British Journal of Anaesthesia **103 (5):** 647–53 (2009)
doi:10.1093/bja/aep234 Advance Access publication August 27, 2009

CARDIOVASCULAR

N-terminal pro-B-type natriuretic peptide levels and early outcome after cardiac surgery: a prospective cohort study

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Background. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a powerful predictor of cardiovascular outcome in many circumstances. There are, however, limited data regarding the utility of NT-proBNP or BNP levels in patients undergoing cardiac surgery. The current study assesses the ability of NT-proBNP to predict early outcome in this setting.

Methods. One thousand and ten patients undergoing non-emergent cardiac surgery were recruited prospectively. Baseline clinical details were obtained and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and Parsonnet score were calculated. Preoperative NT-proBNP levels were measured using the Roche Elecsys assay. The primary endpoint was 30 day mortality.

Results. Median NT-proBNP levels were 624 ng litre^{-1} among patients who died within 30 days of surgery (n=29), compared with 279 ng litre^{-1} in survivors [odds ratio (OR) 1.03 per 250 ng litre^{-1}, 95% confidence interval 1.01–1.05, P=0.001). NT-proBNP levels remained predictors of 30 day mortality in models including either the additive EuroSCORE (OR 1.03 per 250 ng litre^{-1}, P=0.01), the logistic EuroSCORE (OR 1.03 per 250 ng litre^{-1}, P=0.004), or the Parsonnet score (OR 1.02 per 250 ng litre^{-1}, P=0.04). Levels of NT-proBNP were also predictors of prolonged (>1 day) stay in the intensive care unit (OR 1.03 per 250 ng litre^{-1}, P<0.001) and of a hospital stay >1 week (OR 1.07 per 250 ng litre^{-1}, P<0.001). They remained predictive of these outcomes in regression models that included either the EuroSCORE or the Parsonnet score and in a model that included all study variables.

Conclusions. NT-proBNP levels predict early outcome after cardiac surgery. Their prognostic utility is modest—but is independent of traditional indicators and conventional risk prediction scores.

Br J Anaesth 2009; **103**: 647–53

Keywords: complications, death; complications, morbidity; hormones, atrial natriuretic peptide; surgery, cardiovascular

Accepted for publication: June 30, 2009

An ability to accurately predict the hazard associated with cardiac surgery provides patients with an indication of their individual risk, facilitates the effective use of healthcare resources, and allows valid comparisons of different cardiac surgical units. Several scoring systems predict early outcome from cardiac surgery. Among the most extensively validated are the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Parsonnet score.[1 2] EuroSCORE is calculated using either the additive or the logistic versions—the latter being less easy to calculate, but potentially more accurate in high-risk patients.[3] Although frequently used, these scoring

systems have well-recognized limitations.[4 5] A biochemical test that, either alone or in combination with existing clinical tools, could improve the accuracy of risk prediction would be of considerable value.

The natriuretic peptides are produced in the myocardium in response to myocyte stretch, predominantly due to pressure or volume overload.[6 7] This leads to the release of a precursor molecule (proBNP), which is subsequently split into B-type natriuretic peptide (BNP) and an N-terminal pro-peptide (NT-proBNP). BNP promotes natriuresis, diuresis, and vasodilatation, whereas NT-proBNP is biologically inactive. Blood levels of BNP and NT-proBNP are raised in patients with cardiac disease, particularly those with heart failure.[6 7] They are not, however, merely a measure of systolic function, but may be raised in patients with elevated left ventricular (LV) filling pressure due to valve disease, diastolic dysfunction, and/or myocardial ischaemia. This underpins their prognostic utility in many settings.[6 7]

Natriuretic peptide levels predict cardiovascular outcome in patients undergoing non-cardiac surgery.[8–11] Data relating to patients undergoing cardiac surgery are more limited. Small studies suggest that preoperative natriuretic peptide levels might predict the outcome after cardiac surgery.[12–14] Limited sample size has, however, precluded comparisons with existing methods of risk stratification. To address this issue, we have assessed the ability of NT-proBNP and conventional risk scores (EuroSCORE and Parsonnet score) to predict early cardiovascular outcome in a large unselected cohort.

Methods

Patients and measures

The study protocol was approved by the local research ethics committee and consent was obtained from all patients. The study was a prospective single-centre observational cohort study of 1010 consecutively recruited adult patients undergoing non-emergent cardiac surgery.

