Incidence and aetiology of heart failure

A population-based study


Cardiac Medicine, Imperial College School of Medicine at the National Heart & Lung Institute, *Department of Medical Statistics and Evaluation, Imperial College School of Medicine at the Hammersmith Hospital, London; †Hillingdon Hospital, Uxbridge, Middlesex, U.K.

Aims To determine the incidence and aetiology of heart failure in the general population.

Methods and Results New cases of heart failure were identified from a population of 151,000 served by 82 general practitioners in Hillingdon, West London through surveillance of acute hospital admissions and through a rapid access clinic to which general practitioners referred all new cases of suspected heart failure. On the basis of clinical assessment, electrocardiography, chest radiography and transthoracic echocardiography, a panel of three cardiologists decided that 220 patients met the case definition of new heart failure over a 20 month period (crude incidence rate of 1.3 cases per 1000 population per year for those aged 25 years or over). The incidence rate increased from 0.02 cases per 1000 population per year in those aged 25–34 years to 11.6 in those aged 85 years and over. The incidence was higher in males than females (age-adjusted incidence ratio 1.75 [95% confidence interval 1.34–2.29, P<0.0001]).

The median age at presentation was 76 years. The primary aetiologies were coronary heart disease (36%), unknown (34%), hypertension (14%), valve disease (7%), atrial fibrillation alone (5%), and other (5%).

Conclusions Within the general population, new cases of heart failure largely occur in the elderly, and the incidence is higher in men than women. The single most common aetiology is coronary heart disease, but in a third of cases the aetiology cannot be determined on the basis of non-invasive investigation alone. To be relevant to clinical practice, future clinical trials in heart failure should not exclude the elderly.

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Key Words: Epidemiology, heart failure, incidence, aetiology

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Introduction

The contemporary epidemiology of heart failure within Europe is not well described despite the apparent ever increasing number of hospital admissions due to heart failure[1], and the economic burden the management of this condition places on the health care system in developed countries[2]. Routinely collected data from primary care or hospitals cannot be used to describe the epidemiology of heart failure because of the poor validity of the clinical diagnosis of heart failure in primary care[3,4], and the problem of miscoding in routine hospital discharge records[5] and death certificates[6–8].

We report the results of a survey of the incidence and aetiology of heart failure from a population of 151,000 in Hillingdon District, West London, U.K.

Methods

Study population and identification of cases

The study population was that registered with 31 general practices (82 general practitioners) within the southern half of Hillingdon District, west London. The general practitioners agreed to refer all suspected cases of new heart failure to a rapid access clinic held at Hillingdon Hospital. Patients who were acutely ill were sent directly to the Accident & Emergency Department of Hillingdon Hospital in the usual way and were identified by daily surveillance of all hospital admissions by a research nurse. In addition, the general practitioners were asked
to inform the study team of any patient in whom the
diagnosis of heart failure had been made for the first
time elsewhere e.g. whilst the patient was on holiday.

The age and sex structure of this population was
obtained from Hillingdon Health Authority, which
holds the age and sex register for each practice. The total
study population was 150,582 as of February 1996 (the
mid-point of the study which ran from 6 April 1995 to
5 December 1996). The Health Authority figures for the
district agree to within 5% of that enumerated at the
last national census (1991) for the corresponding
geographical area.

Ethical approval for this study was granted by
the local health authority ethics committee.

A cardiologist (M.R.C. or V.S.) took a standard-
ized medical history and examined all the patients except
those who died rapidly after hospital admission. In
such cases, the clinical findings of the admitting doctors
were noted. Whenever possible an electrocardiogram,
chest radiograph, transthoracic echocardiogram, serum
biochemistry and haematology and thyroid function
tests were performed. The echocardiogram was done
as part of the standard protocol and according to accepted
guidelines[9–11] by either one cardiologist (M.R.C.) or
one of two experienced cardiac technicians, and the
two-dimensional, M-mode, Doppler and colour-flow
images were recorded on video-tape for subsequent
analysis. Of the 220 new cases of heart failure identified,
217 (99%) had an electrocardiogram, 216 (98%) a chest
radiograph, and 201 (91%) an echocardiogram.

