Predicting long-term morbidity of ACS patients: can NT-proBNP succeed where other biomarkers have failed?

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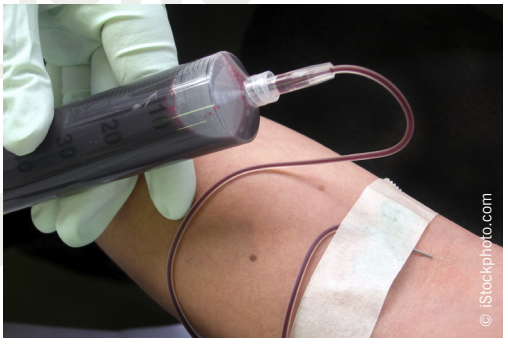
Identification of those at low risk of developing heart failure (HF) after acute coronary syndrome (ACS) would aid clinical management, but it is unclear whether N-terminal pro-brain natriuretic peptide (NT-proBNP) adds to the predictive accuracy of troponin. There were 229 subjects recruited into a prospective cohort study. Subjects were assessed for acute heart failure (AHF) prior to discharge and for readmission within 30 days of their ACS event (cohorts A+B). Cohort A (n=116) were further assessed for readmission within 12 months. Troponin I (TnI) and NT-proBNP levels were measured at ACS onset and at 6–12 hours. Readmissions were identified using electronic records. In total, 23.6% of subjects developed AHF during the index admission: 10.0% were readmitted within 30 days of admission; 17.2% within three months; 26.7% within six months and 36.2% within 12 months. At presentation, NT-proBNP, but not TnI, was significantly elevated among subjects who developed AHF compared with non-AHF subjects. Compared with non-readmitted subjects, readmission within 30 days was associated with significantly lower baseline NT-proBNP, and readmission after 30 days with higher baseline NT-proBNP. For all periods, TnI level was lower among readmitted compared with non-readmitted subjects. In conclusion, NT-proBNP has a potential role for rule out of those at low risk of AHF development and readmission.

Introduction

For patients with acute coronary syndrome (ACS) who survive to reach hospital, the majority of mortality and morbidity over the following five years occurs after discharge.[1] Of all complications,



development of acute heart failure (AHF) and left ventricular systolic dysfunction (LVSD) are key determinants of adverse outcome. Approximately half of patients with ACS are readmitted to hospital, constituting a profound burden on healthcare resources.[1] In several healthcare systems there are financial penalties when ACS patients are readmitted within 30 days.[2] Prediction of the development of AHF and hospital readmission following ACS would aid clinical management, but widely used biomarkers have limited accuracy. Troponin is the only biomarker routinely measured in ACS management despite evidence that more reliable predictors of ACS complications exist.[3-6]

Brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) have been proposed as alternatives to troponin for predicting heart failure (HF) in ACS patients.[7-10] They are produced by cleavage of their common precursor, proBNP, after its release from cardiac ventricles.[11] Measurement of NT-proBNP within the first few days after ACS provides valuable prognostic information, independent of left ventricular ejection fraction. De Lemos *et al.*[9] demonstrated that baseline BNP level was higher among subjects who experienced new or worsening HF within 30 days or 10 months of their ACS event compared with subjects who did not. Of note, few studies have evaluated the predictive value of baseline NT-proBNP level in early HF, specifically that developing during index admission.

Study rationale

To determine whether biomarkers (troponin I [TnI] and NT-proBNP) are useful in identifying risk of developing AHF and hospital readmission following ACS.

Hypotheses

1. NT-proBNP is superior to TnI for predicting development of AHF and hospital readmission after ACS.
2. Surrogate markers of LVSD, e.g. developing AHF during index admission, pre-existing ischaemic heart disease (IHD), predispose to hospital readmission.

Materials and methods

Subjects

The study population comprised 229 subjects. Patients presenting to the Royal Infirmary of Edinburgh with possible ACS were consented and prospectively recruited in two phases during November to December 2011 (cohort A, n=116), and February to March 2013 (cohort B, n=113). The use of two cohorts is a product of the compilation of two student-led projects, and takes advantage of examining the outcomes in two independent, temporally separated patient cohorts.

Patients who received a non-ACS diagnosis at discharge were excluded. Patients with a pre-existing diagnosis of HF were excluded so that any clinical evidence of AHF could be attributed to the concurrent ACS.

Data collection

Data, including clinical history and examination, cardiovascular risk factors, comorbidities and medications, were collected from subjects' medical notes.

Subjects were classified into three groups according to admission electrocardiogram (ECG) and serial TnI values: unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI), consistent with European Society of Cardiology (ESC) guidelines.[12,13]

Subjects were assessed for evidence of new-onset AHF using clinical examination findings, chest radiography (CXR) and echocardiography. Significant signs of AHF for each modality are bulleted in **table 1**, which was developed from ESC AHF diagnosis guidelines.[14] Presence of at least one significant sign in at least two assessment modalities constituted a diagnosis; symptoms were not sufficient.