Preoperative data collection included patient characteristics, cardiovascular risk factors, medication, and prior medical history. A baseline 12-lead ECG was recorded and reported by a cardiologist, blinded to NT-proBNP levels. LV function was assessed by echocardiography, ventriculography, or both. It was classified as normal (LV ejection fraction >50%) or mildly (LV ejection fraction 40–50%), moderately (LV ejection fraction 30–40%), or severely (LV ejection fraction <30%) impaired, on the basis of visual assessment by a cardiologist, again blinded to NT-proBNP results. New York Heart Association (NYHA) functional class was determined and the EuroSCORE and Parsonnet scores were calculated.[1 2] Intraoperative data collection included details of surgery and anaesthesia, duration of cardiopulmonary bypass and aortic cross-clamp times, and the requirement for cardiovascular support (pharmacological, mechanical, or both). Postoperative data collection included the requirement for cardiovascular support, duration of ventilation, and the duration of intensive care unit (ICU) and hospital stay.

Plasma NT-proBNP levels were determined before operation using an electro-chemiluminescence immunoassay, performed on a Roche Elecsys 2010 automated platform (Roche Diagnostics, Basel, Switzerland). The assay has an effective measuring range of 5–35 000 ng litre^{-1}. The within-run coefficient of variation was 2.7% at a concentration of 175 ng litre^{-1} and 1.9% at 1068 ng litre^{-1}. The between-run coefficients of variation were 13.4%, 5.4%, and 4.3% at levels of 37.8, 236.3, and 473.2, respectively.

Clinicians responsible for patient care were blinded to the preoperative NT-proBNP levels. All preoperative data were also collected by individuals blinded to these levels. Preoperative glomerular filtration rate was estimated (eGFR) using the Modification of Diet in Renal Disease equation.[15]

Endpoints

Deaths after surgery were identified using a computerized system linked directly to the General Register Office for Scotland. The primary study endpoint was all-cause mortality within 30 days of surgery. Secondary endpoints included the requirement for postoperative cardiovascular support, the length of stay in the ICU, and the duration of hospital stay. Prolonged ICU and hospital stay were prospectively defined as >1 day and >1 week, respectively, based on local audit data.

Statistics

Categorical data are summarized as absolute values (percentage). Continuous data are presented as median [interquartile range (IQR)] or, when normally distributed, as mean (SD). Characteristics of patients with differing quartiles of NT-proBNP levels and differing grades of LV systolic function were compared using the χ^2 test for trend, the Jonckheere–Terpstra test, or analysis of variance depending on the distribution and nature of the data.

Estimations of risk were performed using logistic regression and quoted as odds ratio (OR) with 95% confidence interval (CI). NT-proBNP levels were entered into logistic regression models along with, in separate models, the logistic and additive EuroSCORE and the Parsonnet score as continuous variables. Backward conditional multivariable models were also developed. For the primary endpoint of 30 day mortality, the number of variables in each model was limited by the small number of deaths. Variables were selected on the basis of them being known or likely to influence NT-proBNP levels, reflective of the results of other preoperative tests that might convey

similar prognostic information, or being powerful ($P<0.01$) univariable predictors of this outcome. Regression models were also developed assessing the independent predictive value of NT-proBNP levels for prolonged ICU and hospital stay. These models contained all study variables except for composite risk scores and mathematically related factors. Retention in the regression models was set at $P<0.05$. Statistical analyses were performed using SPSS version 15 (SPSS Inc., Chicago, IL, USA).

Power calculation

In 2001–2, 450 coronary artery bypass grafting (CABG) operations were performed in Aberdeen with a hospital mortality of 3.5%. We originally powered the study to look at the ability of BNP to predict hospital mortality which was expected to be 3.5%. The original power calculations, based on logged BNP, suggested that with 1000 patients, there was more than 90% power to detect the difference between the mean of logged BNP between those patients expected to live or to die equivalent to BNP measurements of 30 and 100 ng litre^{-1}, respectively, assuming a standard deviation of logged BNP of 0.35. This power would be reduced after adjustment for known confounding variables and existing risk scores. Experimental conditions necessitated the use of NT-proBNP and the difference above is equivalent to a comparison of 120 and 400 ng litre^{-1} under the assumption that a conversion factor of four to one between NT-proBNP and BNP is appropriate in this range (local data, $n=735$, Pearson's correlation coefficient=0.82, $P<0.001$).