**Case definition**

There is no gold standard for the diagnosis of heart
failure, and there has been much variation in the diag-
nostic criteria used in previous studies[2]. We adopted the
criteria recommended by the Working Group on Heart
Failure of the European Society of Cardiology[12]. To
meet the case definition of heart failure, patients had
to have appropriate symptoms (shortness of breath,
fatigue, fluid retention or any combination of these
symptoms) with clinical signs of fluid retention (pul-
monary or peripheral) in the presence of an underly-
ing abnormality of cardiac structure and function. If
an element of doubt remained, a beneficial response
to therapy for heart failure (e.g. a brisk diuresis
accompanied by substantial improvement in breathless-
ness) was taken to confirm the diagnosis. All data
collected were presented to a panel of three cardiologists
(A.C., G.C.S., D.A.W.) who determined on the basis of
a majority decision whether the case definition had been
met, and the aetiology. An underlying abnormality of
cardiac structure or function was necessary to confirm a
case as heart failure, but echocardiographic abnor-
malities were not sufficient in themselves to diagnose heart
failure; patients had to satisfy the full case definition.

Patients’ hospital and general practitioner notes
were checked to ensure that only those without a
previous history of heart failure were included in the
study. If a patient had been assessed at another hospital
in the past, the physician in charge of the patient’s
care at that hospital was contacted for details of the
consultation and investigations performed.

**Allocation of aetiology**

Coronary artery disease was considered the primary
aetiology if the patient had a documented history of
myocardial infarction (acute or in the past); unstable
angina pectoris; a history of stable angina supported by
evidence of reversible myocardial ischaemia; or cor-
onary artery disease confirmed at coronary angiogra-
phy. Such cases were subdivided into those with acute
ischaemic syndromes (acute myocardial infarction or
unstable angina pectoris), and those without.

Hypertension was considered the aetiology if there was
a history of hypertension from the general practice records
or sustained hypertension (blood pressure greater than
160/95 mmHg) during hospital admission and there was
no documented history of myocardial infarction or
angina, and no evidence of other cardiac pathology. The
presence and severity of underlying valvular heart dis-
ease was assessed from the history, clinical examination
and echocardiographic findings. The presence of cardiac
arrhythmias were noted and the temporal relationship of
these to the development of heart failure ascertained.

**Reproducibility of panel decisions**

The repeatability of the panel’s decisions were assessed
by re-presenting blindly a random sample of 25 cases on
a second occasion at least 4 weeks after the first presen-
tation. The panel decision regarding whether the case
definition had been met had good reproducibility
(Cohen’s $\kappa=0.67$) as did the allocation of aetiology
(Cohen’s $\kappa=0.63$).

**Audit of case ascertainment**

An audit of case ascertainment was performed by iden-
tifying within a random sample of 10 practices all new
prescriptions for diuretic drugs during the study period.
Two of the 10 practices were not fully computerized and
therefore could not take part and two practices declined.

In the remaining six practices (involving 19 general
practitioners and approximately a quarter of the study
population) the case notes of these patients were scru-
tinized by an audit nurse. With the help of the general
practitioner she identified which of these patients had a
suspected diagnosis of new heart failure. Sixty-eight such
patients were identified, of which 61 (90%) had been
assessed by the study team either in the rapid access
clinic or as a result of acute admission to Hillingdon
hospital.

**Data analysis**

All data were initially entered onto a case record form
and subsequently into a computerized database by
double data entry. The age-adjusted incidence ratio of heart failure by sex was calculated by grouped logistic regression. Proportions were compared using a chi-square test. Two-tailed tests of significance are reported.

