Hospitalization of patients with heart failure

A population-based study

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Aims To describe the clinical course of heart failure in a population-based sample of incident cases, and to identify factors predicting hospitalization and mortality.

Methods and Results Three hundred and thirty-two incident cases were identified over 15 months; 208 inpatients and 124 outpatients. Thirty-eight inpatients died during the first hospital admission (case fatality 18%) leaving 294 at risk of subsequent hospitalization. Over an average follow-up of 19 months, 173 cases were hospitalized on 311 occasions. Two hundred and twenty-four (72%) of these admissions were unplanned, with 51% due to worsening heart failure. One hundred and ten cases died over the same period. Cases diagnosed as an inpatient had 26 more admissions for worsening heart failure per 100 cases during follow-up (95% CI 9 to 44) compared to cases diagnosed as an outpatient, and also a higher mortality (hazard ratio 3·1 (95% CI 1·9 to 5·1)). Age was the only factor associated with an increased risk of hospitalization for worsening heart failure, but age, functional class and serum creatinine were predictive of mortality.

Conclusions New cases of heart failure are at high risk of subsequent hospitalization, especially during the first months after diagnosis. Whilst predicting which patients will be hospitalized is difficult, interventions designed to reduce hospitalizations for worsening heart failure should be targeted at elderly inpatients with a new diagnosis.


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Introduction

Heart failure is one of the most common reasons for hospital admission in the developed world. In Europe, approximately 5% of all acute medical admissions relate to heart failure[1] and in the U.S.A. heart failure is the most common diagnostic group among hospitalized patients aged over 65[2]. The number of hospitalizations related to heart failure has been rising steadily in every age group since the 1980s[3–6], although recent evidence suggest the rate of rise may be slowing[7]. The rise in hospitalization may be related to an increased

prevalence of heart failure, although changes in medical practice also probably play a part[8]. Patients with heart failure are at high risk of readmission to hospital[9,10]. A survey in the Netherlands reported that 16% of patients were readmitted within 6 months of their first admission[5], and data from the U.S.A. suggest that almost a third of patients are readmitted within 6 months[11].

However, routinely collected data from hospitals cannot be used to describe the epidemiology of heart failure, either in terms of its clinical course (hospitalizations) or prognosis because of the poor validity of the clinical diagnosis of heart failure and the problem of miscoding in routine hospital discharge records and death certificates[8].

Since hospitalization contributes over 60% of the total cost of heart failure to the health service[12], it is not surprising that considerable effort has been expended in developing programmes that reduce the risk of hospitalization in patients with heart failure[13–17]. However, the
Factors that identify a patient as being at high risk of readmission to hospital for heart failure are not clearly identified\(^{18}\). Previously published reports are mainly from selected series of patients (often from heart transplantation assessment programmes)\(^{13,15,19,20}\) which include individuals who are, on average, younger, more often male, and with considerably less comorbidity than the typical patient with heart failure\(^{8}\).

We report the results of the prospective follow-up for hospitalization and death of a cohort of incident cases of heart failure identified from a population of 292,000 in Bromley District, South London, and explore the factors associated with an increased risk of hospitalization for worsening heart failure and mortality in this general population of heart failure cases.

**Methods**

**Study population and identification of cases**

The method of patient identification and characterization has been described previously\(^{21}\). Briefly, the study population of 292,000 was that registered with 151 primary care physicians working within Bromley Health Authority, South London, U.K. during February 1996 to April 1997. These physicians referred all suspected cases of new heart failure to a daily rapid-access heart failure clinic\(^{22}\). In addition, patients who were acutely ill were admitted to the local hospital in the normal manner and were identified by daily surveillance of all hospital admissions by a research nurse. From an audit of medical notes in a random sample of 10 of the 59 primary care practices involved in the study, it was estimated that 82% of new heart failure cases (95% confidence interval 78–86%) had been successfully identified in this study.

