OPeRA-HF

An **O**bservational study to assess and **P**redict the in-patient course, risk of **R**e-Admission and mortality for patients hospitalised for or with **H**eart **F**ailure

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Background:

Heart failure (HF) is a complex syndrome, the final common pathway of many different pathological processes and usually accompanied by other serious co-morbid conditions. It is a common reason for urgent hospitalisation. The subsequent health trajectory of such patients discharged after an admission for HF is variable. Identifying those patients at high risk of re-admission or death and understanding the causes could improve discharge planning and the targeting of monitoring and community support. At present, there is no robust model for clinical practice.

Previous risk models of HF re-admission or death have usually been derived from registries or clinical trial data; have shown limited predictive accuracy and their results have not been reproduced. They have also focused on clinical and demographic variables with little attention to the effects of frailty, cognitive function, mood, social network, deprivation and lifestyle. Very few models have made use of repeated measurements during an admission. Designing or identifying a model that can characterise patients with HF in order to predict those at highest risk of (cardiovascular) re-admission and death could make a substantial difference to care by facilitating management tailored to the individual patient.

PANEL A: Study aims

1. To establish the causes of admission or re-admission of patients with HF to the Hull & East Yorkshire Hospitals NHS Trust and classify them according to primary and contributory causes, severity, urgency and whether they were avoidable or appropriate.
2. To identify the primary reason and contributory factors to death within the first 6 months after discharge, including the events leading up to death and the place of death
3. To develop one or more risk stratification models to identify patients with HF at high risk of early death and re-admission, who are in need of intensive support and early hospitalisation and to identify those at very low risk who could be discharged early. Importantly, unlike conventional prognostic models of HF, information on measures of patient-frailty, cognition and social support network will be collected. This will create a holistic picture of the challenges facing patients with HF and the services required to support them.
4. To use the data captured in this study to validate previously published risk models.

Measurement	Enrol-ment*	Pre Dis-charge	Dis-charge
Demographics and socio-economic status	X		
Clinical and family history	X		
HF related symptoms (e.g. breathlessness, orthopnoea, nocturnal dyspnoea, chest pain, etc)	X		
Lifestyle	X		
Quality of sleep	X		
Mood and cognitive function	X		
Medication and devices e.g. CRT, ICD	X		
Social deprivation and support	X		
Admission procedures performed / discharge details	X		X
Results of ECG, Echo (if available)	X		X
Frailty test result (if available)	X		
Prediction of outcome (clinician/patient perceived)	X		X
Mobility tests – 50m corridor walk test	X	X	
Vital signs: Blood pressure lying/standing, heart rate, height and weight, presence of lung and peripheral oedema jugular venous pressure, transcutaneous arterial oxygen saturation, lung function	X	X	
Routine haematology/biochemistry blood tests	X	X	X
Charlson co-morbidity index score (where recorded)	X		
Questionnaires: Berlin Sleep, Hospital Anxiety & Depression Scale, HF Knowledge, Dutch HF Knowledge and EQ-5D	X		
Bio-impedance	X	X	

Table 1: Measurement schedule (*3-7 days after admission)

Study design:

A prospective observational study collecting demographic, clinical and psycho-social data during hospital admission, in-patient stay and pre discharge timeframes. Patients with a confirmed diagnosis of HF will be invited to take part. Patients will be identified from cardiology, medical elderly and acute admission wards at the two main hospitals serving the Hull & East Yorkshire area. Written consent will be obtained from the patient by a doctor or research nurse. Ethics approval was sought and granted in October 2012.

The study aims are shown in ***Panel A*** and the inclusion and exclusion criteria in ***Panel B***.

PANEL B: Inclusion and exclusion criteria

Inclusion criteria: (a) Age > 18 years; (b) In hospital; (c) Usual residence is in the catchment region for Hull & East Yorkshire Hospitals NHS Trust; (d) Either treated with loop diuretics or with a clinical diagnosis of HF (prior research has shown that patients treated with loop diuretics have a similar prognosis to patients with HF, suggesting that the diagnosis of HF may often be over-looked.); (e) Willing and able to consent.

Exclusion criteria: Unable to understand and comply with the protocol or to give informed consent

