Prognostic value of psychosocial factors for first and recurrent hospitalizations and mortality in heart failure patients: insights from the OPERA-HF study

I. Sokoreli[1,4,*], S.C. Pauws[1,2], E.W. Steyerberg[3,4], J.J.G. de Vries[1], J.M. Riistama[1], A. Tesanovic[1], S. Kazmi[5], P. Pellicori[5], J.G. Cleland[5,6,7], A.L. Clark[5]

(1) Philips Research - Healthcare, High Tech Campus 34, 5656 AE Eindhoven, the Netherlands; (2) TiCC – University of Tilburg, Tilburg, the Netherlands; (3) Department of Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, the Netherlands; (4) Department of Public Health, Centre for Medical Decision Making, Erasmus MC, Rotterdam, the Netherlands; (5) University of Hull, Hull, UK; (6) National Heart & Lung Institute, Imperial College, London, UK; (7) Robertson Centre for Biostatistics & Clinical Trials, University of Glasgow, UK.

* I.Sokoreli (ioanna.sokoreli@philips.com)

Abstract

Aims: Psychosocial factors are rarely collected in studies investigating the prognosis of patients with heart failure (HF), and only time to first-event is commonly reported. We investigated the prognostic value of psychosocial factors for predicting first or *recurrent* events after discharge following hospitalization for HF.

Methods and results: OPERA-HF is an observational study enrolling patients hospitalized for HF. In addition to clinical variables, psychosocial variables are recorded. Patients provide the information through questionnaires which include social information, depression and anxiety scores, and cognitive function. Kaplan-Meier, Cox regression and the Andersen-Gill model were used to identify predictors of first and recurrent events (re-admissions or death).

Of 671 patients (age 76±15 years, 66% men) with one-year follow-up, 291 had no subsequent event, 34 died without being readmitted, 346 had one or more unplanned readmissions and 71 patients died after a first readmission. Increasing age, higher urea and creatinine, the presence of co-morbidities (diabetes, history of MI, COPD), were all associated with increasing risk of first or recurrent event. Psychosocial variables independently associated with both the first and recurrent events were: presence of frailty, moderate to severe depression and moderate to severe anxiety. Living alone and the presence of cognitive impairment were independently associated only with an increasing risk of recurrent events.

Conclusion: Psychosocial factors are strongly associated with unplanned recurrent readmissions or mortality following an admission to hospital for HF. Further research is needed to show whether recognition of these factors and support tailored to individual patients' needs will improve outcomes.

Keywords: Heart Failure; Readmission; Mortality; Recurrent events; Psychosocial factors; Frailty.

1. Introduction

Patients with heart failure (HF) are at high risk of readmissions and death. About 25% of patients admitted with HF are readmitted within one month of leaving hospital.[1] In European studies, the readmission rate is up to 44% at 1 year after discharge.[1] Commonly, studies investigating risk factors for readmission only consider the first readmission. However, they are often recurrent, reflecting progression of the underlying disease or exacerbations due to co-morbidities and sub-optimal self-care and medication adherence. Understanding the causes, precipitants and risk factors for recurrent readmissions may help to prevent them. By focusing only on first event analysis, any subsequent events are ignored and the impact of potential risk factors can be greatly under- or over- estimated.

Several demographic or clinical variables, such as age, sex, the presence of co-morbidities, left ventricular ejection fraction, New York Heart Association class of symptoms and serum markers are important predictors of readmissions and death among patients with HF.[2] The impact of psychosocial factors on first readmission or mortality has also been studied. [3] The presence of some psychosocial factors, such as depression, are significant predictors of mortality among patients with HF.[4,5] The presence of frailty is also associated with increasing risk of first readmission or mortality.[6,7] However, there is no report about the effect of depression, frailty and other psychosocial factors on recurrent events.

Accordingly, we explored the effect of psychosocial factors on first and recurrent unplanned readmissions or death in a cohort of patients discharged after a hospitalization for worsening HF.

2. Methods

2.1. Study design

OPERA-HF is an ongoing prospective observational study, enrolling patients hospitalized for HF in the Hull & East Yorkshire Hospitals NHS Trust, UK. The aim of the study is to create a holistic view of the patients, their general condition and co-morbidities, and to identify predictors of mortality and re-admission to hospital. Additional assessments, including assessments of depression/anxiety and cognitive function, were performed during hospital admission using questionnaires completed by the patient.

Patients had to fulfill all of the following criteria to be included in the present study: age >18 years; usual residence in the region served by the Hull & East Yorkshire Hospitals Trust; hospitalization for HF; treatment with loop diuretics; and at least one of the following: left ventricular ejection fraction (LVEF) ≤ 40%, left atrial dimension >4.0 cm [8] or NT-ProBNP >400 pg/ml (if in sinus rhythm) or >1200 pg/ml (if in atrial fibrillation). [9] Patients who were unable to understand and comply with the protocol or unable or unwilling to give informed consent were not included in the study. The study has full ethical approval from the South Yorkshire Research Ethics Committee (REC ref: 12/YH/0344) and is conducted in accordance with ICH-GCP, Declaration of Helsinki, the Data Protection Act 1998 and the NHS Act 2006.

