Scottish Heart Failure Hub Business case for the funding of NT-proBNP for the diagnosis and management of patients with Heart Failure in NHS Scotland

Drs Clare Murphy, Ross Campbell, Colette Jackson,
Roy Gardner, Mark Petrie, David Murdoch and Professor John McMurray
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Objective

To secure funding for NT-proBNP in NHS Scotland.

This will:

1) Make the diagnosis of heart failure (HF) more accurate and efficient. (breathless or oedematous patients with a low NT-proBNP are very unlikely to have HF and do not need a cardiology assessment or echocardiogram).
2) Reduce the number of cardiology outpatient referrals and outpatient echocardiograms. The existing HF diagnostic pathway (HFDP) in NHS Greater Glasgow and Clyde (NHS GG&C) reduced echocardiography and cardiology outpatient appointments for HF diagnosis by 50%.
3) Facilitate early discharge of low risk (i.e. low NT-proBNP) patients from clinic follow up.
4) Reduce the number of patients admitted from A+E (low NT-proBNP patients are very unlikely to have HF and are at low risk of cardiac events).
5) Among patients admitted, reduce the number of inpatient cardiology referrals and inpatient echocardiography.
6) Improve the triage of high risk (i.e. high NT pro BNP) patients with HF in secondary care to the cardiology team and cardiology areas rather than non-specialist areas. Specialist management of HF in the England and Wales audit was associated with a 50% reduction in mortality.
7) Reduce length of stay in secondary care. Patients with elevated NT-proBNP levels that fall with treatment are at lower risk and can be discharged early.
8) Identify the most appropriate patients for management by the HF liaison nurse service and facilitate early discharge of low-risk, low NT pro BNP, patients from this service.
9) Improve the ability of NHS Scotland to institute the Scottish Patient Safety Programme's HF Bundle.
10) Align NHS Scotland with International and National (NICE) guidelines for the management of acute HF.
11) Update existing HFDPs that use BNP at the interface between primary and secondary care.
12) Improve on the prognostic information available to clinicians and patients.

Cost saving and efficiency

1. Reduction in echocardiography.
2. Reduction in cardiology clinic appointments.
3. Reduction in length of stay.
4. Reduction in admission and readmission rates.
5. Reduction in CT scan and Doppler ultrasound requests: Of the 50 most recently recruited patients into a HF project in the Western Infirmary, Glasgow, 8 patients underwent CT pulmonary angiogram, CT chest /abdomen/pelvis or Doppler ultrasound of their legs to investigate the cause of their symptoms. Evidence of HF and no alternative diagnosis was found in all of these scans. These patients were all subsequently found to have very high natriuretic peptide levels when recruited to the HF study. If a natriuretic peptide had been measured at the outset, the CT and ultrasound scans would not have been requested.
6. More accurate diagnosis of HF and more accurate diagnostic exclusion of HF resulting in more accurate patient management.
7. Cost saving by replacing BNP with NT-proBNP for NHS Scotland HFDPs.
8. Cost saving when introducing the new HF drug, Sacubitril/valsartan

Background

HF represents a rising healthcare concern

HF is associated with frequent, recurrent and prolonged hospital admissions, high morbidity, poor quality of life and therefore a large burden of cost.

HF is associated with high mortality

One-year mortality rates for HF are around 27% following a hospital admission for HF which is worse than many types of cancer.

HF is common

Approximately 1-2% of the adult population in developed countries has HF with the prevalence rising to ≥10% in those aged ≥70 years of age.

There is much we can do to manage these patients well

Recent advances in medical therapy, including ACE inhibitors, beta-adrenoceptor antagonists and mineralocorticoid receptor antagonists together with multidisciplinary team working has given us an armamentarium to manage these patients well and keep them out of hospital. Published data from the 2013-14 national HF Audit in England and Wales demonstrated an almost 50% in-patient mortality reduction for HF patients if they receive the correct diagnosis, are managed on a cardiology ward and are followed up by a specialist HF team, in comparison to HF patients who are managed by a non-specialist team for example on general medical wards.

