Is The Diagnostic Position of Acute Heart Failure (AHF) Related to Mortality? - A report from the Euro Heart Failure survey-1 (EHFS1)

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Abstract

Background

Most previous publications on AHF exploring the relation between admissions to hospital for heart failure (HF) and subsequent outcomes have focused only on those patients with HF coded as the primary discharge diagnosis, which might be only a minority of all patients. Failure to quantify the size of the problem is likely to lead to an under-estimate of the health economic impact of heart failure and under-provision of resources for its care.

Methods & Results

EHFS1 screened consecutive deaths and discharges during 2000-2001, to ascertain patients with known or suspected HF. Information on presenting symptoms and signs were gathered. Of all 10,701 patients, HF was considered to be the primary reason for admission in 4,234 (40%), secondary reason for admission if complicated or prolonged stay in further 1,772 (17%), and in 4, 695 (43%) it was uncertain that HF is actively contributing in index admission. 278 (16%) from secondary HF, 286 (9%) from primary HF and 183 (4%) from uncertain group were died during index admission. Hazard ratio of death was 3.26 ($P<0.001$) in secondary, 1.72 ($P<0.001$) in primary as compare to uncertain group. Total death after 12 weeks of discharge were again higher in secondary HF, 389 (22%), 558 (13%) in primary and 412 (9%) in uncertain group.

Conclusion

Heart failure at secondary position has very high mortality even most of HF registries and clinical trial reported patients on primary position only. Significant number of patients was died from that group where diagnosis of HF was uncertain.

Key words: Acute heart Failure, EHFS1, Diagnostic position, Prognosis

Introduction

Heart failure (HF) is a common reason for hospitalization and also commonly complicates hospitalization for other reasons.[1] Indeed, about 80% of hospitalisations caused or complicated by heart failure will have another diagnosis in the primary position. Most patients with heart failure will have other medical problem many of which cause, contribute to, complicate or are complicated by heart failure.[2, 3] Heart failure as a secondary diagnosis is important for several reasons.[4]

- The diagnosis of heart failure is usually first made during a hospital admission and this will often be due to a precipitating cause such as an acute coronary syndrome, arrhythmia or infection.[5]
- An acute medical problem that is complicated by heart failure might be more likely to lead to admission.
- Although heart failure might not cause admission it might be the key illness that dictates the length of hospital stay and prognosis.
- When heart failure is due to left ventricular systolic dysfunction (LVSD), it should usually be treated with disease modifying agents whether it is a primary or secondary diagnosis. Hospitalisation offers an opportunity to review and improve management, although sadly the reverse is often the case on general medical wards, although this may be improving with the introduction of cardiology-based heart failure 'out-reach' services for patients with heart failure on general medical or surgical wards.

Most previous audits, registries and publications reporting on deaths and discharges for heart failure focussed only on patients with heart failure as a primary discharge diagnosis; a small minority of all hospitalisations complicated by heart failure. [1, 6-8] Little is known about the outcome of patients admitted for other reasons but in whom heart failure is either a secondary or incidental diagnosis. Moreover, it is likely that the diagnosis of heart failure is often overlooked during a hospital admission. Many patients are treated with and discharged on loop diuretics for no obvious reason other than symptoms and signs of congestion. Even if these patients do not have heart failure, it should be suspected and investigated, although this is often not the case.[9] Failure to consider all admissions with suspected heart failure will lead to a serious under-estimate of the health economic impact of heart failure and under-provision of resources for its care.

The Euro Heart Failure Survey 1 (EHFS-1) enrolled patients either discharged on loop diuretics or with a diagnosis of heart failure preceding, causing or complicating hospitalisation.[4] We explored the nature and importance of heart failure as a secondary or incidental diagnosis in this data-set.