2.1.1. Depression and anxiety assessment

Depression and anxiety were assessed by the Hospital Anxiety and Depression Scale (HADS) questionnaire.[10] The HADS consists of two parts of 7 questions each, one focusing on depression and one on anxiety. For each part, the response to each of the 7 questions is graded from 0 to 3, giving a total score that ranges between 0 and 21. A score of 7 or less implies that

there is no depression or anxiety; a score of 8-10 suggests mild depression or anxiety; and a score of 11 or more reflects moderate-to-severe depression or anxiety. [10]

2.1.2. Cognition assessment

This assessment was based on the General Practitioner assessment of Cognition (GPCOG),[11] a brief screening tool for detecting cognitive impairment. It was designed for use by primary care practitioners. The cognitive test includes nine items focusing on time orientation, clock drawing, awareness of a current news event and recall of a name and an address. Each correct answer scores one point leading to a maximum score of 9. A score of 4 or lower indicates cognitive impairment.

2.1.3. Frailty

For frailty, a two-fold assessment was applied. First the patient was asked to respond to a question about having troubles bathing or dressing and then was assessed through the 'get up and go' test. The timed 'get up and go' requires patients to stand up from a chair, walk a short distance (3 m), turn around, return, and sit down again. The normal time to complete the task is less than 10 seconds and abnormal is more than 20 seconds.[12] Patients who reported either troubles in bathing or dressing or completed the 'get up and go' test in more than 20 seconds were defined as frail.

2.1.4. Readmission/Mortality

All patients enrolled in the study are followed subsequent to discharge. All-cause readmissions and mortality are automatically recorded in the hospital's IT system. For the present report, the primary outcome of interest was all-cause unplanned readmissions or mortality. Unplanned readmission is considered any type of emergency readmission such as

emergency fast-track, through the Accident and Emergency department, or an urgent admission requested by the GP.

2.2. Statistical analysis

We report the baseline characteristics of the patients who participated in the study between 14/10/2012 and 30/07/2016. Follow up was censored at 22/08/2016. We describe and compare the baseline characteristics of the patients by the number of their subsequent events. For the comparison among patients having no event with patients having one or multiple readmissions or death after discharge, we used the chi-squared test to compare binary or categorical variables, and Kruskal-Wallis test for continuous variables. In order to avoid comparisons between groups of patients with unequal follow up times, we initially analysed events in patients for whom one year follow up data were available, including only those events which happened in the first year, in order to compare those with and those without an event.

We subsequently included all patients in statistical modeling to determine the relation between a putative risk factor and outcome. The Kaplan-Meier method was used to estimate the cumulative incidence of events (readmissions and mortality).[13] The event rate was calculated by taking into account all available recurrent events. We used univariable Cox regression to calculate the effect of potential risk factors on the first unplanned readmissions or death. The Andersen-Gill model was used to analyze the effect of the same factors when taking into account recurrent unplanned readmissions or death. The counting processes model of Andersen-Gill is a semiparametric model, and is a generalization of the Cox regression model.[14] It takes into account all the recurrent events along the time line, where the time to an event starts at the end of the previous event. All events are treated as being similar and independent of each other.

After identifying predictors of outcome, we calculated the effect of each psychosocial variable whilst adjusting for all significant clinical ones. For the psychosocial variables we used only complete cases and for clinical variables we used multiple imputation to impute missing values. [15] Application of the technique requires three steps: imputation, analysis and pooling. Each missing clinical value was imputed 5 times following the predictive mean matching method, thus producing 5 imputed data sets; each one of these 5 imputed data sets was then analyzed by the aforementioned complete-data procedures. The 5 resulting analyses are then combined into one final analysis following Rubin's method. The means of these pools are reported in the result section.[15,16] All analyses were conducted using R 3.3.2 statistical software (The R Foundation for Statistical Computing, Vienna, Austria).

3. Results

Of 814 patients consented, 35 died during the index admission and 779 were discharged. (Consort diagram: Figure 1) The median follow up amongst survivors was 764 (interquartile range, IQR 411–1069) days. 671 patients either died during the first year or were still alive at one year. The remaining 108 patients were survivors who had not yet completed their first year follow up after discharge.

➔ Figure 1

3.1. First year follow up

Figure 2a shows the outcomes at one year for the 671 patients who had at least one year follow-up or who died within one year and consequently had known one year outcome. During the first year, 291 (43%) patients had no event; 34 (5%) patients died without being readmitted; 346 (52%) had at least one unplanned readmission and 125 (19%) died after one or more further admissions.

➔ Figure 2

Of patients who agreed to complete the psychosocial assessments, 35% had all assessments completed and 54% had at least 4 of them completed. Patients who had no events in the first year were younger, and were less likely to have a history of MI or COPD. (Table 1)

Patients with one or more follow up events were more likely to have moderate-to-severe depression or moderate-to-severe anxiety and were more likely to be frail; they were less likely to complete the “get up and go” test and were more likely to report difficulties in bathing or dressing.

➔ Table 1

3.2. All follow up

Figure 2b shows events for all 779 participants, including patients followed for less than one year and events that happened *after* the first year. Overall, 220 (28%) patients had no event; 41 (5%) died without being readmitted; 518 (66%) had at least one unplanned readmission and 228 (29%) died after one or more further admissions.

The incidence of unplanned readmission and mortality is shown in Figure 3, with a combined event rate of 70% [95% CI 68% - 72%] at one year.