Medical records were accessed post-discharge to identify readmission to hospital within 30 days (cohorts A and B) and within three, six and 12 months (cohort A only) of the ACS event. A readmission is defined as an episode of any cause of elective or emergency admission to hospital.

Medical records of the 25 subjects in cohort A who did not develop AHF during index admission despite an admission NT-proBNP level of >2 × 97.5th percentile were accessed at 22 months to determine subsequent AHF development.

NT-proBNP assay

In current practice, venous blood samples are taken on admission for immediate analysis of TnI in patients presenting with possible ACS using the ARCHITECT® STAT chemiluminescent microparticle immunoassay. For non-STEMI patients a further sample is collected at 6–12 hours to reassess TnI level. Aliquots were collected from these samples and assayed for NT-proBNP levels using the Elecsys proBNP II assay. Levels were considered against evidence-based age- and sex-specific reference ranges.

Investigators and treatment-providing clinicians were blinded to NT-proBNP results at the time of assessment.

Statistical analysis

Statistical analysis was performed using IBM® SPSS® Statistics 19. The Chi-squared test of association determined significance for categorical data where >80% of expected counts were >5. Otherwise, Fisher's exact test was used. The Shapiro-Wilk test generated histograms to determine continuous variable normalities. The two-tailed *t*-test compared those showing parametric distribution. The biomarkers largely showed non-parametric distribution so were analysed using the Mann-Whitney U test.

Table 1. Significant signs of heart failure (HF) for each assessment modality (clinical examination, chest radiography and echocardiography)

Assessment modality	Significant signs
Clinical examination	• Pulmonary oedema (crackles or rales over lungs, effusion) • Cardiogenic shock (poor peripheral perfusion, systolic blood pressure <90 mmHg, anuria or oliguria) • Right HF (raised jugular venous pressure, peripheral oedema, ascites)
Chest radiography	• Prominent upper lobe pulmonary veins and/or increased vascularity of lung fields • Opacification of hilar regions • Septal lines • Pleural effusion • Cardiomegaly
Echocardiography	• Increased left ventricular internal dimension at diastole (LVIDd) • Estimated pulmonary artery pressure >30 mmHg • Investigator's impression that systolic function of the left ventricle is at least mildly impaired

Developed from reference 14. Reference ranges for LVIDd were isolated from the American Society of Echocardiography's 'Recommendations for Chamber Quantification'.[20] In the context of acute coronary syndrome, regional myocardial dysfunction (or even akinaesia) may be compensated for by hyperdynamic function in other myocardial regions and hence global ejection fraction may not be a robust measure of regional dysfunction. For these reasons the investigators used the assessment of left ventricular (LV) function from the full LV echo assessment.

Results

The study population comprised 229 subjects. Baseline characteristics of cohorts A and B did not differ significantly, except that cohort A had a higher prevalence of IHD (data not shown).

Development of AHF during index admission for ACS

This study's criteria for a diagnosis of AHF during index admission were met by 23.6% of subjects (n=54). Cohort A, where 20.7% (n=24) developed AHF, was considered in greater detail. The baseline characteristics of Cohort A are summarised in **table 2**.

Subjects with HF were significantly older than non-HF subjects, less likely to be male and more likely to have pre-existing renal insufficiency.

Table 2. Baseline characteristics of cohort A

Characteristic, % (n)	Heart failure	Non-heart failure	p value
Age	73.33 ± 2.436 (SEM)	61.58 ± 1.344 (SEM)	<0.0001
Male gender	41.7% (10)	68.5% (63)	0.029
Risk factors for ACS			
Hypertension	37.5% (9)	34.8% (32)	ns
Hypercholesterolaemia*	16.7% (4)	23.9% (22)	ns
Diabetes mellitus	41.7% (10)	26.1% (24)	ns
Smoking			ns
Current	33.3% (8)	45.7% (42)	
Ex-	16.7% (4)	23.9% (22)	
Non-	50.0% (12)	30.4% (28)	
Family history of ACS	33.3% (8)	29.7% (27)	ns
Past medical history			
Diuretic usage	50.0% (12)	38.0% (35)	ns
Angina	83.3% (20)	66.3% (61)	ns
Myocardial infarction	45.8% (11)	29.3% (27)	ns
PCI	25.0% (6)	21.7% (20)	ns
CABG	12.5% (3)	6.5% (5)	ns
Renal insufficiency	25.5% (6)	6.5% (6)	0.017
ACS diagnosis			ns
STEMI	50.0% (12)	43.5% (40)	
NSTEMI	50.0% (12)	46.7% (43)	
UA	0.0% (0)	9.8% (9)	
Management			
Aspirin (or prasugrel)	95.8% (23)	97.8% (90)	ns
Clopidogrel	87.5% (21)	97.8% (89)	ns
Beta blocker	83.3% (20)	73.9% (68)	ns
Tirofiban	39.1% (9)	51.6% (47)	ns
PCI	62.5% (15)	72.8% (67)	ns
Thrombolysis	4.2% (1)	3.3% (3)	ns

*Only if documented prior to index-admission.