Study / Data set used / End-point	Model type & Variables in model
Fonarow (2005) / ADHERE / In-hospital mortality	Logistic regression model: *BUN, systolic BP, heart rate, age //* CART model: *BUN, systolic BP, creatinine*
O'Connor (2012) / PROTECT / Combined death, WHF, or re-hospitalization for HF within 7 days of index admission	Cox-regression model: *BUN, respiratory rate, systolic BP, heart rate, albumin, cholesterol, diabetes, prior HF hospitalisation*
O'Connor (2008) / OPTIMIZE-HF / All-cause mortality after discharge Combined mortality or re-hospitalisation after discharge	Cox regression model: *Admission: systolic BP, age, weight, reactive airway disease, depression, sodium, creatinine, liver disease, lower-limb oedema; Discharge: statin, beta-blocker, creatinine, systolic BP* Logistic regression model: *Admission: systolic BP, creatinine, haemoglobin, taking a nitrate/digoxin/diuretic, history of COPD, prior CVA/TIA, HF hospitalisation in last 6 months ;During admission: coronary angiography / mechanical ventilation / ICD implant; Discharge: statin/ACEi/ARB*
Pocock (2006) / CHARM / All-cause mortality Combined mortality & re-hospitalisation	Cox regression model: *Age, LVEF, diabetes, BMI, female, NYHA, current smoker, BBB, cardiomegaly, prior HF hospitalisation <6-months, diastolic BP, diagnosis of HF >2years, prior MI, dependent oedema, heart rate, pulmonary crackles, pulmonary oedema, AF, resting dyspnoea, candesartan (vs placebo).* Cox-regression model: *Age, diabetes, LVEF, prior HF hospitalisation <6-month, cardiomegaly, diagnosis of HF >2 years, NYHA class, diastolic BP, BBB, heart rate, candesartan (vs placebo), dependent oedema, pulmonary crackles, female, AF, BMI, mitral regurgitation, previous MI, pulmonary oedema, current smoker*
Felker (2004) / OPTIME-CHF / 60-day mortality Combined 60-day mortality or re-hospitalisation	Logistic regression model: *Age, NYHA, systolic BP, BUN, sodium* Logistic regression model: *Prior HF admission <12-months, systolic BP, BUN, haemoglobin, history of PCI*
Chin & Goldman (1997) / Routine clinic / 60-day mortality Combined 60-day mortality or re-hospitalisation	Cox regression model: *diabetes, admission systolic BP, non-sinus rhythm* Cox regression model: *Admission systolic BP, no ST wave changes, Charlson's co-morbidity score (22 conditions), single*
Krumholz (2000) / Routine clinic / All-cause re-admission	Cox regression model: *Creatinine, hospitalisation in last year, HF admission history, diabetes*
Keenan (2008) / CMS Medical / 30-day all-cause re-admission	Logistic regression: *Gender, age, history of CABG, plus 34 co-morbidities from CMS medical hierarchical condition categories*

Table 2: Some of the risk models to be validated using the OPERA-HF study data

	Valid n	n (%) or Median [25th – 75th]
Age (years)	185	75 [67 – 81]
Male (%)	182	123 (67.6%)
Clinical History		
Myocardial Infarction	168	53 (31.5 %)
CVA/TIA	165	7 (4.2%)
Peripheral vascular disease	163	6 (3.7%)
Device (ICD, PPM, CRT, CRT-D)	185	31 (16.8%)
Lung disease (COPD, Asthma, etc)	165	44 (26.7%)
Diabetes	166	60 (36.1%)
Chronic kidney disease	164	38 (23.2 %)
Liver disease	165	5 (3 %)
Gastro-intestinal disease	165	14 (8.5 %)
Joint or connective tissue disease	165	45 (27.3 %)
Cancer (inc. leukaemia lymphoma)	164	6 (3.7 %)
Examination		
Main presenting symptom	170	
Acute SOB		75 (44.1%)
Breathless on slight exertion		66 (38.8%)
Chest pain – cardiac		14 (8.2%)
Syncope		3 (1.8%)
Severe oedema		7 (4.1%)
Other symptom		5 (2.9%)
Heart rate (bpm)	159	91 [74 - 112]
Heart Rhythm	163	
Sinus Rhythm		58 (35.6 %)
Atrial fibrillation		80 (49.1 %)
Other rhythm		25 (15.3 %)
Systolic BP (mmHg)	166	125 [110 - 143]
Worst NYHA in last 7-days	147	
Class II		20 (13.6 %)
Class III		89 (60.5 %)
Class IV		38 (25.9 %)
HF Medication		
ACE-inhibitor	161	74 (46 %)
Beta-blocker	159	87 (54.7 %)
Aldosterone Receptor Antagonist	158	39 (24.7 %)
Loop diuretic	161	102 (63.4 %)
Thiazide	155	17 (11%)
Digitalis	158	23 (14.6 %)
LV-Impairment*	154	
None / Trivial		35 (22.7%)
Mild / Mild-to-mod / Moderate		54 (35.1%)
Mod-to-Sever / Severe		65 (42.2%)
NT-proBNP (ng/L)*	144	5063 [2243 – 10468]

Table 3: Admission characteristics of patients recruited (*nearest to discharge)

Study methods:

Data Collection: Patients will be enrolled into the study in the post-acute phase of their care, generally 3-7 day after admission. Data will be collected at enrolment and on or close to the day of discharge. A summary of the data to be collected at enrolment, prior to discharge and at discharge is shown in ***Table 1***. The primary end-points for model development will be death or re-admission for (a) any reason, (b) cardiovascular disease (c) worsening HF at (i) 30-days, (ii) 6-months and (iii) 1-year.

Patient follow-up: Patients will be followed according to their consultant's instructions. They may be discharged back to their General Practitioner or followed up in a medical, cardiology or HF clinic. Follow up will be for up to ten years after the last patient is enrolled.

The data collected will be used to investigate the utility of previously published models (see ***Table 2***) to determine the incremental value of a new model derived from these data.

Results:

So far, 185 patients have been recruited. ***Table 3*** shows a limited set of admission characteristics for these patients.

Conclusion:

This study will provide insight into the factors which influence re-admission after hospitalisation for HF. The data collected will result in a risk stratification model enabling the identification of patients at most risk of 30-day re-admission or death. It is envisaged that such a model will facilitate an improved discharge-planning pathway.

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