### Results

#### The incidence of clinical heart failure

In the 20 month study period, 220 new cases of heart failure were identified within the study population (118 male: 102 female; age range 29–95 years). One hundred and eighty cases were identified from surveillance of admissions to the local hospital and the remainder (40) from 157 referrals to the rapid-access clinic. Amongst those referred to the clinic the proportion with a diagnosis of heart failure confirmed on further assessment was lower in women than men (15/82 [18%] vs 25/75 [33%] \( P=0.03 \)). One hundred and one cases presented with alveolar pulmonary oedema, 55 with a raised jugular venous pressure and dependent oedema, and 64 with raised jugular venous pressure or dependent oedema or raised pulmonary venous pressure on chest radiograph (without alveolar shadowing) that responded to diuretic therapy. The crude incidence rate in the population aged over 25 years was 1.3 cases per 1000 population per year. The incidence rate increased steadily from 0.02 per 1000 population per year in those aged 25 to 34 years to 11.6 in those aged 85 years or over (Table 1) and was higher in males than females (age-standardized incidence ratio 1.75 [95% confidence interval 1.34–2.29] \( P<0.0001 \)) (Fig. 1). There was no statistical evidence that the incidence ratio changed across the age groups (\( P=0.70 \)). The median age at presentation was 76 years (73 years in men and 78 years in women) and 47% of male cases and 64% of female cases were aged 75 years or older.

#### Aetiology of heart failure

The aetiology of heart failure in the 220 cases is shown in Table 2. The single most common aetiology was coronary heart disease (79 cases [36%]), but this frequently co-existed with a history of hypertension (40/79 cases, 51%). Just under half of all cases had a history of hypertension (97/220, 44%) but hypertension was considered the primary aetiology in only 30 (31%) of these cases. Valvular heart disease was an uncommon cause of heart failure (16 cases [7%]).

#### Unknown aetiology

In 75 (34%) of cases no aetiology could be allocated on the basis of the information available at the time of panel review. Over half of such cases with a technically adequate echocardiogram (37/63 [59%]) presented with a dilated globally hypokinetic left ventricle with no obvious aetiology.

#### Atrial fibrillation

Atrial fibrillation was present in 68 (31%) of cases in total (and atrial flutter in a further three patients). In the majority of such cases the atrial fibrillation was either long-standing (present on electrocardiograms recorded months to years before the onset of heart failure) or associated with other cardiac pathology e.g. myocardial infarction, valvular heart disease, or a dilated globally hypokinetic left ventricle of unknown cause. Atrial fibrillation was classified as the primary aetiological factor only in those 10 patients who did not appear to have significant left ventricular systolic dysfunction on echocardiography at the time of presentation (although this was usually assessed when the patient was in fast atrial fibrillation), with no other demonstrable cardiac pathology, and where there was good evidence to suggest that the onset of this arrhythmia coincided with the onset of symptoms. The possibility of underlying myocardial disease (of unknown aetiology) presenting with atrial fibrillation cannot be excluded.

#### Other aetiologies

The remaining cases were allocated to a variety of other causes including alcohol (four cases with a long history of heavy alcohol consumption) and heart failure due to pulmonary causes (five cases) such as idiopathic pulmonary fibrosis, lung cancer, interstitial lung disease, granulomatous disease, and those in whom heart failure developed in association with interstitial lung disease but the underlying cause was not identified. A large number (55) of cases had a history of hypertension, 19/55 (35%) of whom had a primary diagnosis of hypertension.

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![Table 1: Incidence of heart failure by age and sex (for those aged 25 years and over)](Eur_Heart_J_20_6tables_423.png)

*Incidence rate expressed as number of cases per 1000 population per year.
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Incidence (cases per 1000 population per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–34</td>
<td>0.00 0.04</td>
</tr>
<tr>
<td>35–44</td>
<td>0.16 0.18</td>
</tr>
<tr>
<td>45–54</td>
<td>0.26 0.07</td>
</tr>
<tr>
<td>55–64</td>
<td>1.70 0.67</td>
</tr>
<tr>
<td>65–74</td>
<td>3.88 2.31</td>
</tr>
<tr>
<td>75–84</td>
<td>9.82 5.92</td>
</tr>
<tr>
<td>85+</td>
<td>16.76 9.62</td>
</tr>
</tbody>
</table>