Results

Patient population

The cohort was predominantly male with a median age of 67 yr (Table 1). NT-proBNP levels were obtained a median of 1 day (IQR 1–3) before surgery. Seven hundred and thirty-two (72%) patients underwent isolated CABG. Of the remaining patients, 225 received an aortic valve replacement (97 with concomitant CABG, three with associated aortic root replacement, and 16 with concurrent mitral valve surgery) and 50 patients underwent mitral valve surgery (23 with CABG and four with tricuspid valve annuloplasty). One patient had isolated tricuspid annuloplasty in addition to CABG and two patients had aortic root replacement (plus CABG).

The relationship between baseline characteristics and NT-proBNP quartile is shown in Table 2. Patients with normal LV systolic function had a median NT-proBNP level of 227 ng litre^{-1} (IQR 101–613). In comparison, those with mild systolic dysfunction had a median level of 468 ng litre^{-1} (IQR 159–1136), those with moderate dysfunction had median levels of 614 ng litre^{-1} (IQR 263–

Table 1 Baseline patient characteristics and 30 day mortality. Data are presented as number (%), median (IQR), or mean (SD). *OR per 10 μmol litre^{-1}; †OR per 250 ng litre^{-1}; ‡median level for the cohort. CI, confidence interval; ECG, electrocardiogram; LV, left ventricular; ACE, angiotensin-converting enzyme; eGFR, estimated glomerular filtration rate; CABG, coronary artery bypass grafting; IABP, intra-aortic balloon pump; NYHA, New York Heart Association; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Characteristic	Alive ($n=981$)	Dead ($n=29$)	Odds ratio (95% CI)	P-value
Age (yr)	65 (9)	70 (9)	1.07 (1.02–1.13)	0.004
Male	758 (77%)	16 (55%)	0.36 (0.17–0.76)	0.008
Smoker (prior or current)	411 (42%)	13 (45%)	1.13 (0.54–2.37)	0.75
Diabetes	169 (17%)	8 (28%)	1.83 (0.80–4.20)	0.15
Hypertension	721 (73%)	27 (93%)	4.87 (1.15–20.62)	0.03
Prior myocardial infarction	394 (40%)	9 (31%)	0.67 (0.30–1.49)	0.33
History of cardiac failure	84 (9%)	9 (31%)	4.81 (2.12–10.89)	<0.001
Prior cardiac surgery	25 (3%)	3 (10%)	4.41 (1.25–15.55)	0.02
Abnormal preoperative ECG	515 (52%)	18 (62%)	1.61 (0.74–3.52)	0.23
LV ejection fraction <50%	330 (34%)	10 (34%)	1.04 (0.48–2.26)	0.92
LV ejection fraction <40%	124 (13%)	3 (10%)	0.80 (0.24–2.67)	0.71
β-Blocker	685 (70%)	13 (45%)	0.35 (0.17–0.74)	0.006
ACE inhibitor	459 (47%)	14 (48%)	1.06 (0.51–2.22)	0.87
Statin	843 (86%)	25 (86%)	1.02 (0.35–2.99)	0.97
Body mass index	28.7 (4.4)	28.4 (4.4)	0.99 (0.91–1.07)	0.73
Creatinine (μmol litre^{-1})	107 (34)	112 (23)	1.03 (0.96–1.10)*	0.48
eGFR (ml min^{-1} per 1.73 m^2)	63 (14)	55 (11)	0.96 (0.94–0.98)	0.001
Valve/aortic surgery (±CABG)	262 (27%)	16 (55%)	3.38 (1.60–7.12)	0.001
Preoperative IABP	124 (13%)	1 (3%)	0.25 (0.03–1.83)	0.17
Additive EuroSCORE	4 (2–6)	5 (4–8)	1.17 (1.05–1.32)	0.007
Logistic EuroSCORE	2.76 (1.59–5.28)	4.26 (2.69–8.73)	1.05 (1.01–1.10)	0.02
Parsonnet score	6 (3–12)	15 (7–20)	1.11 (1.06–1.16)	<0.001
NYHA functional class III/IV	110 (11%)	7 (24%)	2.52 (1.05–6.03)	0.04
NT-proBNP at baseline (ng litre^{-1})	279 (119–833)	624 (190–1368)	1.03 (1.01–1.05)†	0.001
NT-proBNP ≥289 ng litre^{-1}‡	485 (49%)	20 (69%)	2.27 (1.02–5.03)	0.04

Table 2 NT-proBNP quartiles and baseline characteristics. Data are presented as number (%), median (IQR), or mean (SD). NT-proBNP, N-terminal pro-B-type natriuretic peptide; ECG, electrocardiogram; LV, left ventricular; NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate; ACE, angiotensin converting enzyme; CABG, coronary artery bypass grafting; IABP, intra-aortic balloon pump