Timely diagnosis of HF

The starting point for appropriately treating a patient with HF is making a timely diagnosis. The diagnosis can be difficult however, especially in the early stages of HF, because the symptoms can be non-specific. The ECG and echocardiogram are the most useful tests and National/International HF guidelines together with the Scottish Patient Safety Programme (SPSP) specify that a patient suspected of having acute HF should have an echocardiogram within 48 hours of admission. This places a huge burden upon cardiac departments and therefore is difficult to achieve in

practice. Additionally, because the signs and symptoms of HF are non-specific, many patients referred for echocardiography are found to have no significant cardiac abnormality despite waiting in hospital for many days to have their echocardiogram performed. This creates an unnecessary use of hospital bed days and a delay in proper treatment. More worryingly, the difficulty in making a correct diagnosis of acute HF without an echocardiogram can lead to patients being under diagnosed and inappropriately treated for another pathology such as a respiratory problem. This leads to early readmissions because the patient has not been properly managed.

B-type Natriuretic Peptides for the diagnosis of HF

B-type natriuretic peptide (BNP) and NT-proBNP, a family of hormones secreted in increased amounts when the load on any cardiac chamber is increased (as found in patients with HF) are known to independently predict morbidity and mortality in patients with HF.

A normal natriuretic peptide level in an untreated patient virtually excludes significant cardiac disease making an echocardiogram unnecessary and this has very important implications.

A single elevated measurement of BNP or NT-proBNP, by means of a venous blood test, is associated with an adverse prognosis and an increase in concentration over time or a level that fails to fall is associated with a poor outcome.

BNP is useful in providing a 'rule-out' test for acutely breathless patients, where HF is one of the differential diagnoses, because the presence of a normal natriuretic peptide in this situation virtually excludes a diagnosis of HF.

The International Collaborative of NT-pro-BNP Study (figure 1) demonstrated the use of this particular natriuretic peptide as a 'rule out' test in the investigation of 1256 acutely breathless patients and showed a sensitivity of 99% when using a cut-off point of 300pg/ml to exclude HF as the diagnosis.

In patients with a diagnosis of HF during hospital admission, reduction of natriuretic peptide levels by 30% with appropriate inpatient therapy results in a reduced 30 day readmission rate. Additionally, a HF study performed, by several of the co-applicants, in over 1000 GG&C patients hospitalised with decompensated HF found that elevated BNP concentration 4-6 weeks post-discharge was one of 5 clinical variables that independently predicted mortality risk over a median 3 year period.

In another GG&C HF study over 79 weeks of recruitment, 356 near consecutive, consenting patients presenting with signs and symptoms of HF had blood taken for BNP. 332 had a high BNP, with 279 of them (84%) having confirmed HF on subsequent echocardiography. 24 (7%) had a BNP less than 100pg/ml and these patients had a subsequently normal echo. A number of patients with signs of HF were initially started on an alternative treatment pathway (e.g. for lower respiratory tract infection) and this was appropriately changed early into admission based on the BNP result.

The National Institute for Health and Care Excellence (NICE) have recently published a review (October 2014) of "the diagnostic accuracy of, and economic evidence for, serum natriuretic peptides in patients presenting in an acute care setting with suspected HF". The guideline group included forty-nine studies in its review and concluded that both BNP and NTproBNP were very cost effective. Reduction in resources was mainly driven by fewer admissions, fewer readmissions and reduced

length of stay. As a result, NICE have recommended the measurement of BNP or NTproBNP in their 2014 Acute HF clinical guideline.

Benefits of using this test would therefore include a reduction in the number of echocardiograms being requested; a reduction in patients staying in hospital to wait for an echocardiogram to confirm/refute their diagnosis; more appropriate investigations of the correct aetiology of the patient's symptoms if the natriuretic peptide level is normal; more accurate diagnosis of patients with HF; more appropriate/timely referral to a specialist HF team; improved treatment and management; shorter length of hospital stay; a reduction in readmissions and adherence to National and International guidelines. All of these benefits are to the overall benefit of the patient and the healthboard.

Cost savings when introducing the new HF drug – Sacubitril/valsartan

A new class of HF drug therapy 'Angiotensin Receptor Neprilysin Inhibitor' (ARNI) has recently emerged. The results of the landmark PARADIGM-HF clinical trial comparing the ARNI, Sacubitril/valsartan, against a current gold standard therapy for HF, the Angiotenisn Converting Enzyme (ACE) inhibitor, Enalapril, have been presented and published. PARADIGM-HF was stopped early due to overwhelming benefit of Sacubitril/valsartan over Enalapril in providing a 20% reduction in the risk of death and hospitalisation for HF. Sacubitril/valsartan has already been licenced in Europe and awaits a decision from the Scottish Medicines Consortium (SMC), anticipated in the first quarter of 2016.