Methods

In the EHFS-1 consecutive deaths and discharges primarily from medical wards were screened over a 6 week period during 2000-2001 from 115 hospitals in 24 countries belonging to the European Society of Cardiology, to identify patients with known or suspected HF.[4 10] The design and implementation of the survey have been published in detail previously.[11] Information was gathered from patients' case notes to identify if the patient fulfilled one or more of the following inclusion criteria; the

criteria were deliberately set wide in order to capture as much relevant diagnostic and therapeutic activity as possible:[4]

1. A diagnosis of heart failure on the index admission, irrespective of the primary reason for admission.
2. A diagnosis of heart failure recorded in the hospital records at any time during the previous three years.
3. Loop diuretics given in the 24 hours prior to death or at discharge, unless for renal failure.
4. Administration of treatment for heart failure or major ventricular dysfunction within the 24 hours prior to death or discharge. Investigators especially reviewed the use of angiotensin converting enzyme inhibitors (ACE-I), beta blockers, mineralo-corticoid receptor antagonists (MRA), diuretics and digitalis compounds during this period to ascertain the reason for administration.

Admissions were then classified by investigators, according to their personal opinion, as follows:-

- Heart failure as the primary diagnosis
- Heart failure as a secondary diagnosis, complicating or prolonging admission
- Heart failure as an incidental finding or diagnostically uncertain

Presentation, events contributing to this admission, cardiovascular investigations, comorbid illnesses and therapy were recorded. Deaths occurring during the index

hospital admission and deaths and readmissions up to 3 months after discharge were reported.

Continuous data are summarized by the median (25th/75th centiles); categorical data by percentages. Prognostic models for all-cause mortality were developed using Cox regression. The proportionality of hazards (PH) assumption was verified for all covariates using tests based on Schoenfeld residuals. [12, 13] There was no departure from the proportional hazard assumption for any covariate. Cox metrics include the hazard ratio (HR), 95% confidence intervals (CIs) and pseudo r2 (the square of the correlation coefficient of the actual and predicted values of the dependent variable). This is a measure of goodness-of-fit.[13] Prognostic models were developed using k-fold cross-validation.[14] This procedure splits the data randomly into k partitions. For each partition, it fits the specified model using the other k-1 groups, and uses the resulting parameters to predict the dependent variable in the unused group. We arbitrarily chose k as 25 (hence 25-fold cross-validation). Our group has used this approach before.[15] We started with 50 variables and then selected nine variables that were significant in at least 70% of cross-validations for the final model to assess mortality during the index hospital admission.

Kaplan-Meier curves constructed using the log-rank test was used to compare outcomes in groups during index admission. We used logistic regression to assess mortality and readmission within 12 weeks after discharge from index admission. An arbitrary level of 5% statistical significance (two-tailed) was assumed. The Stata statistical computer package was used to analyse the data.

Results

Of 10,701 patients admitted with suspected HF, heart failure was considered to be the primary reason for admission in 4,234 (40%), the secondary (if HF complicated or prolonged hospital stay) in a further 1,772 (17%), and in 4,695 (43%) it was uncertain whether HF was actively contributing to the admission. The clinical characteristics of each group are shown in **Table 1**. Although there were statistical differences in age and sex amongst the three groups, these were small and of doubtful clinical relevance. More patients with a primary diagnosis of HF were prescribed loop diuretics at admission and discharge (71% & 84%) but this was only slightly greater than amongst patients with an incidental or uncertain finding of HF (58% & 74% respectively) **Table 1**. Indeed, there were remarkably few substantial differences amongst the three groups of patients. More patients with a secondary diagnosis of heart failure had a primary diagnosis of ACS. More patients with a primary diagnosis of heart failure had a dilated cardiomyopathy.

Patients with a primary or secondary diagnosis of HF exhibited broadly similar echocardiographic features although the prevalence and severity of abnormalities tended to be greater in those with a primary diagnosis. Patients with an incidental or uncertain diagnosis were less likely to have had an echocardiogram. This highlights an important point; surveys that include only patients with a confirmed diagnosis of heart failure are an unreliable source of data on the quality of diagnostic investigation. It is possible that a diagnosis of HF would have been confirmed in a substantial proportion of patients had adequate diagnostic investigation been conducted (**Table 2**). There was no substantial difference in laboratory investigations, although patients with an incidental or uncertain diagnosis of HF had, statistically,

better renal function. Most patients in all three groups had either cardiomegaly or signs of pulmonary congestion or both on their chest X-ray although the proportion was substantially greater in those with a primary or secondary diagnosis of heart failure (**Table 2**).