Characteristic	NT-proBNP <120 ng litre^{-1} (n=253)	NT-proBNP ≥120 to <289 ng litre^{-1} (n=252)	NT-proBNP ≥289 to 847 ng litre^{-1} (n=253)	NT-proBNP ≥847 ng litre^{-1} (n=252)	P-value
Age (yr)	62 (9)	64 (8)	67 (9)	70 (9)	<0.001
Male	219 (87%)	205 (81%)	184 (73%)	166 (66%)	<0.001
Smoker (current/prior)	108 (43%)	99 (39%)	103 (41%)	113 (45%)	0.60
Diabetes mellitus	47 (19%)	46 (18%)	42 (17%)	42 (17%)	0.48
Hypertension	183 (72%)	191 (76%)	187 (74%)	187 (74%)	0.82
Prior myocardial infarction	74 (29%)	102 (40%)	105 (42%)	122 (48%)	<0.001
History of cardiac failure	4 (2%)	20 (8%)	17 (7%)	52 (21%)	<0.001
Abnormal preoperative ECG	72 (28%)	106 (42%)	156 (62%)	199 (79%)	<0.001
LV ejection fraction <50%	50 (20%)	72 (29%)	95 (38%)	123 (49%)	<0.001
NYHA functional class III/IV	19 (8%)	17 (7%)	23 (9%)	58 (23%)	<0.001
Creatinine (μmol litre^{-1})	103 (17)	106 (21)	106 (29)	116 (53)	<0.001
eGFR (ml min^{-1} per 1.73 m^2)	67 (11)	64 (13)	63 (14)	57 (14)	<0.001
β-Blocker	170 (67%)	195 (77%)	177 (70%)	156 (62%)	0.06
ACE inhibitor	109 (43%)	122 (48%)	133 (53%)	109 (43%)	0.77
Statin	229 (91%)	231 (92%)	209 (83%)	199 (79%)	<0.001
Body mass index	29.3 (4.1)	29.1 (4.2)	28.8 (4.6)	27.7 (4.4)	<0.001
Prior cardiac surgery	1 (<1%)	6 (2%)	10 (4%)	11 (4%)	0.004
Valve surgery (±CABG)	17 (7%)	31 (12%)	83 (33%)	146 (58%)	<0.001
Preoperative IABP	20 (8%)	25 (10%)	43 (17%)	37 (15%)	0.003
Additive EuroSCORE	2 (1–4)	3 (2–5)	5 (3–7)	6 (4–8)	<0.001
Logistic EuroSCORE	1.72 (1.15–3.07)	2.08 (1.44–3.63)	3.30 (1.85–6.03)	4.99 (2.89–9.28)	<0.001
Parsonnet score	4 (3–8)	5 (3–10)	8 (4–14)	12 (5–18)	<0.001

1356), and those with severe dysfunction had median levels of 818 ng litre^{-1} (IQR 565–9098; P<0.001).

Mortality at 30 days

Data on survival were available for all patients. Twenty-nine (2.9%) patients died within 30 days of surgery. The univariable predictors of 30 day mortality are shown in Table 1 and survival curves with the cohort dichotomized around the median value of NT-proBNP (289 ng litre^{-1}) are shown in Figure 1.

NT-proBNP levels were entered into logistic regression models along with conventional risk-prediction systems. After correction for logistic EuroSCORE, NT-proBNP levels remained predictors of 30 day mortality (OR 1.03 per 250 ng litre^{-1}, 95% CI 1.01–1.05, P=0.004). In separate models with (i) the additive EuroSCORE and (ii) the Parsonnet score, NT-proBNP levels remained independent predictors (OR 1.03 per 250 ng litre^{-1}, 95% CI 1.01–1.05, P=0.01 and OR 1.02 per 250 ng litre^{-1}, 95% CI 1.00–1.05, P=0.04, respectively).

The number of deaths within 30 days of surgery allowed only limited multivariable modelling. In the first model, NT-proBNP was entered along with age, gender, and eGFR. In this model, age, gender, and NT-proBNP remained independently predictive (OR for NT-proBNP 1.03 per 250 ng litre^{-1}, 95% CI 1.00–1.05, P=0.03). In a further model, including an abnormal preoperative ECG and abnormal LV systolic function, only NT-proBNP remained independently predictive (OR 1.03 per 250 ng litre^{-1}, 95% CI 1.01–1.06, P=0.001). In a model including a history of cardiac failure, the requirement for valve or aortic surgery, and the receipt of preoperative β-blockers, a non-significant trend towards NT-proBNP predicting outcome was demonstrated (P=0.21).