Key: ACS = acute coronary syndrome; CABG = coronary artery bypass graft; ns = not significant (p>0.05); NSTEMI = non-ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; SEM = standard error of the mean; STEMI = ST-elevation myocardial infarction; UA = unstable angina

NT-proBNP level on admission was significantly higher among subjects who developed AHF during index admission compared with subjects who did not (p<0.0001) (**figure 1**). This was also true of NT-proBNP levels 6–12 hours after symptom onset (data not shown). By contrast, TnI was not significantly higher in the AHF group on admission (p=0.081) (**figure 2**) or at 6–12 hours (data not shown) (**figure 2**).

Venn diagrams were compiled for admission TnI and NT-proBNP levels in the HF and non-HF groups (**figure 3**). Data were analysed to calculate the positive-predictive value (PPV) and negative-predictive value (NPV) of serum markers for predicting HF (**table 3**). The NPVs of TnI and NT-proBNP exceeded 90% when used individually or combined.

By contrast, the PPVs for both markers were low (**table 3**). Twenty-five non-AHF subjects had an admission NT-proBNP concentration exceeding twice the upper reference range limit (**figure 3**). The clinical outcome of these 25 patients at 22 months is represented in **figure 4**.

Readmission to hospital within 12 months

The data from both cohorts for 30-day readmission rates are considered together. Altogether 10.0% (n=23) of subjects were readmitted within 30 days of the index ACS event. Among cohort A, 17.2% (n=20) were readmitted within three months, 26.7% (n=31) within six months and 36.2% (n=42) within 12 months of ACS. The majority of these were emergency readmissions, predominantly to medical firms (general medicine or cardiology). Complaints included recurrent chest pain or shortness of breath. These are detailed further in **appendix 1**.

Compared with non-readmitted subjects, readmissions within 30 days had lower TnI levels on index admission (p=0.043); lower mean NT-proBNP levels (not significant) (**figure 5**; **appendix 3**); and were more likely to be diagnosed with UA (**appendix 3**). Readmissions beyond 30 days were more likely to have a history of IHD (particularly angina); significantly lower TnI level at baseline (**figure 5**; **appendix 3**); and were less likely to have been diagnosed with STEMI compared with non-readmissions (**appendix 3**). In keeping with this, those readmitted after three months were less likely to have received tirofiban (reserved for STEMI patients). Those readmitted within three to six months were less likely to have undergone percutaneous coronary intervention (PCI). Readmissions after 30 days had significantly higher baseline NT-proBNP level compared with non-readmissions (**figure 6**; **appendix 3**).

The NPV of NT-proBNP for readmission within 30 days exceeded 90%, though its value subsequently decreased (**table 4**). By contrast, the PPV of NT-proBNP for readmission within 30 days was low; this is unsurprising given that most readmitted patients had a positive NT-proBNP assay (i.e. exceeding the age- and sex-corrected 97.5th percentile), with mean NT-proBNP values lower among subjects readmitted within 30 days compared with non-readmissions. The NPV and PPV for TnI were insignificant for all periods. The addition of TnI to NT-proBNP did not increase its negative-predictive power.

Table 3. Predicting heart failure: NPVs and PPVs of serum markers when they are used individually or in combination

Serum marker on admission	PPV	NPV
NT-proBNP concentration >97.5th percentile	37.5%	92.2%
Positive TnI (>0.05 μg/L)	27.0%	95.0%
Both of the above	40.5%	94.7%

Key: NPV= negative-predictive value; NT-proBNP = N-terminal pro-brain natriuretic peptide; PPV = positive-predictive value; TnI = troponin I

Table 4. Predicting 30-day readmission: NPVs and PPVs of serum markers when they are used individually or in combination

Highest serum marker	PPV	NPV
30 days		
NT-proBNP >97.5th percentile	10.59%	91.53%
Positive TnI (>0.05 μg/L)	9.30%	78.57%
Both of the above	10.43%	90.91%
3 months		
NT-proBNP >97.5th percentile	18.89%	88.46%
Positive TnI (>0.05 μg/L)	15.60%	57.14%
Both of the above	17.65%	83.87%
6 months		
NT-proBNP >97.5th percentile	28.89%	80.77%
Positive TnI (>0.05 μg/L)	25.69%	57.14%
Both of the above	28.24%	77.42%
12 months		
NT-proBNP >97.5th percentile	37.78%	69.23%
Positive TnI (>0.05 μg/L)	35.78%	57.14%

Key: NPV= negative-predictive value; NT-proBNP = N-terminal pro-brain natriuretic peptide; PPV = positive-predictive value; TnI = troponin I

Readmission of patients who developed AHF during the index admission

AHF was observed in increasing frequency for patients readmitted in each subsequent time period, but this trend did not reach statistical significance.