A cardiologist (K.F.) took a standardized medical history and examined all patients except those who died soon after hospital admission. In such cases, the clinical findings of the admitting doctors were noted. Of the 332 new cases of heart failure identified, 331 (100%) had an electrocardiogram, 326 (98%) a chest radiograph, and 310 (93%) an echocardiogram. The echocardiogram was performed to a standard protocol and according to accepted guidelines\(^{23,24}\) by either one cardiologist (K.F.) or one experienced cardiac technician.

**Case definition**

All data collected were presented to a panel of three cardiologists (A.J.S.C., G.C.S., D.A.W.) who determined on the basis of a majority decision whether the case definition had been met. The diagnostic criteria were based on those recommended by the Working Group on Heart Failure of the European Society of Cardiology\(^{25}\). The reproducibility of the panel decision regarding whether the case definition had been met was estimated by re-presentation of a random sample of 25 cases and was excellent (Cohen’s \(\kappa = 1.0, 95\%\) confidence interval 0.68–1.00). Patients’ hospital and primary care notes were checked to ensure that only those without a previous history of heart failure were included in the study.

**Follow-up**

During the follow-up period patients were managed by cardiologists through the rapid access heart failure clinic or a specialized outpatient heart failure clinic, or the general physicians and/or primary care physicians. Hospitalizations were identified by prospective follow-up of each patient by research nurses (S.B., P.D.). Each admission was classified according to pre-set criteria as either a planned, or unplanned, admission. If the admission was unplanned it was subclassified into one of the following categories: worsening of the severity of heart failure; new medical problem related to the aetiology of heart failure (e.g. further myocardial infarct in a patient with heart failure due to previous myocardial infarction); new medical problem directly related to heart failure (e.g. cellulitis of oedematous lower limbs); new medical problem not related to heart failure or its aetiology; social reasons; unplanned admission for change in therapy, improved compliance or further investigation; iatrogenic; and other (including surgical admissions). Date and certified cause of death were identified by flagging of each patient’s record at the NHS Central Registry using their unique National Health Service number. Death was classified as cardiovascular if it was coded as 390 to 459 on the 9th International Revision of the International Classification of Death\(^{26}\). Follow-up was to the end of February 1999, giving a mean follow-up of 19 months (90% range 12–26 months). Thirteen patients (4%) were lost to follow-up for hospitalization but follow-up for death was complete for all 332 cases.

**Data analysis**

The cumulative survival probabilities were estimated using the method of Kaplan–Meier for all-cause mortality, and unplanned hospitalization for worsening heart failure. The relationship between each of seven baseline measurements (age, sex, New York Heart Association (NYHA) functional class, aetiology of heart failure (heart failure in context of acute myocardial infarction compared with other causes of heart failure), systolic blood pressure, qualitative assessment of left ventricular systolic function on transthoracic echocardiography, and serum creatinine) and subsequent mortality was examined using univariate proportional hazards regression.

The relationship between the combination of these seven measures and mortality was investigated using a further multivariate model. The relationships between
the seven measures and subsequent hospitalization were evaluated using both number of admissions and days spent in hospital over the follow-up period as separate measures of hospitalization. In each case seven univariate models and a single multivariate model, including all seven measures, were estimated. The method of least squares was used to calculate estimates, accompanied by 95% percentile boot strap confidence intervals[27], because of the skewness of the distributions. Two tailed tests of significance are reported.

Data were not collected on the socioeconomic status of the patients. The majority (85%) were over the age of retirement and the most recent (1991) Jarman index of the postcode of the patient’s residence was taken as a proxy of adulthood socioeconomic status. Within the catchment population the index varied from −25 to +29 where 0 is the average for England and Wales, and socioeconomic status increases as the index number increases.

**Ethical approval**

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

**Results**

Table 1 gives the basic features of the 332 new cases of heart failure identified. Two hundred and eight cases (63%) were identified from surveillance of admissions to Bromley Hospital and the remaining 124 from 383 referrals to the rapid-access clinic. The aetiology could not be determined in 131 cases (39%) but in the remainder the single most common aetiology was coronary heart disease (113 of 201 cases, 56%). Fifty-four cases occurred in the context of acute myocardial infarction.
The majority of cases were symptomatic at rest (NYHA Class IV) or on mild exertion (NYHA Class III) at the time of first presentation.