➔ Figure 3

3.2.1. Risk factors for first event

There were 559 first events (41 deaths and 518 readmissions). Increasing age, a past history of MI or COPD, LVEF lower than 40%, and increasing urea and creatinine at discharge were all associated with increasing risk of first event. Amongst psychosocial variables, moderate-to-severe depression, moderate-to-severe anxiety, worsening cognitive impairment and the presence of frailty were all associated with adverse events. (Table 2a)

3.2.2. Risk factors for recurrent events

There was a total of 1600 events including 1041 events subsequent to the first. Increasing age, history of MI, the present of diabetes or COPD, and increasing urea and creatinine at discharge were all associated with increasing risk. Amongst psychosocial variables, moderate-to-severe depression or anxiety, cognitive impairment and frailty, assessed by a question on troubles with bathing/dressing and/or by the ‘timed get up and go’ test, were all also associated with adverse events. Patients living alone also had a significantly higher risk (although not facing an increased risk of *first* event alone). (Table 2b)

➔ Table 2

3.2.3. Impact of psychosocial factors adjusted for demographic and clinical variables

In the statistical models adjusting for the clinical variables found to be significant in the univariable analysis (age, diabetes, history of MI, COPD, urea and creatinine), moderate-to-severe depression, moderate-to-severe anxiety, cognitive impairment, the presence of frailty and living alone were significant predictors of adverse outcomes. (Table 3)

Patients having troubles with bathing or dressing were 20% more likely to have one or more follow-up events compare to those not reporting troubles. Patients able to complete the "get up and go" test were 20% less likely to have a first follow up event than those who could not. Being unable to complete the test was a significant predictor of a first event, but not of recurrent events. Amongst those who did manage to complete the test, there was a 1% increase in risk of first or recurrent events for every extra second taken.

➔ Table 3

The impact of psychosocial variables on outcomes is plotted in Figure 4, with the patients grouped by having none or at least one of the following factors: moderate-to-severe depression; moderate-to-severe anxiety; cognitive impairment; more than 20 seconds needed to complete the 'get up and go' test; troubles with bathing or dressing; or living alone.

➔ Figure 4

4. Discussion

Our study is one of the first to evaluate the impact of psychosocial factors on the risk of subsequent events in patients hospitalized for heart failure (HF). We found a high event rate, with 70% of patients being re-admitted or dying at one year follow up. In common with previous studies, we have found that older patients with more co-morbidities, or higher urea or creatinine, are more likely to have one or more unplanned events. We also found that the presence of frailty, anxiety and depression were powerful predictors of outcome, both of first and of recurrent events.

We have previously reported that depression is strongly associated with increasing mortality in this cohort.[5] In the present study, we have found that patients with moderate-to-severe anxiety have a 1.7 times higher risk of a first event and a 1.4 higher risk of recurrent events compared to patients without anxiety. Patients with moderate-to-severe depression have a 1.7 times higher risk of a first event and a 1.8 higher risk of recurrent events compared to patients without depression. Patients living alone or with cognitive impairment have a 1.2 and 1.4 times higher risk of having multiple events after discharge compared to the patients not living alone or without cognitive impairment, respectively.

Psychological factors such as depression,[17,18] and other factors not directly related to the medical reason for an admission to hospital, such as cognitive impairment[19] or frailty,[20] are associated with adverse events in older people. We have found that these are also powerful predictors of adverse outcomes amongst patients hospitalized with HF. We also showed that the presence of at least one adverse psychosocial factor was associated with 1.8 higher risk of one or more recurrent events compared to having none.

Frailty is increasingly recognized as an important factor in managing patients with long term conditions,[21] but although it is easily recognized clinically, it can be difficult to define. Increasing age is an obvious risk factor for frailty, and around a quarter of patients admitted to hospital for HF are over 80 years of age.[22] Frailty is associated with poor nutritional status, itself associated with worse long-term outcome.[23] There are recent studies concluding that an indicator of frailty in routine care is related to first readmission or mortality in HF patients[7] or that amongst patients hospitalized for HF, worsening frailty measured by screening tools, such as the Derby frailty index (DFI) or clinical frailty scale (CFS), is strongly related to increasing mortality. [24] The results of the present study show a strong association between the presence of frailty and the risk of follow up. Even the answer to a simple question about difficulties with daily activities has a similar predictive value as more elaborate screening tools. We also found that the 'get up and go' test, a simple test of mobility, is strongly related to outcome. For every extra second needed to complete the test the risk of recurrent events increased by 1%. As an indicator of "social frailty", living alone was also associated with a worse outcome.

Previous studies have not found an association between anxiety and mortality in HF although depression is associated with worse outcomes.[4] We found that both depression and anxiety are related to the risk of recurrent events. The mechanism is not clear, but may be related to the reduced self-care seen amongst patients with depression.[25] Further research is needed to see if any specific intervention targeted at psychological factors is helpful. Anti-depressant therapy in patient with HF does not affect mortality and morbidity [26] but psychotherapy in primary care has a limited beneficial effect on reducing depression in patients with a cardiac condition.[27]

Cognitive impairment is a risk factor for adverse events in patients with HF. [28] We found that cognitive impairment is also associated with an increased risk of recurrent post discharge events. Cognitive impairment is also an impediment to HF patients' ability to self-care. [29]

We have thus found that a range of related conditions not directly associated with the HF syndrome itself – frailty (both physical and social), cognitive impairment, depression and anxiety – are all associated with an increased risk of adverse outcomes following discharge from hospital after an admission for HF. The individual patient should always be treated within his or her individual social context, and proper management should always consider whole patient, something of which it can be easy to lose sight in a busy hospital.

It's not clear from the present study whether targeted interventions for the conditions we have identified as predictors of a poor outcome might have a beneficial effect. Multidisciplinary interventions have shown some evidence of benefit,[30] and exercise therapy can also help in frail subjects.[31] Intervention trials are needed to see whether such interventions as providing extra help at home, day care or telemonitoring might be helpful.