Discussion

The role of biomarkers for predicting AHF during index admission

Elevated TnI at the index ACS event does not predict subsequent development of AHF. This justifies evaluation of alternative biomarkers for predicting AHF. NT-proBNP levels, both on admission and at 6–12 hours after symptoms onset, were significantly higher in patients who developed AHF during the index admission compared with those who did not. This is in keeping with findings by De Lemos *et al.* who demonstrated higher baseline BNP level among subjects with new or worsening HF within 30 days of ACS.[9]

Both NT-proBNP and TnI had a high NPV for development of AHF during the index admission. Our data support a role for either of the serum markers in identifying those patients at low risk of developing AHF.

The role of biomarkers for predicting readmission to hospital after ACS event

NT-proBNP concentrations were lower for patients readmitted within 30 days than for those who were not. For every other period the inverse was true. Given that LVSD is reflected by elevated NT-proBNP, only late readmissions may be reasonably attributed to LVSD and HF. Indeed, the higher prevalence of underlying IHD among the late readmission group would reasonably increase these patients' susceptibility to LVSD following ACS. By contrast, early readmissions were more likely to have suffered UA (as opposed to STEMI), hence, extensive infarction and the LVSD associated with it is less likely in this group.[15,16] The underlying cause for early readmissions is probably multi-factorial and has been described by Keith *et al.*[15] For our cohort, potential reasons include initial burden of infarction, patient factors and complications of ACS treatment. Higher incidence of readmission following complications of ACS treatment has been reported previously.[16]

For all periods, TnI levels were significantly lower among readmissions. The PPV and NPV of TnI for readmission were low for all periods. The NPV of NT-proBNP for readmission was reduced by the addition of TnI. This is an interesting new finding given the focus of recent research into high-sensitivity troponin assays.

The NPV of NT-proBNP for readmission within 30 days exceeded 90% and may play a role in excluding readmission for lower-risk patients. However, a positive assay does not correlate with an increased risk. The value of NT-proBNP for a risk-stratification tool in NSTEMI has been advocated by Eggers *et al.*,[17] who found it independently predictive of clinical outcome up to six months, and superior to TnI and C-reactive protein. Indeed, the ESC has labeled NT-proBNP the most useful 'rule-out test' for HF.[18]

Our finding that a greater NT-proBNP value among readmissions beyond 30 days did not reach statistical significance may reflect our small sample size. A larger multi-centre study with a longer follow-up period presents a next step.

Our study highlights the unreliability of using single markers (even troponin) to predict outcomes for ACS patients. This has been documented in the international GRACE (Global Registry of Acute Coronary Events) study.[19] Our results support using NT-proBNP as part of overall risk assessment; the NPV of NT-proBNP for adverse outcome is high and superior to TnI. However, given the poor PPV of NT-proBNP for predicting AHF and readmission, research into alternative markers of adverse outcome for this patient population is indicated

Conflict of interest

None declared.

Figure 1. Histograms to show N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration on admission in subjects with and without heart failure. Data labels indicate the actual number of subjects per group

