pulmonary rales, raised jugular venous pressure, hepatomegaly, peripheral oedema and others clinical signs.

Table 3. NYHA classification for patients with and without hospital admission within first six months after the diagnosis of heart failure

	Hospital admission (n=274) n (%)	No hospital admission (n=283) n (%)	p-value
NYHA I	7 (2.6)	11 (3.9)	0.37
NYHA II	28 (10)	82 (29)	<0.001
NYHA III	135 (49)	137 (48)	0.84
NYHA IV	106 (39)	40 (14)	<0.001

at the time of the diagnosis. The physical examination of these patients revealed significantly more pulmonary rales ($p<0.001$) and significantly less peripheral oedema ($p<0.006$).

To determine the symptoms and clinical signs with the highest association with mortality, we built a model on the basis of patient characteristics using backward stepwise logistic regression, with heart failure mortality within six months as the dependent variable. Age and pulmonary rales had the best association with mortality and peripheral oedema had an inverse association with mortality.

Patients dying from heart failure within six months after the diagnosis had a higher NYHA classification at the time of the

Table 4. Symptoms and clinical signs for patients with and without mortality within first six months after the diagnosis of heart failure

	Death (n=108) n (%)	Survivors (n=449) n (%)	p-value
Nocturnal dyspnoea	29 (27)	114 (25)	0.75
Orthopnoea	57 (53)	201 (45)	0.13
Limitations of physical activity	60 (56)	274 (61)	0.30
Breathlessness on exercise	69 (64)	303 (68)	0.48
Tiredness on exercise	47 (44)	211 (47)	0.52
Other symptoms	14 (13)	51 (11)	0.64
Third heart sound	14 (13)	44 (10)	0.33
Cardiac murmurs	28 (26)	95 (21)	0.28
Pleural effusion	28 (26)	100 (22)	0.42
Pulmonary rales	82 (76)	262 (58)	<0.001
Raised jugular venous pressure	31 (29)	114 (25)	0.48
Hepatomegaly	19 (18)	68 (15)	0.53
Peripheral oedema	62 (57)	319 (71)	0.006
Other clinical signs	14 (13)	75 (16)	0.34

Table 5. Logistic regression stepwise backwards last step for mortality

					95% Confidence Interval for O.R.	
	B	Std. Error	p-value	O.R.	Lower Bound	Upper Bound
Age	0.06	0.01	<0.001	1.07	1.04	1.10
Pulmonary rales	0.72	0.22	0.001	2.06	1.33	3.18
Peripheral oedema	-0.44	0.21	0.035	0.64	0.43	0.97

Logistic regression with in the first step gender, age, nocturnal dyspnoea, orthopnoea, limitations of physical activity, breathlessness on exercise, tiredness on exercise, others symptoms, third heart sound, cardiac murmurs, pleural effusion, pulmonary rales, raised jugular venous pressure, hepatomegaly, peripheral oedema and others clinical signs.

Table 6. NYHA classification for patients with and without mortality within first six months after the diagnosis of heart failure

	Death (n=108) n (%)	Survivors (n=449) n (%)	p-value
NYHA I	3 (2.8)	15 (3.3)	0.77
NYHA II	8 (7.4)	102 (23)	<0.001
NYHA III	41 (38)	231 (51)	0.012
NYHA IV	52 (48)	94 (21)	<0.001

diagnosis than those not dying from heart failure. NYHA IV was found in 48% of the dying compared to 21% among the survivors ($p<0.001$). The mortality within the first six months among patients with NYHA IV was 36%, for those with NYHA III it was 15%, those with NYHA II in 7% and patients with NYHA I in 17%.

DISCUSSION

Half of the patients with newly diagnosed heart failure are hospitalized within the first months after the diagnosis. Six months after the initial diagnosis of heart failure the mortality was 19%. Many symptoms and clinical signs may appear among patients with newly diagnosed heart failure. However, peripheral oedema, nocturnal dyspnoea and pleural effusion are highly associated with hospital admission. But, none of the symptoms or clinical signs are associated with mortality.

Sentinel Network

Medical records do not always provide detailed information concerning the care provided. Therefore, a registration with predefined questions directly with GP's has an important surplus value. Since primary health care is highly accessible in Belgium, a representative sample of the entire population can be monitored. The Belgian sentinel network of general practices is since many years very stable in terms of participating GP's. The sentinel network is highly performant to monitor health-related problems over long and repeated periods. The participating GP's have not been selected on the basis of a specific interest in heart failure research.

Comparisons between the incidence of stroke mortality and suicide registered with the Belgian Sentinel Network and the figures from the National Institute for Statistics on the one hand, and between the cancer incidence registered via the Belgian Sentinel Network and several national and international cancer registries on the other hand, have shown that the Sentinel Network can provide information representative for the entire Belgian population (8, 14).

Because of the weekly registrations, which are leaving little time between the onset of heart failure and the registration, retrospective recall bias found in other retrospective research designs, will be limited (15, 16).

Besides the many strengths of the Belgian sentinel network, the system also has some weaknesses. The registration and follow-up forms are to be kept simple, and time-consuming questions should

be avoided. Consequently, the in-depth study of some specific aspects of heart failure is not feasible (17). However, for the present registration of heart failure, the participating GP's completed two in-depth follow-up questionnaires after 6 and 12 months.