Limitations The Anderson-Gill approach assumes the recurrent events to be identically distributed and independent of each other, which might not always be the case. It also treats death as an event similar to readmission. Missing data is also a limitation in this study. However, there is evidence to support the method that we followed to impute part of the data. [15] Our analysis is based on patients hospitalized only in one location. Further external validation of the results is needed in order to support their generalizability.

Our methods have been developed for research and have not been extensively tested in routine practice for HF patients. The HADS survey will not give the same diagnostic certainty as ICD-9 or similar codes. The surveys were only administered once, and we may have missed changes during or after hospitalization or subsequent events. The questionnaires use some colloquial language which may not be understood by patients from different backgrounds.

Conclusion. Moderate-to-severe depression and anxiety, living alone, cognitive impairment and the presence of frailty are strongly associated with unplanned recurrent admissions and mortality in the year following discharge after a HF admission to hospital. Studies are needed to show whether strategies to support patients from a social perspective and to target those with persistent problems with appropriate non-clinical interventions help to reduce risk.

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Figure legends

Tables

Table 1 Baseline characteristics for all study participants and all participants with follow up at one year stratified by number and type of events. Characteristics are summarized by their count and fraction (N (%)) for categorical or their median and interquartile range (Median [25th – 75th]) for continuous variables respectively; (*) null hypothesis: no significant difference between those with no event and those with at least one event; readmission(s) and/or death within one year, 0.1 level of significance; (**) NYHA class which was evaluated as the worst class during the last 7-days before admission; (***) the closest measurement to discharge. N# = number of patients with this variable available.

	All patient data		*Patients with one year follow-up data*						
Event	**All**		**All Patients**		**No Events**	**One re-admission**	**Death/ No re-admission**	**>1 event**	**Comparison**
	(N = 779)		**(N = 671)**		**(N = 291)**	**(N=121)**	**(N = 34)**	**(N = 225)**	
Characteristics	**N#**		**N#**						**P-value***
Women %	779	271 (35 %)	671	230 (34 %)	109 (37 %)	47 (39 %)	7 (21 %)	67 (30 %)	0.15
Age years	779	75 [67-82]	671	76 [67 -82]	73 [64-80]	75 [68-81]	79 [73-86]	78 [71-84]	<0.01
Diabetes %	779	278 (36 %)	671	243 (36 %)	101 (35 %)	45 (37 %)	14 (48 %)	83 (37 %)	0.53
History of MI %	779	183 (23 %)	671	163 (24 %)	57 (20 %)	34 (28 %)	12 (35 %)	60 (27 %)	<0.05
COPD %	779	136 (17 %)	671	111 (17 %)	35 (12 %)	21 (17 %)	7 (21 %)	48 (21 %)	<0.01
Cancer %	779	69 (10 %)	671	72 (10 %)	31 (11 %)	16 (13 %)	2 (6 %)	20 (9 %)	0.88
NYHA **:	672		569						
Class I/II %		68 (10 %)		67 (12 %)	29 (12 %)	14 (14 %)	0 (0 %)	24 (12 %)	0.61
NYHA: Class III %		427 (64 %)		365 (64 %)	163 (67%)	70 (71 %)	20 (74 %)	112 (56 %)	
NYHA: Class IV %		177 (26 %)		137 (24 %)	52 (21 %)	15 (15 %)	7 (26 %)	63 (32 %)	
Hypertension at ADM %	726	359 (58 %)	622	359 (58 %)	163 (59 %)	64 (55 %)	17 (55 %)	115 (57 %)	0.48
NT-proBNP pg/mL ***	664	4300[1803 – 9456]	570	4599[1934 - 9553]	3931[1894 – 7954]	4280[1576-9023]	6369[3884-16657]	5414[2083 -10843]	0.46
Sinus rhythm at DIS %	779	286 (37 %)	671	250 (37 %)	115 (40 %)	39 (32 %)	12 (35 %)	84 (37 %)	0.33
LVEF at DIS ≤ 40 %	683	286 (42 %)	588	241 (41 %)	95 (37 %)	51 (47 %)	13 (45 %)	82 (42 %)	0.11
Main presentation:	768		660						0.48
-Severe peripheral oedema %		59 (8 %)		50 (8 %)	20 (7 %)	6 (5 %)	5 (16 %)	19 (9 %)	
-Severe breathlessness at rest%		225 (29 %)		204 (31 %)	94 (34 %)	36 (30 %)	8 (25 %)	64 (29 %)	