During the index admission, 16% (290) of those with a secondary diagnosis of HF, 7% (301) of those with a primary diagnosis of HF and 4% (189) of those in whom the diagnosis was uncertain died. The unadjusted Hazard ratios (HR) were 3.26 for secondary HF and 1.73 for primary HF compared to the group with an uncertain diagnosis (**Table 3**)(Figure 1).

Worsening HF was the main factor contributing to death in those with a primary or secondary diagnosis of HF and for 18% of those in the uncertain group. Myocardial infarction contributed to death in 34% of deaths where HF was a secondary diagnosis but only 18% where HF was a primary diagnosis and 16% when the diagnosis of HF was uncertain (**Table 3**). Stroke was an important contributor to death amongst patients with an incidental diagnosis of HF. Length of stay was on average three days longer in patients who had a secondary diagnosis of HF compared to the other two groups. After adjusting for prognostic variables including male sex, MI during index admission, unstable angina during index admission, evidence of dilated cardiomyopathy, history of ventricular tachycardia or fibrillation, history of stroke and moderate to severe left ventricle dilatation present in our final model, the HR for death during the index admission was 3.45 (CI 2.29-5.22) for those with a secondary diagnosis of HF and 2.55 (CI 1.73 – 3.77) for those with a primary diagnosis of HF as compare to uncertain group(**Table 4**). Harrell's C statistic was 0.72 for the overall model, suggesting moderate discrimination.

Drugs at discharge or within 24 hours before death are shown in **Table 5**. There were few substantial differences in prescription rates; only for digoxin was there a >20% difference in prescribing rates, with 48% of those assigned a primary diagnosis being prescribed digoxin versus 26% in those with an uncertain diagnosis. The absolute differences in prescribing rate of loop diuretics, ACE inhibitors and MRA were only 10-20% higher in patients with a primary diagnosis compared to uncertain diagnosis of HF. The proportion of patients prescribed beta blockers was similar in all three groups, although statistically lowest in those with a primary diagnosis of HF (**Table 5**).

In the 12 weeks following discharge, 287 (7%) patients with a primary, 117 (8%) with a secondary and 238 (5%) with an incidental or uncertain diagnosis of HF died (**Table 6**). Worsening heart failure was the single most common reported reason for death in all three groups, contributing to 40%, 25% and 22% of post-discharge deaths for patients with a primary, secondary or uncertain diagnosis of heart failure. The odds ratio (OR) for death was 1.30 (CI 1.01-1.55) for a primary and 1.47 (CI 1.16-1.85) for a secondary diagnosis compared to those with an incidental or uncertain diagnosis. However, no significant difference in mortality was observed on multi-variable analysis. The area under receiver operator characteristics (ROC) curve was 0.55 for this model adjusted for all relevant variables, suggesting poor discrimination for post-discharge mortality.

Re-admissions, all-cause, due to cardiovascular reasons or due to heart failure within 12 weeks after discharge were more common in patients with a primary, compared to a secondary or incidental/uncertain HF diagnosis (**Table 6**). For the composite

outcome of cardiovascular re-admissions or death within 12 weeks after discharge, the OR was 1.49 (p-<0.001, CI 1.33-1.66) for those with a primary diagnosis and 1.32 (P<0.001, CI 1.13-1.53) for those with a secondary diagnosis, compared to those with an incidental/uncertain diagnosis of HF. However, again these differences were not statistically significant in multi variable analysis. The area under ROC curve for this model was 0.58 suggesting poor discrimination.

Discussion

Despite limitations, research surveys and registries are a rich source of information on patients encountered in clinical practice that may often be excluded from clinical trials. Although some substantial differences were observed amongst patients with a primary, secondary or incidental/uncertain diagnosis of heart failure they were few; the three populations had greater similarities than differences. Importantly, the outcomes after discharge for each group were broadly similar in terms of mortality and re-admission, although statistical differences driven by large numbers were observed and the causes of readmission and death did differ amongst groups. Most readmissions were for CV reasons amongst patients with a primary or secondary diagnosis of HF but only two-thirds of those with an incidental/uncertain diagnosis.