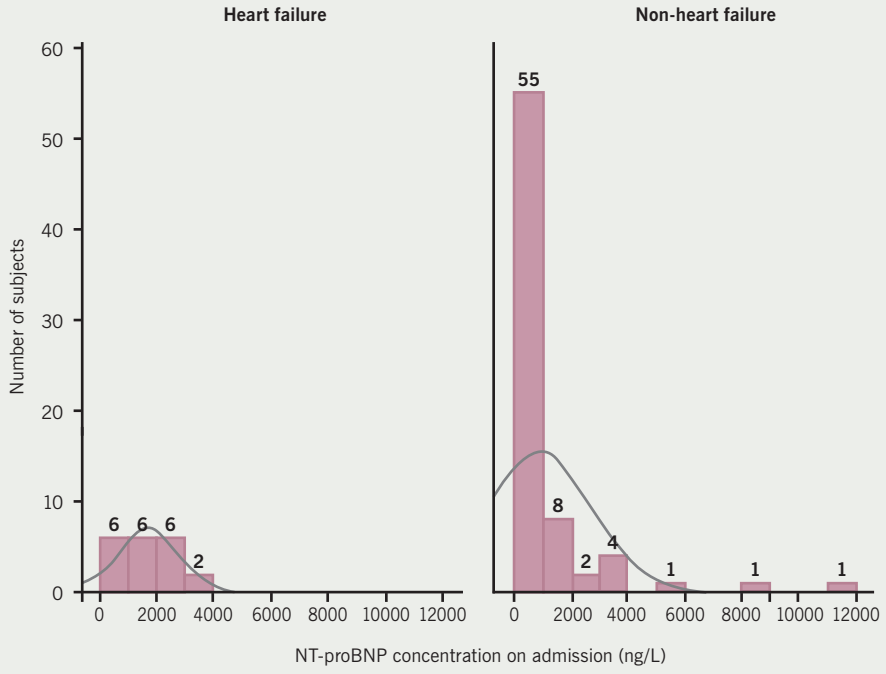


Figure 2. Histograms to show troponin I (TnI) concentration on admission in patients with and without heart failure. Data labels indicate the actual number of subjects per group

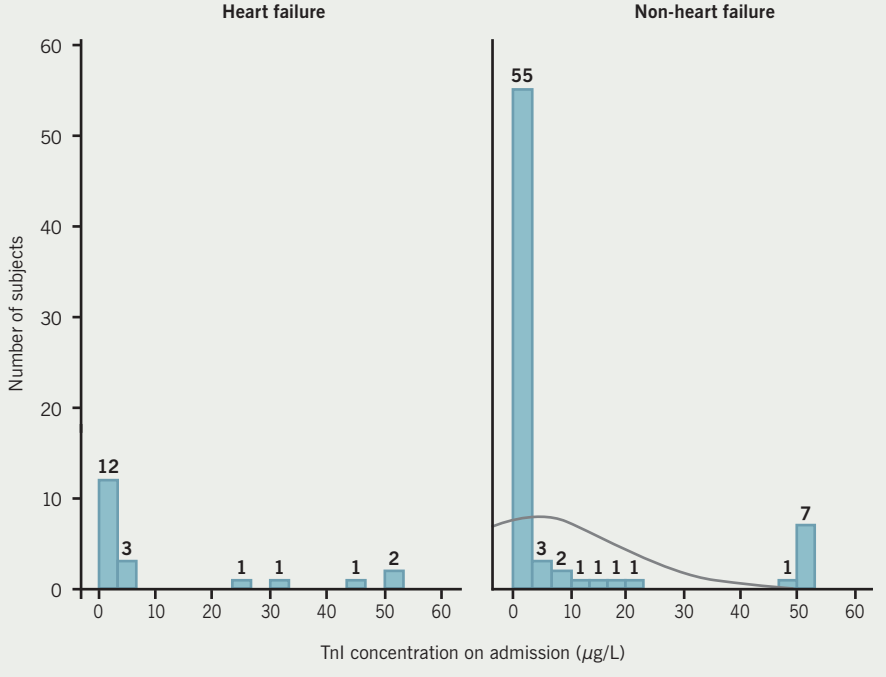
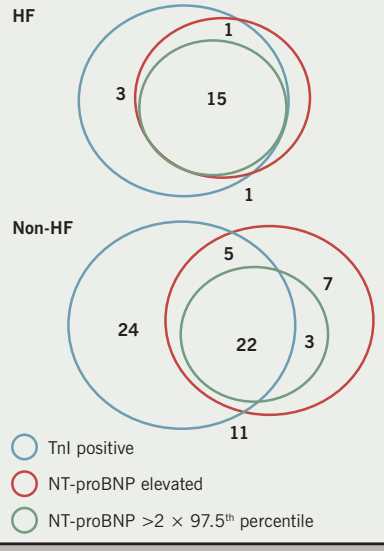


Figure 3. Venn diagrams demonstrating levels of biomarkers in the heart failure (HF) and non-HF groups. Data labels indicate the actual number of subjects per category. Of note, subject numbers do not total 116 because not all patients had serum markers checked on admission



Key: HF = heart failure; NT-proBNP = N-terminal pro-brain natriuretic peptide; TnI = troponin I

Key messages

- Despite progress in recognition of acute coronary syndrome (ACS) and its short- and long-term management, ACS is still associated with a significant burden of post-acute mortality and morbidity, including acute heart failure (AHF) and readmission
- Development of AHF and, therefore, left ventricular systolic dysfunction (LVSD) may predispose to readmission
- Tropinin I (TnI) is an unreliable marker of development of AHF and hospital readmission and does not add to the predictive value of N-terminal pro-brain natriuretic peptide (NT-proBNP) when the two biomarkers are used in combination
- NT-proBNP has a high negative-predictive value (NPV) as a 'rule out' test for both end points, though its positive-predictive value (PPV) is low

Figure 4. Outcome at 22 months post-acute coronary syndrome of subjects who had an admission N-terminal pro-brain natriuretic peptide (NT-proBNP) level of >2 × 97.5th percentile but who did not meet this study's criteria for heart failure during the index admission