-Increasing exertional breathlessness %		356 (46 %)		285 (43 %)	115 (40 %)	53 (44 %)	17 (53 %)	100 (45 %)	
-Chest pain-cardiac %		72 (9 %)		67 (10 %)	28 (10 %)	16 (13 %)	2 (6 %)	21 (9 %)	
-Other symptom %		56 (7 %)		54 (8 %)	24 (9 %)	10 (8 %)	0 (0 %)	17 (8 %)	
Urea at DIS mmol/L	776	9 [7 - 14]	669	9 [6 - 14]	8 [6 - 11]	9 [6 - 14]	18 [11 - 25]	11 [8 - 15]	0.17
Creatinine at DIS µmol/L	774	106 [84-141]	668	106 [84-143]	97 [80-125]	104 [86-141]	161 [111 -210]	119 [91 - 157]	0.26
Depression HADS	371		300						<0.05
-None-to-mild %		316 (85 %)		255 (85 %)	122 (91%)	44 (83 %)	13 (81 %)	76 (78 %)	
-Moderate-to-severe %		55 (15 %)		45 (15 %)	12 (9 %)	9 (17 %)	3 (19 %)	21 (22 %)	
Anxiety HADS	366		296						<0.01
-None-to-Mild %		300 (82 %)		243 (82 %)	120 (89 %)	35 (70 %)	14 (87 %)	74 (78 %)	
-Moderate-to-severe %		66 (18 %)		53 (18 %)	15 (11 %)	15 (30 %)	2 (13 %)	21 (22 %)	
GPCOG score ≤ 4 %	380	28 (7 %)	315	25 (8 %)	7 (5 %)	2 (4 %)	3 (18 %)	13 (13 %)	0.11
Living alone %	660	218 (33 %)	566	184 (33 %)	74 (30 %)	32 (30 %)	9 (36 %)	69 (33 %)	0.29
Trouble bathing/dressing %	644	157 (24 %)	553	134 (24 %)	46 (19 %)	24 (23 %)	10 (42 %)	54 (30 %)	<0.05
Get up and go test:									
-Able to complete %	614	285 (46 %)	520	242 (46 %)	116 (51 %)	40 (42 %)	7 (29 %)	79 (45 %)	<0.1
Time to complete sec	285	9 [6 - 15]	242	10 [6 - 16]	8 [6 - 12]	11 [8 - 20]	15 [4 - 22]	12 [8 - 20]	0.14

MI Myocardial infarction; NYHA New York Heart Association; ADM admission; DIS discharge; LVEF left ventricular ejection fraction; HADS Hospital Anxiety and Depression Scale; GPCOG General Practitioner assessment of Cognition.

Table 2 (a) Univariable Cox regression model for first unplanned readmission or death (b) Univariable Anderson-Gill model for recurrent events. (*) 0.1 level of significance; (**) NYHA class which was evaluated as the worst class during the last 7-days before admission; (***) the closest measurement to discharge.

	(a) First event only				(b) Recurrent events			
	(N*/events)	**HR**	**95% CI**	**P-value***	**(N / events)**	**HR**	**95% CI**	**P-value***
Women yes	(779 / 559)	0.97	0.82 - 1.15	0.70	(2110 / 1600)	1.06	0.88 - 1.27	0.53
Age years	**(779 / 559)**	**1.24**	**1.15 – 1.35**	**<0.001**	**(2110 / 1600)**	**1.29**	**1.16 – 1.43**	**<0.001**
(10 unit increase)								
Diabetes yes	(779 / 559)	1.10	0.93 – 1.30	0.28	**(2110 / 1600)**	**1.34**	**1.12 – 1.59**	**<0.001**
History of MI yes	**(779 / 559)**	**1.29**	**1.07 – 1.55**	**<0.01**	**(2110 / 1600)**	**1.33**	**1.10 – 1.62**	**<0.01**
COPD yes	**(779 / 559)**	**1.43**	**1.14 – 1.79**	**<0.01**	**(2110 / 1600)**	**1.50**	**1.20 – 1.89**	**<0.001**
Cancer yes	(779 / 559)	0.97	0.74 – 1.27	0.83	(2110 / 1600)	1.04	0.78 – 1.40	0.77
NYHA **: Class I or II yes	(672 / 468)	1	-	-	(1785 / 1343)	1	-	-
NYHA: Class III yes		1.05	0.76 – 1.44	0.77		1.10	0.81 – 1.49	0.53
NYHA: Class IV yes		1.19	0.85 – 1.68	0.31		1.29	0.92 – 1.81	0.14
Hypertension at ADM yes	(726 / 515)	1.03	0.86 - 1.23	0.73	(1957 / 1477)	1.04	0.86 - 1.25	0.70
Log(NT-proBNP) pg/mL ***	(664 / 477)	1.05	0.98 – 1.14	0.17	(1833 / 1396)	1.02	0.96 – 1.12	0.32
Sinus Rhythm at DIS yes	(779 / 559)	0.91	0.76 - 1.08	0.28	(2110 / 1600)	0.95	0.79 – 1.13	0.57
LVEF at discharge: ≤40% yes	(683 / 479)	1.20	1.00 – 1.44	<0.05	(1845 / 1395)	1.17	0.97 – 1.41	0.10
Main presentation:	(768 / 548)				(2076 / 1571)			
-Severe peripheral oedema yes		1	-	-		1	-	-
-Severe breathlessness at rest yes -		0.94	0.64 – 1.38	0.74		0.84	0.59 – 1.20	0.35
Increasing exertional		1.07	0.74 – 1.56	0.71		1.02	0.73 – 1.45	0.89
breathlessness yes								
-Chest pain - cardiac yes		1.11	0.72 – 1.70	0.64		1.00	0.65 – 1.53	1.00
-Other symptom yes		1.06	0.68 – 1.64	0.81		0.92	0.61 – 1.37	0.67
Urea at discharge mmol/L	**(776 / 557)**	**1.27**	**1.15 – 1.40**	**<0.001**	**(2099 / 1590)**	**1.25**	**1.15 – 1.36**	**<0.001**
(10 unit increase)								
Creatinine at discharge µmol/L	**(774 / 556)**	**1.54**	**1.38 – 1.72**	**<0.001**	**(2094 / 1587)**	**1.54**	**1.39 – 1.72**	**<0.001**
Depression HADS	**(371 / 227)**				**(866 / 596)**			
-None-to-mild yes		**1.00**	–	–		**1.00**	–	–
-Moderate-to-severe yes		**1.73**	**1.24 – 2.41**	**<0.01**		**1.76**	**1.25 - 2.47**	**<0.001**
Anxiety HADS	**(366 / 222)**				**(848 / 581)**			