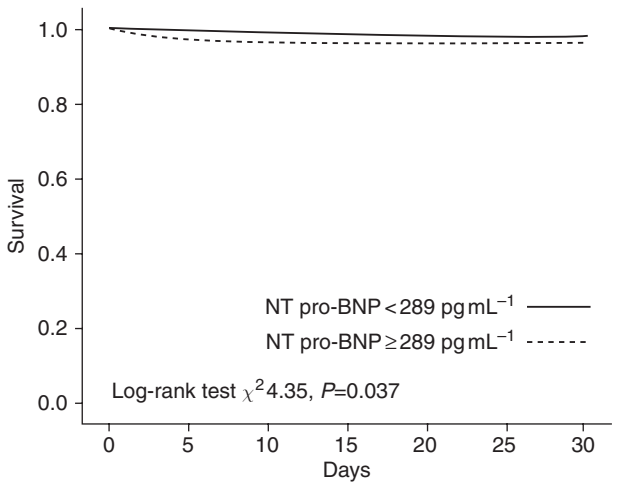

Fig 1 NT-proBNP levels (below and above the median value) and 30 day mortality.

Postoperative course

The relationship between levels of NT-proBNP and early postoperative outcomes is shown in Tables 3 and 4. Patients with NT-proBNP levels <289 ng litre^{-1} stayed a median of 7 (IQR 6–9) days in hospital after operation,

Table 3 NT-proBNP quartiles and peri/postoperative course. IABP, intra-aortic balloon pump; ICU, intensive care unit

Characteristic	NT-proBNP <120 ng litre^{-1} (n=253)	NT-proBNP ≥120 to <289 ng litre^{-1} (n=252)	NT-proBNP ≥289 to 847 ng litre^{-1} (n=253)	NT-proBNP ≥847 ng litre^{-1} (n=252)	P-value
Bypass time (min)	81 (64–97)	79 (62–96)	88 (74–115)	102 (83–138)	<0.001
Cross-clamp time (min)	45 (35–56)	44 (35–55)	51 (40–78)	70 (49–100)	<0.001
'Off-pump' surgery	30 (12%)	17 (7%)	30 (12%)	20 (8%)	0.41
Requirement for postoperative IABP	27 (11%)	27 (11%)	49 (19%)	50 (20%)	<0.001
Requirement for IABP >24 h after surgery	9 (4%)	4 (2%)	12 (5%)	21 (8%)	0.003
Requirement for postoperative inotropes	139 (55%)	144 (57%)	179 (71%)	183 (73%)	<0.001
Requirement for inotropes >24 h after surgery	43 (17%)	41 (16%)	65 (26%)	74 (30%)	<0.001
Requirement for ventilation >24 h after surgery	11 (4%)	3 (1%)	16 (6%)	19 (8%)	0.01
Postoperative atrial fibrillation	74 (29%)	75 (35%)	106 (43%)	109 (44%)	<0.001
Length of stay in ICU (days)	1 (1–2)	1 (1–1)	1 (1–2)	1 (1–2)	<0.001
Postoperative ICU stay >1 day	72 (30%)	77 (31%)	101 (40%)	107 (42%)	<0.001
Length of hospital stay (days)	7 (6–9)	7 (6–9)	8 (7–11)	9 (7–13)	<0.001
Hospital stay >1 week	102 (41%)	106 (43%)	157 (64%)	169 (70%)	<0.001

Table 4 Levels of NT-proBNP and postoperative outcomes. OR presented as per 250 ng litre^{-1} in NT-proBNP level. Levels are median (IQR). IABP, intra-aortic balloon pump; ICU, intensive care unit