**Hospitalization during the follow-up period**

Of the 332 cases, 294 were at risk of subsequent hospitalization (i.e. 170 identified initially as an inpatient and who did not die during that admission, and 124 who were first diagnosed as an outpatient). During the follow-up period, 173 (59%) of these patients were hospitalized on a total of 311 occasions, accounting for a total of 3395 days in hospital.

Two hundred and twenty-four (72%) of the admissions were unplanned, with the causes for these admissions listed in Table 2. Fifty-one percent of these unplanned hospital admissions were due to worsening heart failure. Seventy-seven patients had such an admission during the period of follow-up, with 53 patients being hospitalized for this reason once, 16 twice, 4 three times, 3 four times and 1 five times. The median length of stay for an admission due to worsening heart failure was 8 days (mean 12 days) with a range of 2–68 days (Fig. 1). For the 77 patients admitted to hospital with worsening heart failure during the follow-up period, the total number of days in hospital for that reason ranged from 2–133 days with a median of 12 days.

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**Table 2  Reasons for unplanned hospital admission**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number</th>
<th>Percentage of total unplanned admissions (n=224)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening of heart failure</td>
<td>114</td>
<td>51%</td>
</tr>
<tr>
<td>New medical problem related to heart failure</td>
<td>7</td>
<td>3%</td>
</tr>
<tr>
<td>Medical problem related to aetiology of heart failure</td>
<td>22</td>
<td>10%</td>
</tr>
<tr>
<td>New medical problem unrelated to heart failure</td>
<td>75</td>
<td>33%</td>
</tr>
<tr>
<td>Social reason</td>
<td>10</td>
<td>4%</td>
</tr>
<tr>
<td>To improve compliance with drug therapy, change therapy or for further investigation</td>
<td>5</td>
<td>2%</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>4</td>
<td>2%</td>
</tr>
<tr>
<td>Other reasons</td>
<td>35</td>
<td>16%</td>
</tr>
</tbody>
</table>

*Numbers add up to more than 224, and percentages to more than 100%, because more than one reason could apply to any one admission.

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**Figure 1  Days spent in hospital for the 114 unplanned hospital admissions for worsening of heart failure symptoms.**

The majority of cases were symptomatic at rest (NYHA Class IV) or on mild exertion (NYHA Class III) at the time of first presentation.
Figure 2 divides the study sample into three for each month of follow-up. Those patients above the survival curve have died. Those patients below the survival curve are alive and are further divided into those who have (represented by the bars of the histogram) and who have not (above the bars of the histogram) spent time in hospital for worsening of heart failure symptoms during the month in question. There is a high prevalence of such hospitalization in the first month (8.2%), with a marked reduction to 2.4% during the 6th month, 1.8% during the 12th month, and 1.7% in the 18th month. Eight-two percent of patients remained free of hospitalization for worsening heart failure at 6 months, 76% at 12 months and 72% at 18 months.

Clinical features associated with unplanned hospitalization with worsening heart failure

Table 3 lists the associations between various key baseline clinical features and the number of admissions to hospital with worsening heart failure during the follow-up period. Only age was significantly associated with nine more admissions per 100 patients for a 10-year increase in age at presentation, according to the multivariate analysis. In a supplementary analysis those who had the diagnosis of heart failure made for the first time as an inpatient (almost two thirds of all cases) were at a much higher risk of repeat hospitalization than those
first diagnosed as an outpatient with 26 (95% CI 9 to 44) more admissions for worsening heart failure per 100 people. The hazard ratio for death was also substantially higher at 3·1 (95% CI 1·9 to 5·1) for those identified as an inpatient rather than outpatient. Two other clinical features additional to age were independently associated with the risk of death during the follow-up period: severity of symptoms and serum creatinine at first presentation (Table 4).