Figure 1. Incidence of heart failure by sex and age group.
incidence and aetiology of heart failure

Table 2 Number (and percentage) of cases by primary aetiology

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Number of cases</th>
<th>Percentage of total cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease (acute myocardial infarction)</td>
<td>42</td>
<td>19</td>
</tr>
<tr>
<td>Coronary artery disease (not acute myocardial infarction)</td>
<td>37</td>
<td>17</td>
</tr>
<tr>
<td>Not known</td>
<td>75</td>
<td>34</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30</td>
<td>14</td>
</tr>
<tr>
<td>Valve disease</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Atrial fibrillation or flutter</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Alcohol</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Restrictive cardiomyopathy</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Total</td>
<td>220</td>
<td>100</td>
</tr>
</tbody>
</table>

of chronic excessive alcohol consumption and a dilated globally hypokinetic left ventricle on echocardiography, cor pulmonale (four cases with a long history of chronic lung disease and right heart abnormalities on echocardiography), hypertrophic cardiomyopathy (one case), and restrictive cardiomyopathy (one case).

**Variation in aetiology by sex and age**

There was little evidence that the proportion of cases attributed to coronary artery disease, hypertension, unknown, or other aetiology, was different between the sexes (P=0.11) or as age increased (P=0.65 for those above or below median age at presentation of 76 years).

**Echocardiographic findings by aetiology**

Echocardiographic abnormalities were not sufficient in themselves to diagnose heart failure but were very useful in documenting the underlying cardiac abnormalities. Thirty three of the 35 patients (94%) with a technically adequate echocardiogram who developed heart failure in the context of acute myocardial infarction had at least mild impairment of left ventricular systolic function on qualitative assessment. Regional variation in left ventricular systolic function was common in this group of patients (14/36 [39%]) and mitral regurgitation was almost universal (34/36 [94%]). A left ventricular aneurysm was present in two patients.

Echocardiography was performed in 15 of the 16 patients with heart failure due to valvular heart disease. Seven of these had predominantly aortic stenosis, two had predominantly mitral stenosis, two primary mitral regurgitation, one mixed aortic valve disease, and three both aortic and mitral valve disease.

All 30 patients with heart failure due to hypertension had a technically satisfactory echocardiogram. Only one patient had regional variation in left ventricular systolic function. Left ventricular hypertrophy was common: interventricular septal thickness was ≥1.4 cm in 14/21 (67%) patients in whom this was measurable on M-mode echocardiography and posterior left ventricular wall thickness was ≥1.4 cm in 11/22 (50%). Nineteen of the 30 patients (63%) had at least mild impairment of left ventricular systolic function. In the remaining 11 with normal left ventricular systolic function, prolongation of the isovolumic relaxation time or reversal of the E:A ratio on Doppler examination of left ventricular inflow was common (seven patients).

In those patients for whom an aetiology could not be allocated, the majority with an adequate echocardiogram (55/63 [87%]) had at least mild impairment of left ventricular systolic function. Of the eight with normal systolic function, six demonstrated left ventricular hypertrophy (interventricular septum and posterior wall (≥1.4 cm). In the whole group of 63 patients, regional variation in wall motion was infrequent (8 [13%]). Two patients had complete heart block and two had a small pericardial effusion but no clinical evidence of tamponade. Doppler demonstrable regurgitation across the atriocentric valves was very common (54 [86%] across mitral and 44 [73%] across tricuspid valve).

**Discussion**

Clinical surveys of heart failure in the general population are uncommon. Much of our current knowledge of heart failure is based on highly selected hospital series, or patients selected for clinical trials. Such patients do not reflect the spectrum of heart failure as it presents in the population.