The characteristics of patients admitted to cardiology wards with a primary diagnosis of HF have been described in many surveys. However, the large proportions of patients with a primary diagnosis of HF who are admitted under the care of general physicians or geriatricians are much less well represented. Surveys such as this and some national registries [1] provide valuable insights into less “sanitized” populations with heart failure. However, it is difficult to avoid selection bias, which may have accounted for the relative youth in some countries, such as Germany, in this survey.

It is also likely that the EHFS-1 underestimated the full burden of patients with a secondary or uncertain diagnosis of heart failure. However, in the UK and many Scandinavian countries, EHFS-1 appeared to be successful in recruiting older patients with high rates of co-morbidity.

The management and outcome of heart failure as a secondary diagnosis has been less well-described. This survey shows that ACS is most often the primary diagnosis when HF is considered an important secondary diagnosis and that these patients have a poor in-hospital prognosis although, for those that were discharged, subsequent outcome was no worse than for patients with a primary diagnosis of HF.

The characteristics and outcome of the large number of patients in whom the diagnosis of HF is an incidental finding or diagnostically uncertain has rarely been described. Cleland et al described the outcome of patients discharged on loop diuretics with or without a diagnosis of heart failure in a prospective survey over 18 months from a single large hospital.[9] Only a small proportion (~15%) of patients taking loop diuretics had a primary diagnosis of HF and less than half had a diagnosis of HF in any diagnostic position. However, patients receiving loop diuretics who had not been diagnostically labelled as HF had only a slightly lower mortality at two years compared to those who bore a diagnosis of HF. The study showed that few of these patients underwent diagnostic tests for HF. This diagnostic short-fall was also observed in EHFS-1. It is likely that this population contains a large proportion of patients with HF who have the characteristics and poor prognosis of other patients with HF but diluted by patients treated inappropriately with diuretics with a range of disease, some malign (eg:- stroke and cancer) and others relatively benign (eg:- COPD). Ignoring the diagnostic and therapeutic needs of this

group of patients is likely to be detrimental to their well-being and prognosis and seriously underestimates the resources required to manage HF and the economic burden it imposes.

The diagnostic uncertainty of HF is a dilemma.[16] Diagnostic tests such as echocardiography often require referral to the cardiology team which can be a barrier and rate-limiting step in many hospitals. Conventionally, this is considered part of the gold-standard for diagnosis although problems with reproducibility and interpretation skills have led to its central role being questioned. Natriuretic peptides can be measured in routine blood samples regardless of who is caring for the patient. This greatly democratizes access to the diagnostic pathway in HF. However, although natriuretic peptides are useful to rule out HF they are considered prone to many false-positive results causing confusion for the inexperienced.[16] Symptoms of HF are often mimicked by other conditions especially respiratory problems like chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD) and chest infections which may often co-exist with HF. Peripheral oedema in many older patients may also be due to conditions other than HF. In the presence of many comorbid illnesses, treating clinicians may be uncertain whether HF is contributing to the admission or not, even if these patients have a prior history of heart failure. These patients often receive therapy, such as diuretics, in an attempt to relieve symptoms and signs. Hospitalisation provides an opportunity to correct a patient's diagnosis and rationalise and improve therapy even if HF is not the primary reason for admission.

1.1 Limitations

EHFS1 was conducted at the turn of the century before the roles of beta blockers and cardiac resynchronization of therapy were well established. This will have influenced choice of therapy but should not have affected diagnosis. Natriuretic peptides were not recorded during admission. However, NT-proBNP was <125ng/L in only 47 of 2,368 patients in whom it was measured at the 12 week follow-up and 75% had values >400ng/L.[17] Median serum creatinine was 130umol/L indicating a substantial contribution of moderate renal dysfunction to increases in natriuretic peptides. About 25% were in atrial fibrillation, another cause for elevated plasma natriuretic peptide concentrations. However, even after controlling for renal dysfunction and atrial fibrillation, the increase in natriuretic peptides suggests that the great majority of patients had important cardiac dysfunction. Although, in surveys there are always chances of selection bias, EHFS1 was designed to try and avoid this as far as possible.[11] In particular, the short but intense collection period (more than 10,000 patients enrolled over 6 weeks in115 hospitals), the attempt to recruit from medical wards and the high proportion of non-University hospitals should have reduced bias. However, without 100% ascertainment of suspected cases from a prospectively defined sampling frame it is impossible to be sure that no bias occurred. Indeed, it is likely that there was a bias towards sampling patients from cardiology wards and against patients in whom the diagnosis was in doubt.