The factors associated with the total number of days in hospital after unplanned admission for heart failure show a similar pattern to that for the number of admissions: with 1·3 extra days spent in hospital during the follow-up period for that reason for every 10 year increase in age at presentation (95% CI 0·36 to 2·39 after adjustment for the other factors listed in Table 4). However, in this analysis women also spent significantly longer in hospital — on average 3·4 days more than men during the follow-up period even after adjustment for the other factors (95% CI 0·30 to 6·89).

There was no evidence of an association between the socioeconomic status of the patient (as assessed by the Jarman index for the postcode of area of residence) and the number of hospitalizations for worsening heart failure, or indeed risk of death. There was one less admission for worsening heart failure per 100 patients for a 5 unit increase in the Jarman index (95% CI −4 to +3). The hazard ratio for death was 0·95 for a 5 unit

Table 3 Baseline features associated with number of unplanned hospitalizations for worsening heart failure during the follow-up period (difference expressed in terms of number of hospitalizations per 100 patients)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean difference</td>
<td>95% CI*</td>
</tr>
<tr>
<td>Age (10 year increase)</td>
<td>8</td>
<td>1 to 17</td>
</tr>
<tr>
<td>Sex (M vs F)</td>
<td>−7</td>
<td>26 to 13</td>
</tr>
<tr>
<td>NYHA Class</td>
<td>−19</td>
<td>48 to 13</td>
</tr>
<tr>
<td>II vs IV</td>
<td>−17</td>
<td>39 to 3</td>
</tr>
<tr>
<td>III vs IV</td>
<td>28</td>
<td>8 to 69</td>
</tr>
<tr>
<td>HF in context of AMI</td>
<td>0</td>
<td>−3 to 2</td>
</tr>
<tr>
<td>LV systolic impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild/Moderate vs None</td>
<td>10</td>
<td>15 to 34</td>
</tr>
<tr>
<td>Severe vs None</td>
<td>8</td>
<td>28 to 52</td>
</tr>
<tr>
<td>Serum creatinine (10 μmol l⁻¹ increase)</td>
<td>−1</td>
<td>2 to 1</td>
</tr>
</tbody>
</table>

*Boot strap method. Bold indicates P<0·05.
HF=heart failure; AMI=acute myocardial infarction; SBP=systolic blood pressure; LV=left ventricular.

Table 4 Baseline features associated with risk of death during the follow-up period. Association expressed as the hazard ratio

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age (10 year increase)</td>
<td>1·55</td>
<td>1·22–1·95</td>
</tr>
<tr>
<td>Sex (M vs F)</td>
<td>1·03</td>
<td>0·68–1·55</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II vs IV</td>
<td>0·06</td>
<td>0·01–0·44</td>
</tr>
<tr>
<td>III vs IV</td>
<td>0·40</td>
<td>0·25–0·64</td>
</tr>
<tr>
<td>HF in context of AMI</td>
<td>2·43</td>
<td>1·53–3·88</td>
</tr>
<tr>
<td>SBP (10 mmHg increase)</td>
<td>0·94</td>
<td>0·88–1·01</td>
</tr>
<tr>
<td>LV systolic impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild/Moderate vs None</td>
<td>1·18</td>
<td>0·63–2·18</td>
</tr>
<tr>
<td>Severe vs None</td>
<td>1·59</td>
<td>0·77–3·28</td>
</tr>
<tr>
<td>Serum creatinine (10 μmol l⁻¹ increase)</td>
<td>1·08</td>
<td>1·05–1·11</td>
</tr>
</tbody>
</table>

Bold indicates P<0·05.
HF=heart failure; AMI=acute myocardial infarction; SBP=systolic blood pressure; LV=left ventricular.
increase in the index (95% CI 0.88–1.03). There was also no evidence of an association between socioeconomic status and the total number of days a patient was in hospital for worsening heart failure during the follow-up period (13 more days in hospital per 100 patients for every 5 unit increase (95% CI −38 to +70)).