This is very important when planning services which include measurement of natriuretic peptide levels for two reasons: firstly, Sacubitril/valsartan is expensive at an anticipated cost of between £1200-£1500 per patient per year. PARADIGM-HF however, required patients to have an elevated natriuretic peptide. Access to NTproBNP would therefore ensure that this drug, which will be life saving for eligible patients, will not be prescribed unless patients meet strict criteria including having an elevated NTproBNP. This will result in significant cost savings when Sacubitril/valsartan is introduced by reducing inappropriate use of the drug. Secondly, ARNIs inhibit the breakdown of BNP but not NT-proBNP. This means that whilst NTproBNP would remain useful as a prognostic marker in patients taking this drug, BNP would no longer be useful.

Adherence to National and International Guidelines

NICE, the European Society of Cardiology (ESC) and the forthcoming Scottish Intercollegiate Guidelines Network (SIGN) guidelines for the diagnosis and treatment of HF all recommend measuring the blood concentration of a natriuretic peptide in patients presenting acutely with symptoms suspected to be due to HF.

Timeline for Implementation

Subject to funding of the assay, NT-proBNP would be immediately available in-house on a Roche analyser in all NHS Scotland biochemistry departments. This will require collaboration between NHS Scotland, Roche, Abbott and Siemens as the latter two companies provide the laboratory platforms currently used in NHS Scotland healthboards, but they do not have a NTproBNP analyser.

How will NT-proBNP be used?
See Figures 2 and 3

We would envisage blood being drawn for NT-proBNP in the Emergency departments or Acute Medical Admission Units, as a one off, "rule-out" test for any patient with a 'possible' diagnosis of acute HF where clinical symptoms, signs, ECG, CXR and routine blood tests have neither clearly confirmed a diagnosis of acute HF nor confirmed an alternative cause for the patient's symptoms. A normal NT-proBNP in this situation would allow the examining physician to exclude a diagnosis of HF without requiring further investigations such as echocardiography.
Patients with elevation of NT-proBNP would be treated for a confirmed diagnosis of HF in a timely manner and be triaged to and managed by a specialist HF team. A pre-discharge NT-proBNP would be measured to assess response to therapy and to guide risk stratification and follow-up intensity required, to minimise the risk of multiple readmissions.
We would also envisage the opportunity for General Practitioners (GPs) to access NT-proBNP from the community as part of a locally agreed "diagnostic pathway" protocol. An example of such a pathway is shown in figure 3. In this situation, a normal NT-proBNP would allow GPs to exclude the diagnosis of HF in patients with symptoms that could be due to HF, without the patient requiring echocardiography or assessment in a cardiology clinic.

Financial cost
NT-proBNP costs £15 per assay.

Measurement on admission: It is difficult to quantify how many patients will require a measurement of NT-proBNP. Patients who present to hospital with symptoms compatible with HF (ie breathlessness) often have blood tests to exclude pulmonary embolism (Ddimer) and myocardial infarction (Troponin). In the financial year of 2012-13, combining the three main GG&C hubs of Glasgow Royal Infirmary, the Southern General Hospital and the Royal Alexandra Hospital, approximately 60,000 blood samples were sent at admission for Troponin measurement costing approximately £400,000 and approximately 30,000 blood samples were sent for D-Dimers measurement.
The number of requests expected for NT-proBNP would be significantly less than for troponin because the majority of patients who present with chest pain (requiring troponin measurement) do not have clinical signs of HF.

Pre discharge measurement: In addition to measuring NT-proBNP acutely in the Emergency departments and Acute Medical Admission Units, we addressed how many patients with a diagnosis of HF during admission would require pre discharge NT-proBNP measurements. In the year 2012-2013, from a population of around 1.3 million people in GG&C, there were 3070 discharges of patients with a diagnosis of HF in the 1st or 2nd coding position. If all of these patients had a pre discharge NT-proBNP it would represent a cost of £46,050 per year.

Updating existing HFDPs: HFDPs in Scotland predominantly use BNP at a cost of £22 per measurement. As an example of cost savings that could be made in this area, approximately 1000 patients were seen in the GG&C HFDP in the year 2013-2014 and of them, two thirds had BNP measured. The cost of NT-proBNP is £15 per measurement and therefore if we used NT-proBNP instead of BNP it would represent a cost saving of around £4,600.