1.2 Conclusion

Mortality is high even if heart failure is not main reason of admission but complicates another primary diagnosis. The high mortality may reflect the prognosis of the primary disease or other patient characteristics that impair the delivery of

effective care, including the place of care. Mortality amongst patients with an equivocal diagnosis of HF is also substantial and there appears to be a large diagnostic short-fall. Registries and surveys that do not include patients with HF as a contributory diagnosis may provide an over-optimistic view of prognosis and underestimate the resources required for diagnosis and effective management.

Figures

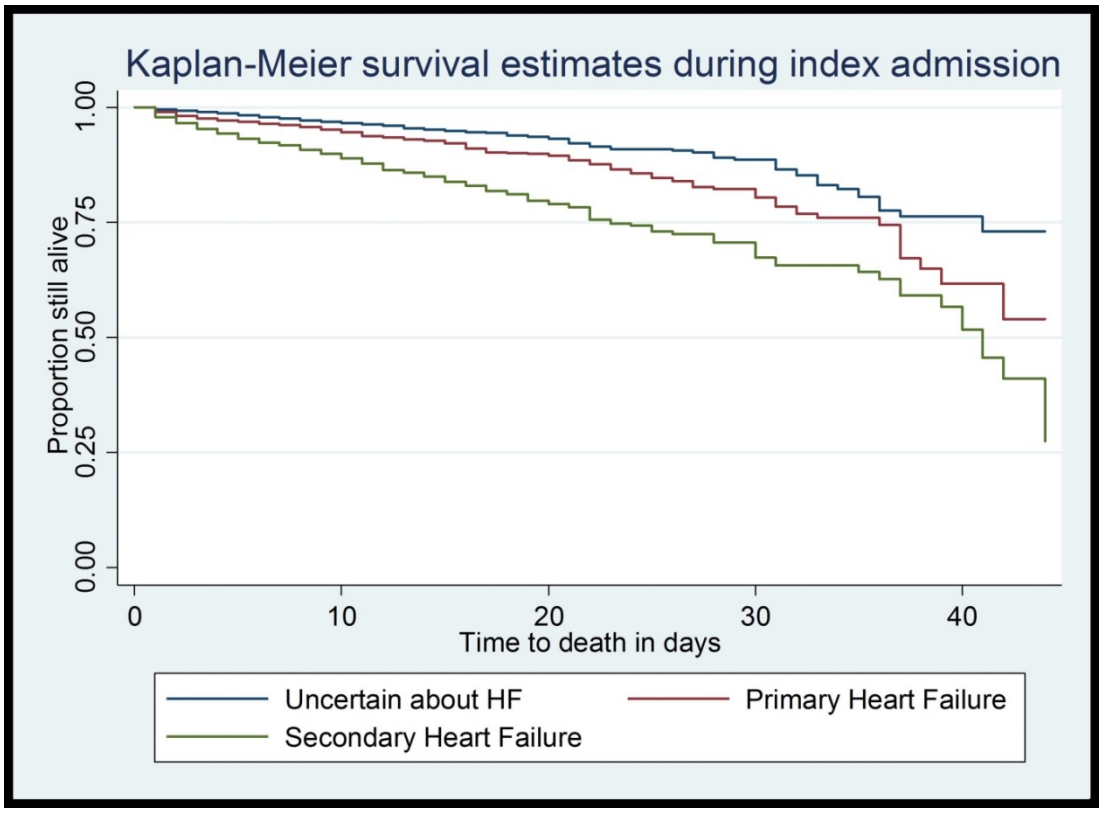

Figure 1: Kaplan- Meier survival estimates during index admission

Tables

Table 1: Clinical Characteristics

	Primary	Secondary	Uncertain	P--Value
N = (%)	4,234 (40%)	1,772 (17%)	4,695 (44%)	
Age in Years (IQR)	72 (63-80)	74 (65-80)	73 (64-80)	<0.001
Women	1,890 (45%)	837 (47%)	2,293 (49%)	<0.001
BMI (kg/m^2)	26 (24-29)	26 (24-30)	27 (24-30)	0.1
Loop diuretics prior to admission	2,782 (71%)	859 (52%)	2,395 (58%)	<0.001
Loop diuretics at discharge	3,532 (84%)	1,359 (77%)	3,455 (74%)	<0.001
MI during this admission	215 (5%)	456 (26%)	413 (9%)	<0.001
MI (anytime)	1,421 (34%)	844 (48%)	1,746 (37%)	<0.001
UA this admission	417 (10%)	331 (19%)	724 (16%)	<0.001
UA (anytime)	902 (21%)	523 (30%)	1,199 (26%)	<0.001
h/o Angina (anytime)	1,785 (43%)	961 (55%)	2,362 (51%)	<0.001