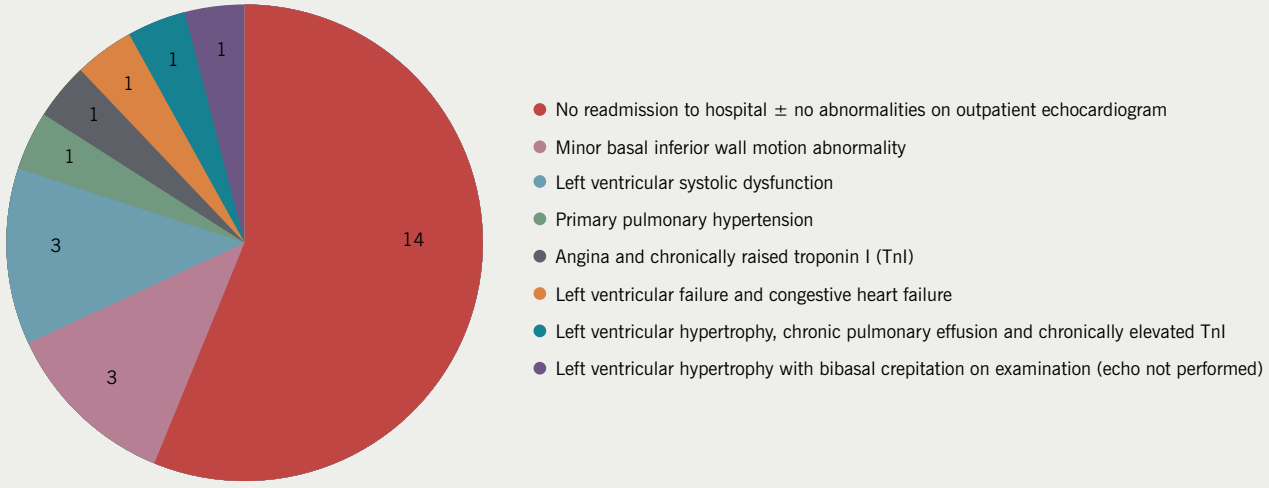


Figure 5. Comparison of troponin I (TnI) concentration at 6–12 hours between non-readmitted subjects and subjects who were readmitted at 30 days (p=0.061), 3 months (p=0.007), 6 months (p=0.004) and 12 months (p=0.006)

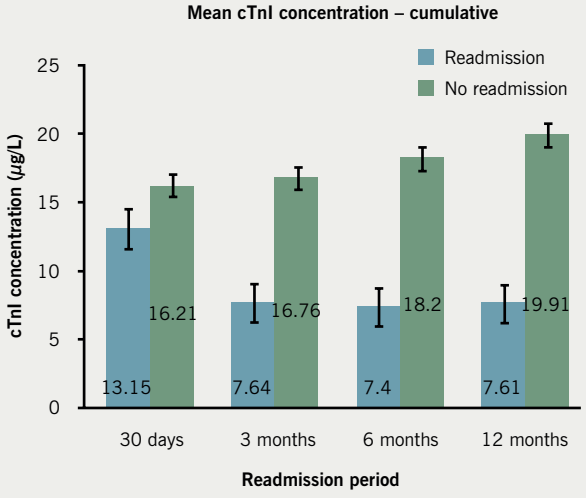
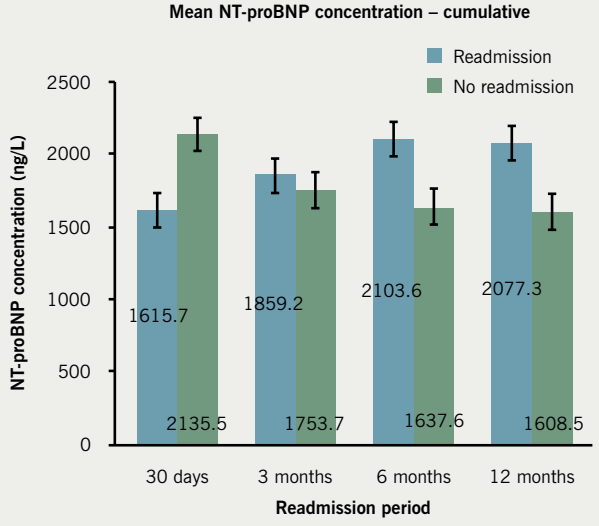


Figure 6. Comparison of N-terminal pro-brain natriuretic peptide (NT-proBNP) levels at 6–12 hours after symptoms onset between readmitted and non-readmitted subjects at 30 days (p=0.90), 3 months (p=0.68), 6 months (p=0.21) and 12 months (p=0.15)



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Appendix 1. Further breakdown of readmissions

Cohort A

Before 30 days
There were 13 episodes of readmission within 30 days, representing 11 patients. All were emergencies:

- Cardiology (9)
- General medicine (2)
- General surgery (1)
- Cardiothoracic surgery (1)

30 days to 3 months
There were 20 episodes in this period, representing 11 patients. 17 were emergency and 3 were elective. Elective presentations were to cardiothoracic surgery (2 episodes) and cardiology (1 episode).