Conclusion

Implementing the routine use of NT-proBNP is an important advance for NHS Scotland and will allow our Health Boards to continue to have an enviable reputation as boards that deliver gold standard care to patients with HF.

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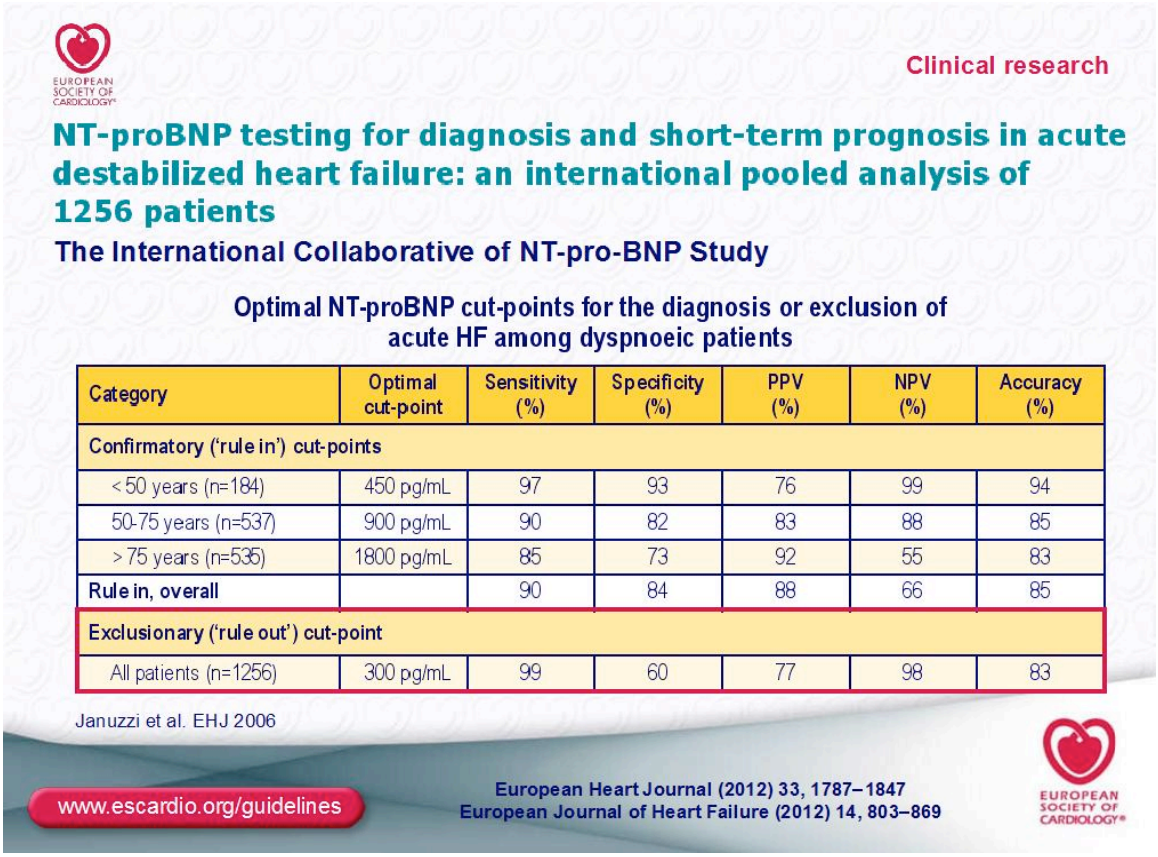
Figure 1: European Heart Journal (2012) 33, 1787-1847. European Journal of Heart Failure (2012) 14, 803-869



Clinical research

NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients

The International Collaborative of NT-pro-BNP Study

Optimal NT-proBNP cut-points for the diagnosis or exclusion of acute HF among dyspnoeic patients

Category	Optimal cut-point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Confirmatory ('rule in') cut-points						
< 50 years (n=184)	450 pg/mL	97	93	76	99	94
50-75 years (n=537)	900 pg/mL	90	82	83	88	85
> 75 years (n=535)	1800 pg/mL	85	73	92	55	83
Rule in, overall		90	84	88	66	85
Exclusionary ('rule out') cut-point						
All patients (n=1256)	300 pg/mL	99	60	77	98	83

Januzzi et al. EHJ 2006

www.escardio.org/guidelines

European Heart Journal (2012) 33, 1787–1847
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Figure 2: Suggested flow diagram to guide the use of NTproBNP in Emergency Departments and Acute Medical Admission Units.