Prospective Registration

In many studies, such as the Framingham Heart Study, heart failure was identified by examining at certain intervals individuals within a cohort (3). This implicates a retrospective registration of cases. In more recent registrations data were accessed by population-based surveillance systems in which individuals developing heart failure were prospectively included (18–20). The present registration by the Belgian sentinel network also uses a prospective registration of heart failure which has the advantage that incident cases may be fully characterized at the time of the diagnosis.

Clinical Diagnosis

The diagnosis of heart failure was strictly clinical in this study. The diagnosis is very difficult in primary health care and many definitions of heart failure have been used over the last 50 years (21). Most of the definitions emphasized the combination of symptoms of heart failure and clinical signs of fluid retention (22). According to the guidelines of the European Society of Cardiology (ESC) heart failure is defined as a clinical syndrome in which patients have symptoms as well as clinical signs typical for heart failure and objective evidence of a structural or functional abnormality of the heart at rest (2). According to the ESC the symptoms typical of heart failure include breathlessness at rest or on exercise, fatigue, tiredness and ankle swelling. The clinical signs typical of heart failure are defined by the ESC as tachycardia, tachypnoea, pulmonary rales, pleural effusion, raised jugular venous pressure, peripheral oedema and hepatomegaly. Objective evidence of a structural or functional abnormality of the heart at rest can be found in cardiomegaly, third heart sound, cardiac murmurs, abnormality on the echocardiogram and raised natriuretic peptide concentration. These diagnostic procedures were not always performed in our study. The participating family physicians were free to perform these procedures, if they thought they might be contributive to the diagnosis. However, it is well known that some clinical examinations with a good specificity and sensitivity are underused in family practice (23).

The strength of our study is that the diagnosis of heart failure was confirmed after one month, giving the family physicians the opportunity for further investigations and excluding most of the inaccurate diagnoses. But, most of the diagnostic procedures are not very specific for heart failure. An abnormal electrocardiography has little predictive value for the diagnosis of heart failure. Chest X-ray permits the differential diagnosis with other causes of dyspnoea but has only little power to exclude heart failure. Echocardiography provides insight into the function of the several parts of the heart but can not always confirm or exclude heart failure (24). A normal concentration of natriuretic peptides makes the diagnosis of heart failure unlikely but increased levels have only little predictive value for heart failure. Baseline serum copper is significantly higher in patients with chronic heart failure but the value of copper concentrations in the diagnosis of heart failure is poor (25).

Hospital Admission and Mortality

It can be assumed that all hospital admission were related to heart failure because only the hospital admission for heart failure were recorded. But for mortality all cases were taken into account, those related to heart failure as well as those not related to heart failure. Therefore, the present mortality figures need to be interpreted as a total mortality and not only as a heart failure-related mortality.

The participating physicians were asked to provide optimal treatment to their patients. We can assume that the hospitalisation figures and mortality rates are not confounded by insufficient treatment of heart failure.

It is generally accepted that more than 50% of patients diagnosed with heart failure will die within five years of diagnosis (1). This mortality rate is comparable with those for the worst types of cancers (26). Patients requiring hospital admission for heart failure have the worst prognosis. Mortality rates are 10–20% in the first month after hospital admission and 30–45% after one year (27–29). These figures are in line with the results of our study where half of the patients are hospitalised within the first month after diagnosis and where 19% died within the first six months. After 12 months the mortality was 26% in our study.

Hospital admission was evaluated after one month and mortality after six months. From the registration it was possible to evaluate hospital admission and mortality after 12 months.

Hospital admission within the first month after diagnosis was best predicted by the NYHA classification. NYHA IV was found in 39% of the hospitalized patients compared to 14% in those not hospitalized. The patients with NYHA IV were hospitalised in 73% of the cases.

Patients dying from heart failure within six months after the diagnosis had a higher NYHA classification at the time of the diagnosis than those not dying from heart failure. NYHA IV was found in 48% of the dying compared to 21% among the survivors. The mortality within the first six months among patients with NYHA IV was 36%.

Surprisingly, hospital admission rates and mortality rates were higher among patients with NYHA IV compared to those with NYHA III. However, these figures are probably biased by the low number of patients with NYHA IV.

In our study heart failure was classified according to the NYHA classification. This is a functional classification based on the symptoms of the patients. Other classifications such as the ACC/AHA (30), Forrester (31) and Killip (32) classification exist. They are based on the symptoms and the structure of the heart. Because the functional status of the heart was not investigated for all patients, it was not appropriate to use another classification.

In our study there is no obvious relationship between the occurrence of symptoms and clinical signs at the time of the diagnosis and the risk for hospital admission or mortality. Therefore symptoms and the clinical examination alone should not influence the optimal titration of the treatment. Even for patients with few or mild symptoms the optimal treatment should be initiated from the moment of the diagnosis.

CONCLUSIONS

Many symptoms and clinical signs may appear among patients with newly diagnosed heart failure. However, peripheral oedema,

nocturnal dyspnoea and pleural effusion are highly associated with hospital admission within the first month after diagnosis. But, none of the symptoms or clinical signs are associated with mortality within the first six month after diagnosis. All patients with heart failure should benefit from the most optimal treatment from the moment of the diagnosis.

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