Emergency readmissions:

- Cardiology (9)
- General medicine (5)
- General surgery (2)
- Vascular surgery (1)

3 months to 6 months
There were 36 episodes of readmission representing 18 patients. 35 were emergency and 1 was elective (cardiothoracic surgery).

Emergency readmissions:

- Cardiology (18)
- General medicine (13)
- General surgery (1)
- Gastroenterology (1)
- Vascular surgery (1)
- Neurology (1)

6 months to 12 months
There were 37 episodes of readmission in this period representing 19 patients. 34 of these were emergency and 3 were elective (gynaecology – 2 episodes, general surgery – 1 episode).

Emergency readmissions:

- Cardiology (21)
- Orthopaedics (5)
- General medicine (4)
- Oncology (1)
- Respiratory medicine (1)
- Dermatology (1)
- Intensive care (1)

Cohort B

30 days
There were 15 episodes of readmission representing 12 patients. 14 of these were emergency and 1 was elective (cardiothoracic surgery).

- Cardiology (11)
- General medicine (2)
- Urology (1)

Appendix 2. Biomarker costings

After correspondence with Abbot Diagnostics UK & Ireland who supplied the cardiac troponin (TnI) assay used in the Royal Infirmary of Edinburgh, and through consultation of National Institute for Health and Care Excellence (NICE) documentation for the N-terminal pro-brain natriuretic peptide (NT-proBNP) assay cost, we were able to obtain the average cost of each assay throughout the UK. The exact cost is moderated by a range of variables, including the number of tests run annually by each centre among several others.

TnI: £1.50

NT-proBNP: £15–25

Appendix 3. Baseline characteristics of readmitted and non-readmitted subjects

30 days

Characteristic	Baseline n=229	Readmission n=23	No readmission n=206	p value
ACS diagnosis				0.022
STEMI	48.0% (110)	39.1% (9)	49.0% (101)	
NSTEMI	44.5% (102)	39.1% (9)	45.1% (93)	
UA	7.4% (17)	21.7% (5)	5.8% (12)	
NT-proBNP (ng/L)	2,083.3 ± 261.9 SEM	1,615.7 ± 432.9 SEM	2,135.48 ± 287.1 SEM	ns
cTnI (μg/L)				
Admission	8.82 ± 1.18 SEM	4.11 ± 2.58 SEM	9.35 ± 1.13 SEM	0.043
6–12 hours	15.90 ± 1.37 SEM	13.15 ± 4.69 SEM	16.21 ± 1.43 SEM	ns

3 months

Characteristic	Baseline n=116	Readmission n=20	No readmission n=96	p value
Medical history				
MI	32.8% (38)	65.0% (13)	26.0% (25)	0.001
Angina	69.8% (81)	100.0% (20)	63.5% (61)	0.001
CKD	10.03% (12)	5.0% (1)	12.1% (11)	ns
PCI	22.4% (26)	45.0% (9)	16.5% (15)	0.002
CABG	7.8% (9)	15.0% (3)	6.3% (6)	ns
Diuretic Rx*	40.5% (47)	55.0% (11)	37.5% (36)	ns
ACS diagnosis				0.002
STEMI	44.8% (52)	20.0% (4)	50.0% (48)	
NSTEMI	47.4% (55)	55.0% (11)	45.8% (44)	
UA	7.8% (9)	25.0% (5)	4.2% (4)	
NT-proBNP (ng/L)				
Admission	1,103.5 ± 184.9 SEM	1,071.7 ± 259.0 SEM	1,109.6 ± 215.6 SEM	ns
6–12 hours	1,791.1 ± 239.5 SEM	1,859.2 ± 523.9 SEM	1,753.7 ± 267.8 SEM	ns
TnI (μg/L)				
Admission	7.99 ± 1.70 SEM	1.85 ± 1.31 SEM	3.17 ± 7.64 SEM	0.033
6–12 hours	15.05 ± 1.90 SEM	9.18 ± 1.98 SEM	16.76 ± 2.19 SEM	0.007
Management				
Aspirin	97.4% (113)	100.0% (20)	96.9% (93)	ns
Clopidogrel	94.8% (110)	85.0% (17)	96.9% (93)	0.036
Beta blocker	75.9% (88)	75.0% (15)	76.0% (73)	ns
Tirofiban	48.3% (56)	20.0% (4)	54.2% (52)	0.018
PCI	70.7% (82)	50.0% (10)	75.0% (72)	0.026
Thrombolysis	3.4% (4)	0.0% (0)	4.2% (4)	ns