-None-to-mild yes		**1.00**	–	–		**1.00**	–	–
-Moderate-to-severe yes		**1.64**	**1.24 – 2.18**	**<0.001**		**1.37**	**1.03 - 1.84**	**<0.05**
GPCOG score ≤ 4 yes	**(380 / 232)**	**1.70**	**1.06 – 2.71**	**<0.05**	**(903 / 628)**	**1.58**	**1.00 – 2.50**	**<0.1**
Living alone yes	(660 / 465)	1.14	0.94 - 1.39	0.18	**(1781 / 1341)**	**1.37**	**1.12 – 1.67**	**<0.01**
Trouble bathing or dressing yes	**(644 / 453)**	**1.48**	**1.20 – 1.83**	**<0.001**	**(1736 / 1303)**	**1.27**	**1.02 – 1.57**	**<0.05**
Get up and go test:								
-Able to complete yes	**(614 / 421)**	**0.72**	**0.59 – 0.87**	**<0.001**	**(1646 / 1229)**	**0.81**	**0.66 – 0.99**	**<0.05**
-Time to complete sec	**(285 / 169)**	**1.02**	**1.01 – 1.03**	**<0.001**	**(701 / 495)**	**1.02**	**1.01 – 1.03**	**<0.001**

HR Hazard Ratio; CI Confidence Interval NYHA New York Heart Association; LVEF left ventricular ejection fraction; HADS Hospital Anxiety and Depression Scale; GPCOG General Practitioner assessment of Cognition.

Table 3 (a) Adjusted Cox regression model for first unplanned readmission or death (b) Adjusted Anderson-Gill model for recurrent events. (*) 0.1 level of significance; (**) each variable is adjusted for the most significant (P<0.01) clinical variables including age, diabetes, history of MI, COPD, urea and creatinine at discharge (see Table 2).

	(a) First event only **			(b) Recurrent events **		
	HR	**95% CI**	**P-value ***	**HR**	**95% CI**	**P-value ***
Depression HADS						
-None-to-mild yes	**1.00**	–	–	**1.00**	–	–
-Moderate-to-severe yes	**1.74**	**1.24 - 2.44**	**<0.01**	**1.77**	**1.44 - 2.17**	**<0.001**
Anxiety HADS						
-None-to-mild yes	**1.00**	–	–	**1.00**	–	–
-Moderate-to-severe yes	**1.67**	**1.21 - 2.30**	**<0.01**	**1.35**	**1.11 - 1.65**	**<0.01**
GPCOG score ≤ 4 yes	1.43	0.90 – 2.28	0.12	**1.40**	**1.06 – 1.85**	**<0.05**
Living alone yes	1.04	0.85 – 1.27	0.71	**1.24**	**1.11 – 1.39**	**<0.001**
Trouble bathing or dressing yes	**1.33**	**1.07 – 1.65**	**<0.01**	**1.18**	**1.04 – 1.35**	**<0.05**
Get up and go test:						
-Able to complete yes	**0.81**	**0.66 – 0.99**	**<0.05**	0.95	0.84 – 1.07	0.38
-Time to complete sec	**1.02**	**1.01 – 1.03**	**<0.01**	**1.01**	**1.01 – 1.02**	**<0.001**

HR Hazard Ratio; CI Confidence Interval; HADS Hospital Anxiety and Depression Scale; GPCOG General Practitioner assessment of Cognition.