Survival

One hundred and ten patients died before the end of the follow-up period, of which 88 (80%) were due to cardiovascular causes. The in-hospital mortality of the 208 cases identified from hospital admission was 18% (38 deaths). The survival estimates are shown in Table 5 and displayed graphically in the top section of Fig. 2.

Discussion

In this population-based survey of patients presenting with a new diagnosis of heart failure, over half are subsequently hospitalized (either for the first time or re-hospitalized) on one or more occasion over 19 months. Almost three quarters of these admissions are unplanned and worsening heart failure is responsible for half of these. By 6 months, 18% of patients had been admitted due to worsening heart failure, and this is very similar to that reported from a hospital-based survey in the Netherlands[5]. This proportion had risen in our survey to 28% at 18 months.

A third of unplanned admissions were due to medical problems unrelated to either heart failure or the underlying aetiology of the heart failure. This is not surprising considering the age and extent of co-morbidity within this unselected group of patients with heart failure. There are no comparable population-based studies, but our data are in keeping with that from a study of 42 elderly patients with heart failure in Israel who had been enrolled in a home care programme for heart failure for over 12 months[16]. Half of their patients were admitted to hospital during a 12-month period, with the majority of admissions related to cardiovascular disease, although not necessarily worsening heart failure. Series from the U.S.A. have also reported that approximately 40% of readmissions are related to conditions other than heart failure[13,15,19]. Such findings imply that intervention programmes designed to control the heart failure syndrome better and reduce the need for hospitalization for worsening heart failure[13–15] may have somewhat less impact on total hospital usage in unselected patients with heart failure compared with younger patients with few other medical problems. Such a conclusion requires confirmation from a randomized controlled trial.

In our cohort of patients with a new diagnosis of heart failure, the mortality was high with a 1-month survival of 85%, dropping to 68% at 18 months. This is very similar to that reported from our first epidemiological study of heart failure[28], and other population-based studies where the diagnosis was based on clinical examination and cardiac assessment[28–30]. The mortality rate is higher than that reported from the placebo arm of randomized trials of pharmacological therapy presumably because unselected patients with heart failure are older and sicker, on average, than the patients recruited to enter clinical trials. The majority of patients entering clinical trials have survived the early high-risk period and are, to a certain extent, natural survivors[28].

The analysis of prognostic factors in this study has been conducted in three parts to identify those factors predictive of the subsequent rate of admission, time spent in hospital, and mortality rate. This contrasts with the more commonly employed approach of analysing time to first hospital admission or death using proportional hazards regression. Discarding information on further admissions and on duration of admission, and failing to distinguish death from hospitalization, prevents this usual approach from forming a full picture of the disease burden. The analysis we have conducted incorporates more of the important information in the data, but care must be exercised in the interpretation of the results. A relationship between a prognostic factor and hospitalization may be obscured by a stronger relationship with mortality. That is, an individual who dies at the start of the follow-up period is likely to have had an unfavourable risk profile, but will not be subject to repeated hospital admissions during that follow-up because of their early death. For a clinical factor to be identified as predicting hospitalization for worsening heart failure in our analyses the clinical factor must make them ill enough to be repeatedly hospitalized, but not so ill that they die early.

In our series, mortality was independently associated with advancing age, higher serum creatinine and greater severity of symptoms at first presentation. Those developing heart failure in the context of a myocardial infarction had a worse prognosis than patients with other aetiologies. These associations have been described previously in a similar cohort of patients[28]. However, of the variables examined only age was an independent predictor of the number of hospitalizations with worsening heart failure. Similarly, age was the only independent predictor of the total time spent in hospital during readmissions during the follow-up period. The length of stay reported in this study (median of 8 days for a single admission for worsening heart failure) is similar to those reported from other studies in the

Table 5 Cumulative survival probability in the cohort of 332 patients from the time of initial admission or diagnosis