PCI this admission	82 (2%)	79 (4%)	203 (4%)	<0.001
PCI (anytime)	277 (7%)	147 (8%)	455 (10%)	<0.001
CABG	400 (9%)	199 (11%)	613 (13%)	<0.001
Heart Transplant (	13 (<1%)	2 (<1%)	36 (<1%)	<0.001

	Primary	Secondary	Uncertain	P--Value
LVAD implanted	23 (<1%)	8 (<1%)	9 (<1%)	0.02
Evidence for DCM	755 (18%)	115 (7%)	336 (7%)	<0.001
Valve replacement	278 (7%)	70 (4%)	290 (6%)	<0.001
Valve repair	93 (2%)	28 (2%)	99 (2%)	0.28
New onset or paroxysmal AF/SVT	1,018 (24%)	482 (27%)	1,046 (22%)	<0.001
Chronic AF/SVT	1,228 (29%)	351 (20%)	903 (19%)	<0.001
VT/VF this admission	239 (6%)	156 (9%)	143 (3%)	<0.001
VT/VF (anytime)	382 (9%)	196 (11%)	296 (6%)	<0.001
PPM	393 (9%)	139 (8%)	347 (7%)	0.004
ICD implanted	70 (2%)	23 (1%)	60 (1%)	0.29
h/o Hypertension	2,245 (53%)	982 (56%)	2,452 (53%)	0.06
h/o Disabling stroke	303 (7%)	198 (11%)	438 (9%)	<0.001
h/o Renal failure	882 (21%)	358 (20%)	593 (13%)	<0.001
Respiratory disease	1,332 (32%)	653 (37%)	1,392 (24%)	<0.001
DM	1,193 (28%)	494 (28%)	1,220 (26%)	0.05
h/o Pulmonary embolism	129 (3%)	78 (4%)	145 (3%)	0.02

HF; Heart failure, BMI; Body mass index, MI; Myocardial infarction, UA; Unstable angina, PCI; Percutaneous coronary intervention, CABG; Coronary artery bypass grafting, DCMP; Dilated cardiomyopathy, AF; Atrial fibrillation, SVT; Supraventricular tachycardia, VT; Ventricle tachycardia, VF; Ventricle fibrillation, TIA; Transient Ischaemic attack, DM; Diabetes Mellitus