Heart failure is difficult to diagnose in primary care. Our findings that fewer than 30% of patients referred to the rapid access clinic had heart failure accords with previous studies in Finland[4] and Scotland[9], which suggested that only 25–50% of patients with a primary care diagnosis of heart failure have evidence of this disorder on further cardiological assessment. The greater problem with the correct diagnosis in women has been reported previously[4,14].

We found the incidence of heart failure rises very steeply with age, reaching over 1% per annum in those aged 85 years or over, but very uncommon in those aged
less than 55 years (Fig. 1). The incidence is higher in males than females at all ages (best estimate 75% higher). Within the general population, therefore, the median age at presentation is 76 years, considerably higher than the median age of patients included in most clinical trials of pharmacological therapy in heart failure [15–18]. Clinical trials in heart failure should recruit patients from population-based registries: this will ensure that the findings of such trials are relevant to clinical practice and the majority of patients developing heart failure. In particular, the elderly should not be excluded from such trials. With the ageing of the population in Europe over the next decades, such patients will become ever more numerous.

A direct comparison with the two other population-based studies of the incidence of heart failure in Europe is difficult because of differences in case definition [2]. In a population of 11,000 aged 45–74 years in eastern Finland [19], 60 cases of heart failure were identified during a 2-year study period. Patients were identified using similar methodology, but the case definition was based on the scoring system used in the Framingham Heart Study [20] or a modified form of the Boston classification [21]. These case definitions are based on weighted scoring systems dependent on symptoms, signs and chest radiograph findings. Although sensitive for the diagnosis of heart failure, they are relatively non-specific compared with the clinical diagnosis of a cardiologist [22].

Although the age range of the Finnish study was limited, and the number of cases (especially for females) was small the incidence of heart failure increased with advancing age, and was higher in men than women, as found in our study, with an age-adjusted incidence ratio of 2.51 (95% confidence interval 1.4–4.0). The incidence of heart failure in the Finnish study is higher for both men and women than in our study. This may be related to the difference in case definition. A true difference in the incidence of heart failure in the two populations cannot be excluded: deaths from coronary artery disease have been higher in Finnish men than in English men over the last decade [23] and thus it is possible the incidence of heart failure due to coronary artery disease may also be higher in Finland than in England.

The Study of Men Born in 1913 in Gothenburg, Sweden, was a prospective cohort study of men from age 50 to 67 years [24] with a case definition unique to that study, and reported an average annual incidence of 5 per 1000 population for ‘manifest’ heart failure. The case definition was designed to be less strict than that of Framingham to include milder cases of heart failure, but at the risk of a higher rate of false positive diagnoses [25].

The incidence rate in the Gothenburg Study is somewhat higher than that found in this study for men of the same age (1.5 per 1000 population per year), but this presumably reflects the differences in case definition.

The other major population study of the incidence of heart failure is the Framingham Study in the U.S.A., which identified 650 cases of heart failure over 40 years since the late 1940s [20,26]. This compares with 220 cases over 20 months in this study. The incidence of heart failure in the Framingham cohort was found to increase steeply with age from 3 per 1000 per year in men aged 50 to 59 years to 27 per 1000 per year in men aged 80 to 89, with lower rates in women (age-adjusted odds ratio for men compared to women of 1.7 [95% confidence interval 1.4–2.0]) [26].

Heart failure occurs as the end-result of cardiac damage caused by a number of disease processes e.g. coronary artery disease, hypertension, valve disease, alcohol misuse or viral infection. Classification of aetiology critically depends on the criteria used. This population study illustrates the difficulties in establishing a precise aetiology for heart failure from non-invasive investigations: the aetiology was not determined in one third of cases. A predominantly elderly population is unlikely to be systematically investigated in detail for possible underlying coronary artery disease by coronary arteriography: the medical background, including hypertension, may be poorly documented; and simple non-invasive investigations, such as echocardiography, in many instances do not provide a precise aetiological diagnosis.