Figures

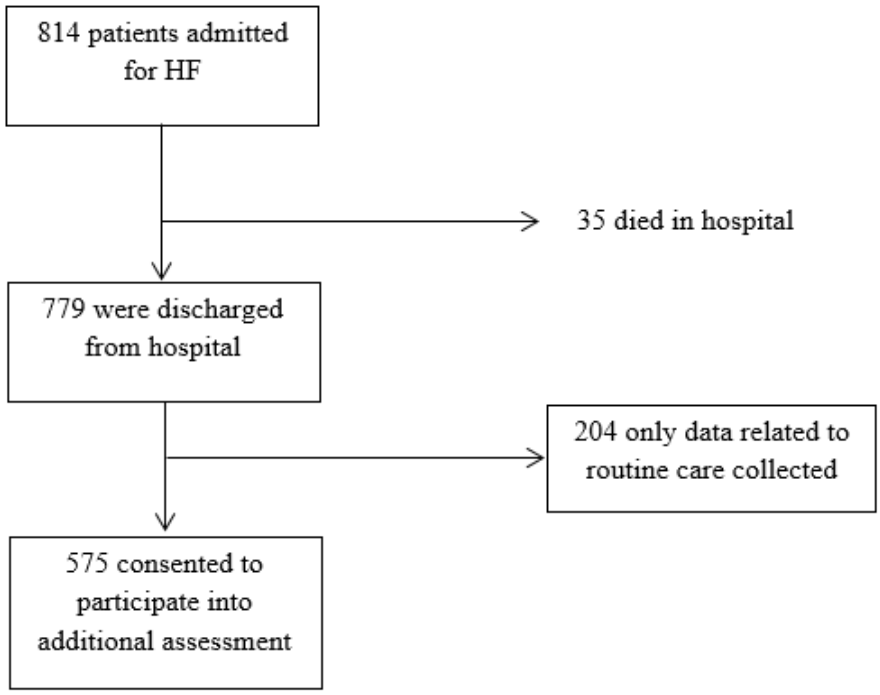

Figure 1 Consort Diagram

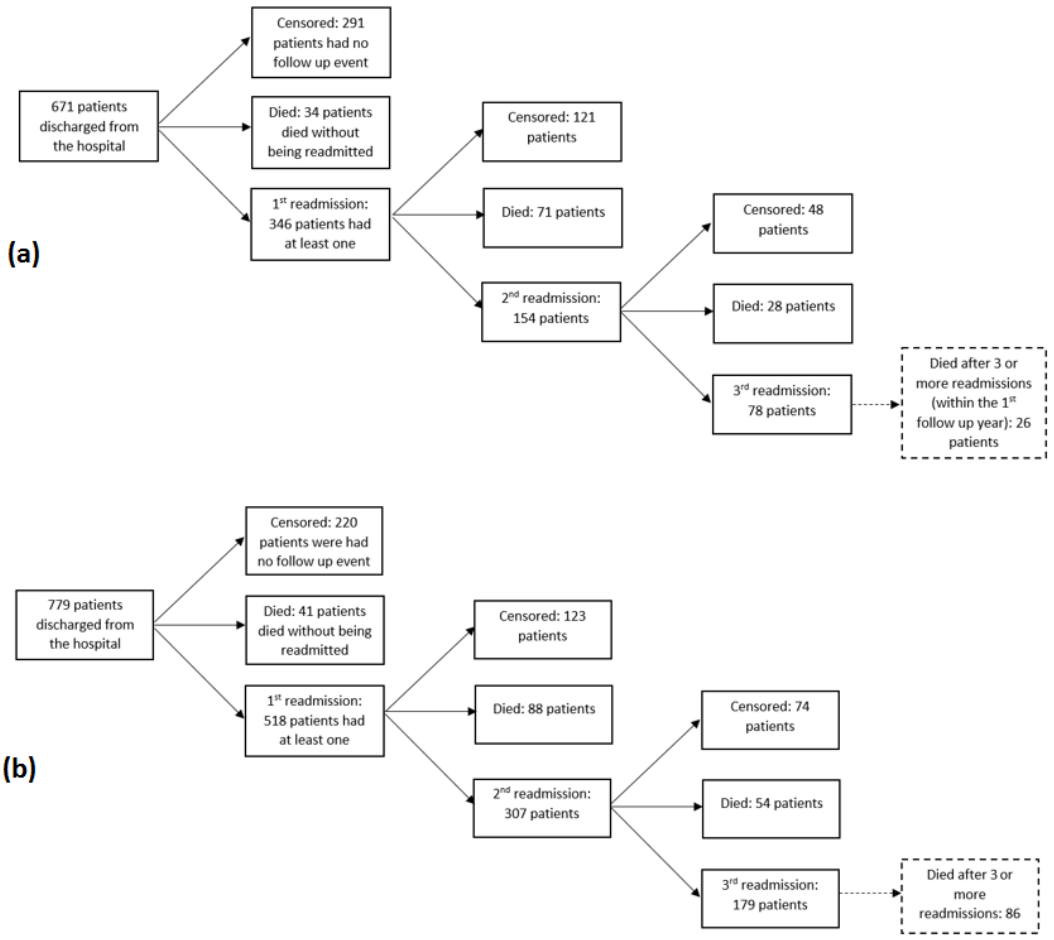

Figure 2 (a) Diagram of events within first year of discharge, based on 671 patients surviving to index-admission discharge and with known outcome at one year; (b) Diagram of all events for 779 patients discharged after the index-admission (including those not censored at one year).