Table 2: Clinical investigations

	Primary	Secondary	Uncertain	P--Value
N = (%)	4,234 (40%)	1,772 (17%)	4,695 (44%)	
Number with echo data	**2,854**	**945**	**2,339**	
Mild LVSD	451 (16%)	187 (20%)	469 (20%)	<0.001
Moderate / Severe LVSD	1,652 (58%)	**489 (52%)**	**951 (41%)**	<0.001
Moderate / Severe LV diastolic dysfunction	415 (15%)	139 (15%)	**266 (11%)**	<0.001
LVEDD (cm)	5.8 (5-6.6)	5.4 (4.9-6.1)	**5.3 (4.8-6)**	<0.001
LVESD (cm)	4.5 (3.6-5.4)	4 (3.3-4.8)	3.9 (3.2-4.8)	<0.001
Moderate / Severe LA dilatation	1,139 (40%)	265 (28%)	**574 (25%)**	<0.001
Moderate / Severe Mitral Stenosis	111 (4%)	22 (2%)	73 (3%)	0.06
Moderate / Severe Mitral Regurgitation	1,080 (38%)	271 (29%)	**574 (25%)**	<0.001
Moderate / Severe Aortic stenosis	275 (10%)	59 (6%)	163 (7%)	<0.001
Moderate / Severe Aortic regurgitation	268 (9%)	64 (7%)	169 (9%)	0.004
Moderate / Severe Right ventricle dysfunction	262 (9%)	62 (7%)	**93 (4%)**	<0.001
Moderate / Severe Pulmonary hypertension	674 (24%)	**131 (14%)**	**266 (11%)**	<0.001
Haemoglobin (g/dl)	12.9 (11.4-14.2)	12.7 (11.3-14.2)	12.9 (11.3-14.2)	0.15

	Primary	Secondary	Uncertain	P--Value
Sodium (mmol/l)	139 (136-142)	139 (136-142)	139 (136-142)	0.06
Potassium	4.3 (3.9- 4.7)	4.3 (3.9-4.7)	4.2 (3.9-4.6)	0.01
Urea mmol/l	10.71 (7-17.6)	11.02 (7-17.85)	8.9 (6.2-14.5)`	<0.001
Creatinine (umol/l)	106 (88.4-135)	106 (88.4-141)	101 (83-126)	<0.001
Cholesterol most recent (mmol/l)	4.89 (3.9-5.8)	5.1 (4.1-5.93)	5.1 (4.3-5.92)	<0.001
Chest X-Ray:	3,218 (86%)	1,205 (78%)	**2,281 (61%)**	<0.001
Cardiomegaly/Pulmonary congestion				

HF; Heart Failure, LVSD; Left ventricle systolic dysfunction, IQR; Interquartile Range, LVEDD; Left ventricle end diastolic diameter, LVESD; Left Ventricle end systolic diameter, LV; Left ventricle, LA; Left atrium.

*Median and Interquartile range (IQR) are shown in continuous variables.

Table 3: Mortality & Length of stay (LOS) during index admission

N = (%)	4,234 (40%)	1,772 (17%)	4,695 (44%)	
Deaths	301 (7%)	**290 (16%)**	189 (4%)	<0.001
Unadjusted HR (95% CI)	1.73 (1.43-2.08)	3.26 (2.70-3.93)		
Events Contributing to death (proportion deaths)				
MI	53 (18%)	**100 (34%)**	31 (16%)	<0.001
Worsening HF	239 (79%)	203 (70%)	**35 (18%)**	<0.001
Renal Failure	79 (26%)	76 (26%)	**21 (11%)**	<0.001
Ventricular Arrhythmia	42 (14%)	35 (12%)	13 (7%)	<0.001
Atrial Arrhythmia	35 (12%)	39 (13%)	8 (4%)	<0.001
Infection	87 (29%)	93 (32%)	57 (30%)	<0.001
Stroke	6 (2%)	31 (11%)	**32 (17%)**	<0.001
Cancer	10 (3%)	22 (8%)	**30 (16%)**	<0.001
Other	43 (14%)	**76 (26%)**	**72 (38%)**	<0.001
Median LOS during index admission in days (IQR)	8 (4-14)	11 (8-17)	8 (4-13)	<0.001

HF; Heart Failure, HR; Hazard ration, CI; Confidence interval, MI; Myocardial Infarction, IQR; Interquartile range, LOS; Length of stay

Table 4: Multi variable Cox Model Showing Variables Associated with Death during the Index Admission

	Hazard Ratio	Standard error	Z Statistics	P Value	95% Confidence interval
Primary HF	2.55	0.50	4.74	<0.001	1.73 - 3.76
Secondary HF	3.45	0.72	5.90	<0.001	2.28 – 5.22
Male	0.81	0.11	-1.55	0.12	0.62 – 1.05
MI during index admission	1.79	0.30	3.45	0.001	1.29 – 2.50
Admission for UA during this admission	0.96	0.20	-0.22	0.83	0.64 – 1.42
Evidence for DCMP	1.19	0.23	0.91	0.36	0.82 – 1.73
VT/VF diagnosed	1.78	0.29	3.54	<0.001	1.29 – 2.45
Disabling stroke	1.47	0.29	1.89	0.06	0.98 – 2.19
Moderate / Severe LV dilatation	0.94	0.15	-0.37	0.71	0.69 – 1.28
Creatinine (umol/l)	1.07	0.001	4.70	<0.001	1.04 – 1.09