The conventional criteria for diagnosing coronary artery disease in an individual patient include documented myocardial infarct, a history of angina supported by evidence of reversible myocardial ischaemia, or evidence of coronary artery disease on arteriography. If the presence of a pathological Q wave on the 12 lead resting ECG is added to the criteria for diagnosing coronary artery disease in this study, 10 cases in the ‘unknown aetiology’ group would be reclassified as due to coronary artery disease. However, in the absence of coronary arteriography in all cases the above criteria will almost certainly underestimate the prevalence of coronary artery disease in these patients. The extent of this underestimation is currently being examined in another population based study by our group (The Bromley Heart Failure Study). The prevalence and clinical relevance of coronary artery disease in incident cases of heart failure in this further study is determined by performing coronary arteriography and myocardial perfusion imaging. In this study five cases whose aetiology could not initially be determined were subsequently shown to have extensive coronary artery disease at angiography (two cases) or coroner’s post-mortem (three cases).

The retrospective diagnosis of hypertension as the primary aetiological factor is even more difficult. Hypertension frequently co-exists in patients with cardiac damage due to coronary artery disease, and it is impossible to determine the precise aetiological role of hypertension (independent of coronary artery disease) in such individuals. In this study, evidence of coronary heart disease took precedence over hypertension in the aetiological classification. Hypertension may ‘burn out’ as heart failure develops, leaving the patient normotensive at the time of presentation, and equally heart failure itself may produce a hypertensive response in a previously normotensive patient. Differential ascertainment
of hypertension in those with other medical problems is also likely as such patients are more likely to visit their general practitioner and have blood pressure recorded. All of these factors pose considerable difficulties in allocating hypertension as the primary aetiology of heart failure and this matter cannot be resolved retrospectively.

The role of arrhythmias, and in particular, atrial fibrillation in heart failure is also difficult to define because, without full previous cardiac investigation, it is impossible to conclude that a patient who develops heart failure in the context of new atrial fibrillation has no cardiac pathology other than the arrhythmia. The assessment of left ventricular systolic function in the presence of atrial fibrillation, especially if the ventricular rate is fast, is unreliable\textsuperscript{27}. Ventricular systolic function may appear markedly impaired only to return apparently to normal on reverting to sinus rhythm in some patients\textsuperscript{28}, but this does not imply the absence of underlying myocardial disease which became apparent with the stress of a rapid and irregular ventricular rate. In this study, we decided to allocate atrial fibrillation as the aetiology only in those cases where the heart appeared structurally normal (no significant valve abnormality and left ventricle not more than mildly hypokinetic whilst in fast atrial fibrillation) and the onset of atrial fibrillation was most probably associated with the onset of symptoms. The majority of patients whose rhythm was atrial fibrillation (85\%) at the time of presentation were allocated to other or unknown aetiologies. The role of atrial fibrillation in the development of heart failure requires further investigation but it is the cardiac rhythm in a substantial minority of patients (31\%) presenting with heart failure for the first time. In an elderly heart lacking myocytes and with increased interstitial fibrosis due to age-related changes\textsuperscript{29}, the onset of atrial fibrillation may be sufficient to cause heart failure even in the absence of concomitant coronary artery disease or hypertension.

The aetiology of heart failure would be expected to reflect the cardiac pathologies which develop in a particular community. Coronary artery disease (with or without hypertension) should be the dominant aetiology of heart failure in the U.K. In this study the single most common aetiology was ischaemic heart disease (36\%), and a past history of hypertension was common (44\%). This is very similar to the findings in both Finland and Sweden\textsuperscript{19,24}, and is not dissimilar to that reported from Framingham\textsuperscript{30}.

The incidence rates reported in this study should be considered an underestimate of the true population incidence. The case ascertainment was high at 90% within the audited practices, but a small number of possible new cases of heart failure may have been missed. The study design was also dependent on patients presenting to a doctor either in primary or secondary care when they developed symptoms of heart failure and will have missed those that did not. Cases may also have been misdiagnosed in general practice. However, heart failure is a progressive condition and without appropriate treatment is associated with deteriorating and troublesome symptoms over a short period, and thus the number of cases not becoming clinically apparent should be small in a study with case identification over 20 months.

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