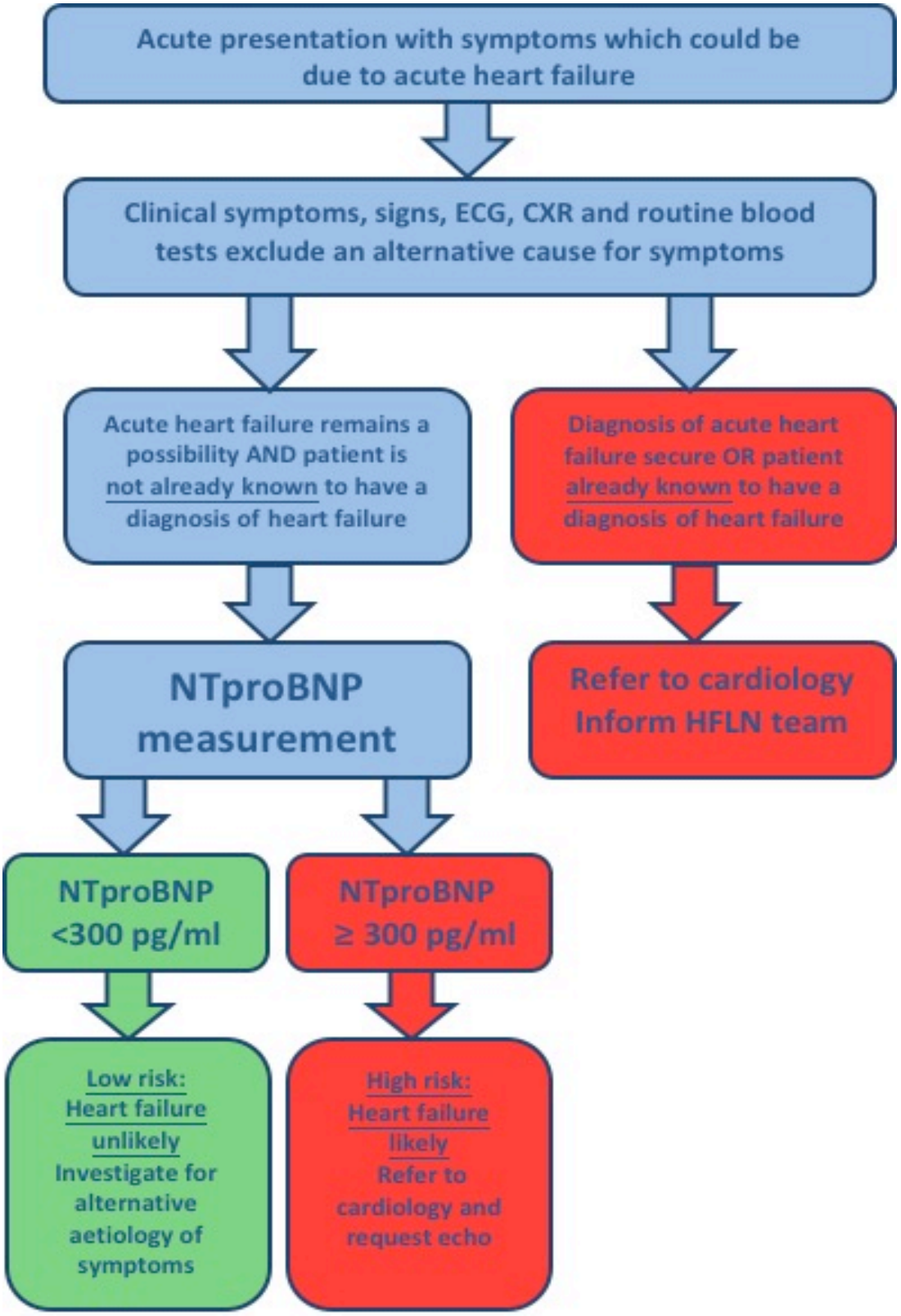

Figure 3: Flow chart of a "Heart Failure Diagnostic Pathway" protocol using Natriuretic peptides in primary care.