HF; Heart failure, MI; Myocardial Infarction, UA; Unstable angina, DCMP; Dilated cardiomyopathy, VT; Ventricle tachycardia, VF; Ventricle fibrillation, LV; Left ventricle, umol/l; Micro mole / per liter

Table 5: Drugs at discharge

	Primary	Secondary	Uncertain	P—Value
	4,234 (40%)	1,772 (17%)	4,695 (43%)	
Spironolactone	**1,357 (32%)**	300 (17%)	540 (12%)	<0.001
Furosemide	**3,489 (82%)**	1,335 (75%)	3,327 (71%)	<0.001
Bumetanide	126 (3%)	4 (2%)	110 (2%)	0.16
Torasemide	163 (4%)	64 (4%)	140 (3%)	0.07
Metolazone	77 (2%)	19 (1%)	21 (<1%)	<0.001
Thiazide diuretic	508 (12%)	163 (9%)	397 (8%)	<0.001
ACEI	**2,964 (70%)**	1,069 (60%)	2,577 (55%)	<0.001
ARB	218 (5%)	50 (3%)	213 (5%)	<0.001
Nitrate	1,872 (44%)	817 (46%)	2,005 (43%)	0.04
Calcium channel blockers	773 (18%)	361 (20%)	1,131 (24%)	<0.001
Beta blockers	1,459 (34%)	695 (39%)	1,790 (38%)	<0.001
Digoxin	**2,036 (48%)**	562 (32%)	1,227 (26%)	<0.001
Antiarrhythmic drugs	703 (17%)	272 (15%)	599 (13%)	<0.001
Lipid lowering drugs	747 (18%)	343 (19%)	1,097 (23%)	<0.001

HF; Heart Failure, ACI; Angiotensin converting enzyme inhibitor, ARB; Angiotensin receptor blockers

Table 6: Mortality & Readmission within 12 Weeks after discharge

	Primary	**Secondary**	**Uncertain**	**P--Value**
Deaths	287 (7%)	117 (8%)	229 (7%)	0.001
Unadjusted OR (95% CI)	1.30 (1.01-1.55)	1.47 (1.16-1.85)		
Events contributing to death (proportion deaths)				
MI	27 (9%)	10 (9%)	25 (11%)	0.88
Worsening HF	**114 (40%)**	**29 (25%)**	50 (22%)	<0.001
Renal Failure	23 (8%)	12 (10%)	12 (6%)	0.02
Ventricular Arrhythmia	22 (8%)	2 (2%)	7 (3%)	0.002
Atrial Arrhythmia	8 (3%)	4 (3%)	8 (3%)	0.87
Infection	24 (8%)	17 (15%)	40 (17%)	0.16
Stroke	19 (7%)	9 (8%)	19 (8%)	0.87
Death caused by cancer	16 (6%)	9 (8%)	28 (12%)	0.27
Other events contributing to death	**43 (15%)**	30 (26%)	63 (28%)	0.07

	Primary	Secondary	Uncertain	P--Value
Readmission within 12 weeks after discharge				
All cause	961 (23%)	344 (19%)	980 (21%)	0.01
	OR 1.12 (CI 1.01-1.22)	OR 0.91 (CI 0.80 – 1.04)		
Due to cardiovascular cause	772 (18%)	240 (14%)	580 (13%)	<0.001
	OR 2.92 (CI 2.38-3.58)	OR 1.61 (CI 1.24-2.09)		
Due to Heart Failure	517 (12%)	134 (8%)	240 (5%)	<0.001
	OR 3.8 (CI 3.03-4.46)	OR 1.99 (CI 1.53-2.59)		

HF; heart failure, MI; Myocardial infarction, OR; Odd ratio, CI; Confidence interval

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