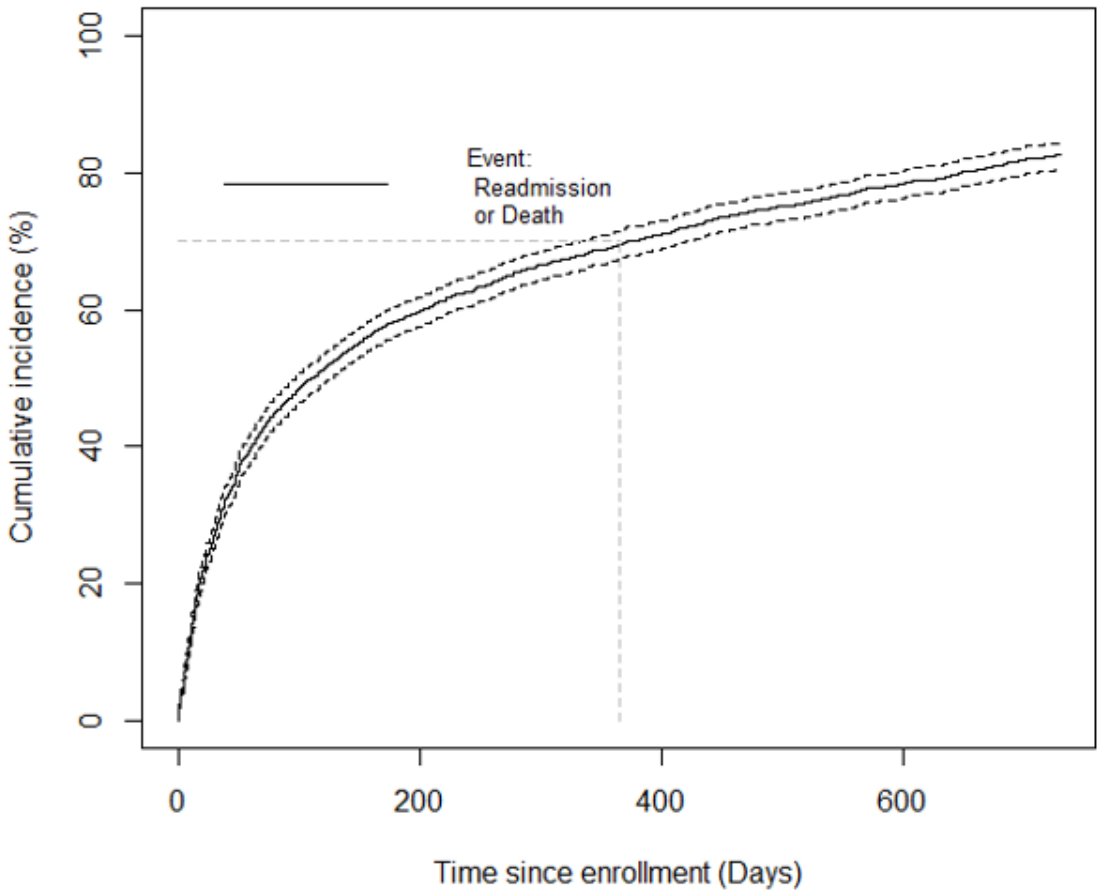

Figure 3 Cumulative incidence plot of events; recurrent readmissions and mortality. For the plot gap times are used. That means that every recurrent event of a patient is taken into account as a new sample for the calculations starting from point zero. Dotted grey lines: incidence rate at 1 year; Dotted black lines: 95% confidence interval.

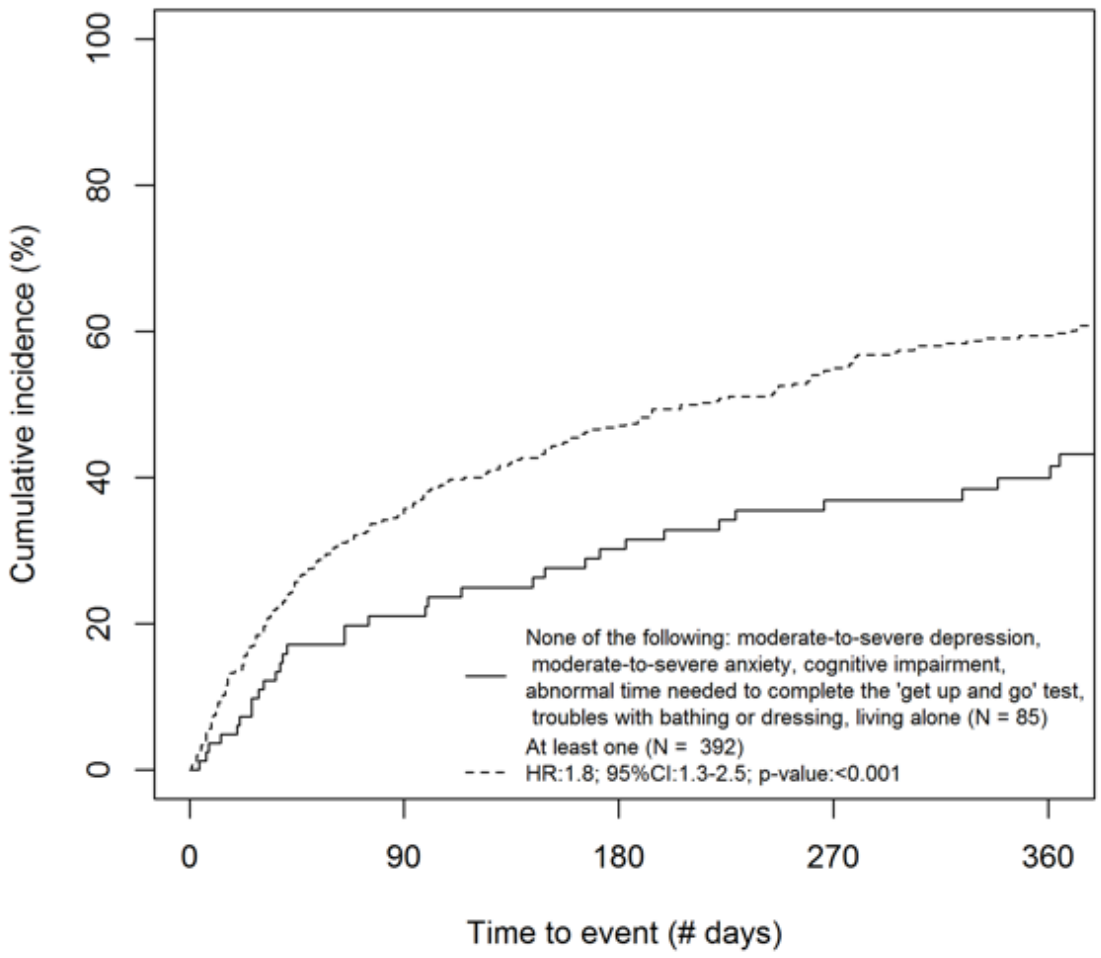

Figure 4 Cumulative incidence plot of events (recurrent readmissions and mortality) of patients having at least one psychosocial factor assessed negatively compared to those with none, adjusted for significant demographic and clinical factors. We used data of the 477 patents who had participated to at least one of the psychosocial assessments.