6 months

Characteristic	Baseline n=116	Readmission n=31	No readmission n=85	p value
Medical history				
MI	32.8% (38)	61.3% (19)	22.4% (19)	0.001
Angina	69.8% (81)	90.3% (28)	62.4% (53)	0.004
CKD	10.03% (12)	6.5% (2)	11.8%(10)	ns
PCI	22.4% (26)	41.9% (13)	15.3% (13)	0.002
CABG	7.8% (9)	9.7% (3)	7.1% (6)	ns
Diuretic Rx*	40.5% (47)	54.8% (17)	35.3% (30)	ns

6 months				
Characteristic	**Baseline n=116**	**Readmission n=31**	**No readmission n=85**	**p value**
ACS diagnosis				0.002
STEMI	44.8% (52)	19.4% (6)	54.1% (46)	
NSTEMI	47.4% (55)	64.5% (20)	41.2% (35)	
UA	7.8% (9)	16.1% (5)	4.7% (4)	
NT-proBNP (ng/L)				
Admission	1,103.5 ± 184.9 SEM	1,260.4 ± 223.4 SEM	1,054.1 ± 233.0 SEM	0.013
6–12 hours	1,791.1 ± 239.5 SEM	2,103.6 ± 451.1 SEM	1,637.6 ± 279.8 SEM	ns
TnI (μg/L)				
Admission	7.99 ± 1.70 SEM	1.56 ± 0.93 SEM	10.01 ± 2.16 SEM	0.004
6–12 hours	15.05 ± 1.90 SEM	7.40 ± 2.62 SEM	18.20 ± 2.37 SEM	0.004
Management				
Aspirin	97.4% (113)	100.0% (31)	96.5% (82)	ns
Clopidogrel	94.8% (110)	83.9% (26)	98.8% (84)	0.016
Beta blocker	75.9% (88)	83.9% (26)	72.9% (62)	ns
Tirofiban	48.3% (56)	25.9% (8)	56.5% (48)	0.002
PCI	70.7% (82)	54.8% (17)	76.5% (65)	0.024
Thrombolysis	3.4% (4)	3.2% (1)	3.5% (3)	ns
12 months				
Characteristic	**Baseline n=116**	**Readmission n=42**	**No readmission n=74**	**p value**
Medical history				
MI	32.8% (38)	52.4% (22)	21.6% (16)	0.001
Angina	69.8% (81)	85.7% (36)	60.8% (45)	0.006
CKD	10.03% (12)	7.1% (3)	12.2% (9)	ns
PCI	22.4% (26)	33.3% (14)	16.2% (12)	0.011
CABG	7.8% (9)	11.9% (5)	5.4% (4)	ns
Diuretic Rx*	40.5% (47)	50.0% (21)	48.6% (36)	ns
ACS diagnosis				0.001
STEMI	44.8% (52)	21.4% (9)	58.1% (43)	
NSTEMI	47.4% (55)	66.7% (28)	36.5% (27)	
UA	7.8% (9)	11.9% (5)	54.1% (4)	
NT-proBNP				
Admission	1,103.5 ± 184.9 SEM	1,206.2 ± 231.6 SEM	1,048.6 ± 256.2 SEM	ns
6–12 hours	1,791.1 ± 239.5 SEM	2,077.3 ± 398.9 SEM	1,608.5 ± 298.8 SEM	ns
TnI (μg/L)				
Admission	7.99 ± 1.70 SEM	1.19 ± 0.64 SEM	11.61 ± 2.46 SEM	0.002
6–12 hours	15.05 ± 1.90 SEM	7.61 ± 2.10 SEM	19.93 ± 2.68 SEM	0.006
Management				
Aspirin	97.4% (113)	100.0% (42)	100.0% (74)	ns
Clopidogrel	94.8% (110)	85.7% (36)	100.0% (74)	0.005
Beta blocker	75.9% (88)	78.6% (33)	74.3% (55)	ns
Tirofiban	48.3% (56)	28.6% (12)	59.5% (44)	0.002
PCI	70.7% (82)	61.9% (26)	75.7% (56)	ns
Thrombolysis	3.4% (4)	2.4% (1)	4.1% (3)	ns

*Only if documented prior to index-admission.
Key: ACS = acute coronary syndrome; CABG = coronary artery bypass graft; CKD = chronic kidney disease; MI = myocardial infarction; ns = not significant (p>0.05); NSTEMI = non-ST-elevation myocardial infarction; NT-proBNP = N-terminal pro-brain natriuretic peptide; PCI = percutaneous coronary intervention; Rx = prescription; SEM = standard error of the mean; STEMI = ST-elevation myocardial infarction; TnI = troponin I; UA = unstable angina