<table>
<thead>
<tr>
<th>Time from identification (months)</th>
<th>Survival</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>85%</td>
<td>81–89%</td>
</tr>
<tr>
<td>6</td>
<td>77%</td>
<td>72–81%</td>
</tr>
<tr>
<td>12</td>
<td>72%</td>
<td>67–77%</td>
</tr>
<tr>
<td>18</td>
<td>68%</td>
<td>63–73%</td>
</tr>
</tbody>
</table>

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U.K.\cite{6,7}, the Netherlands\cite{31}, and New Zealand\cite{32}. Our
data suggest that although the number of admissions for
worsening heart failure is the same in women and men, women
have a longer duration of hospital stay. This has
been reported previously\cite{3} and may be at least partially
related to social factors such as a lower likelihood of a
healthy spouse at home who would be able to provide
care after hospital discharge.

Others have noted that the prediction of readmission
to hospital in patients with heart failure is difficult\cite{38}.
Two risk scoring systems have been developed in the
U.S.A., but these have not been widely adopted as they
do not appear to clearly stratify the risk of readmission
in routine practice and are largely based on administrative
data\cite{33,34}. Both patient and health care system
factors are recognised as important. Age is generally
associated with a higher risk of hospital readmission, but
the effect is often weak and may be acting as a marker of
other factors such as social support, co-morbidity and
compliance with treatment.

A study from North America reported that single
marital status and increasing co-morbidity strongly pred-
icts the risk of hospitalization in patients with heart
failure\cite{35}. A hospital-based study in Scotland also
reported a strong association between socioeconomic
status and the risk of emergency readmission for a
cardiac reason\cite{36}. This association was independent of
disease severity and non-adherence with diuretic pre-
scription. We did not find such an association when
using the Jarman index of area of residence as a proxy of
socioeconomic status.

The proportion of unplanned admissions due to
worsening heart failure that are related to poor com-
plicity with drug and lifestyle prescriptions varies con-
siderably according to the patient population\cite{20,37}.
It was not feasible within the constraints of this study to
collect meaningful data on patient compliance.

High quality care and good discharge planning are
seen as key to reducing hospital readmission rates in
patients with heart failure. Most intervention pro-
grames are nurse-led and involve patient and carer
education, good discharge planning and contact with the
patient after discharge from hospital. Virtually all pro-
grames reduce both the number of hospital readmis-
sions (especially for worsening heart failure) and the
number of patients being readmitted multiple times\cite{38}.
The experience of those that have led such programmes
is that the elderly, those with co-morbidity and those
with previous admissions for worsening heart failure are
those most likely to benefit from such intervention\cite{38}.

Our data would support such observations. This study
took place prior to the widespread acceptance of the
benefits of β-blockade, and spironolactone, in patients
with heart failure due to left ventricular systolic dysfunc-
tion. Notwithstanding this, patients identified in this
study are likely to have been managed more carefully
than is the case in routine care. While our data demon-
strate a large burden of mortality and hospitalization,
they reinforce the need to ensure that patients are given
the opportunity to benefit from modern, evidence-based
therapy. The elderly and those who have been hospital-
ilized, who may represent a more challenging group of
patients, should not be excluded. Closer collaboration
between cardiologists and care of the elderly specialists
should be encouraged.

In conclusion, patients with a new diagnosis of heart
failure in the population tend to be elderly with con-
siderable co-morbidity. If they survive the early high-
risk period after diagnosis they are at high risk of
subsequent hospitalization, with almost half of such
admissions relating to worsening heart failure. Our
study shows the highest risk for hospital admission for
worsening heart failure is in the first few months after
the initial diagnosis has been made, and is higher in
those diagnosed as an inpatient rather than as an
outpatient. The older the patient the higher the risk and
once admitted female patients are likely to stay in
hospital longer. With limited resources it would be
sensible to target heart failure management programmes
to older patients, especially those with other medical
problems, presenting for the first time with this clinical
syndrome.

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of death.

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