Postoperative outcome	Yes	No	Odds ratio (95% CI)	P-value
Requirement for postoperative IABP	456 (189–1154) ng litre^{-1}	266 (114–790) ng litre^{-1}	1.01 (1.00–1.03)	0.18
Requirement for IABP >24 h after surgery	705 (248–1316) ng litre^{-1}	27 (118–793) ng litre^{-1}	1.02 (1.00–1.04)	0.03
Requirement for postoperative inotropes	356 (143–1002) ng litre^{-1}	207 (100–605) ng litre^{-1}	1.04 (1.01–1.06)	0.002
Requirement for inotropes >24 h after surgery	419 (169–1160) ng litre^{-1}	254 (114–768) ng litre^{-1}	1.03 (1.01–1.06)	0.001
Requirement for ventilation >24 h after surgery	468 (209–1318) ng litre^{-1}	274 (119–813) ng litre^{-1}	1.03 (1.01–1.05)	0.001
Postoperative atrial fibrillation	388 (150–1004) ng litre^{-1}	246 (105–747) ng litre^{-1}	1.02 (1.00–1.03)	0.02
Postoperative ICU stay >1 day	391 (158–1080) ng litre^{-1}	249 (110–753) ng litre^{-1}	1.03 (1.01–1.05)	<0.001
Hospital stay >1 week	419 (166–1169) ng litre^{-1}	199 (95–502) ng litre^{-1}	1.07 (1.04–1.10)	<0.001

compared with 9 (IQR 7–12) days in patients with NT-proBNP levels above the median (P<0.001).

In a logistic regression model incorporating NT-proBNP and the Parsonnet score, the former was an independent predictor of a prolonged (>1 week) hospital stay: OR 1.05 per 250 ng litre^{-1} (95% CI 1.02–1.07, P=0.001). In models incorporating the additive and logistic EuroSCORE, NT-proBNP levels remained independently predictive: OR 1.03 per 250 ng litre^{-1} (95% CI 1.00–1.06, P=0.02) and OR 1.04 per 250 ng litre^{-1} (95% CI 1.01–1.07, P=0.005), respectively. In similar models, NT-proBNP was independently predictive of a prolonged (>1 day) stay in ICU (P<0.05 for all).

A multivariable model was developed that included all preoperative study variables (Table 1) except creatinine (which is mathematically related to eGFR but has inferior prognostic utility) and the patient's EuroSCORE and Parsonnet scores (which incorporate many of the other variables). The independent predictors of a prolonged hospital stay are shown in Table 5. In a similar model, NT-proBNP was also an independent predictor of a prolonged stay in the ICU (OR 1.03 per 250 ng litre^{-1}, 95% CI 1.01–1.05, P=0.003).

Table 5 Independent predictors of hospital stay >1 week. ORs are presented as per 250 ng litre^{-1} change in NT-proBNP. IABP, intra-aortic balloon pump; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Variable	Odds ratio	95% CI	P-value
Age (yr)	1.04	1.03–1.06	<0.001
Male gender	0.53	0.38–0.75	<0.001
Valve/aortic surgery	1.67	1.19–2.35	0.003
Preoperative IABP	1.67	1.11–2.52	0.01
NT-proBNP	1.03	1.00–1.05	0.04

Discussion

The current data demonstrate that preoperative levels of NT-proBNP predict 30 day mortality after cardiac surgery and are independent of the patient's EuroSCORE and Parsonnet scores. Elevated levels also predict an increased and more prolonged requirement for postoperative cardiovascular support and longer ICU and hospital stays.

NT-proBNP and cardiac risk

The prognostic value of BNP and NT-proBNP has been demonstrated in many settings.[6 7] This appears to be due to the ability of these peptides to reflect several factors

that influence survival, including cardiac dysfunction (systolic and diastolic), the presence and severity of myocardial ischaemia, age, and renal impairment. Indeed, several of the factors that influence BNP and NT-proBNP, such as LV filling pressure/diastolic function and kidney function, are themselves influenced by multiple cardiovascular risk factors and are powerful determinants of outcome.[16 17] This may explain the utility of NT-proBNP in preoperative risk stratification.[8–11] There are, however, only limited data relating to cardiac surgery.

Prior studies

We have previously reported that preoperative BNP levels predicted the level of cardiovascular support and the duration of ICU stay in 46 patients undergoing CABG.[14] Likewise, in 98 male patients undergoing cardiac surgery, BNP levels predicted the requirement for an intra-aortic balloon pump, prolonged hospitalization, and 1 yr mortality.[12] There were few deaths (three within 30 days and 11 within 1 yr) and few other morbidities within this small cohort precluding comparisons with conventional methods of risk assessment.[12] The current study reports our findings in a far larger mixed cohort of patients with an increased number of outcomes. This allows us to conclude, with some certainty, that NT-proBNP levels predict mortality and also a large number of perioperative events in this setting. In addition, they do so independently of standard methods of risk prediction. Certainly, there would be advantages to a biochemical test that would provide an objective measure. There are, however, limitations to the predictive utility of BNP and NT-proBNP, just as there are well-documented limitations to clinical risk scores.[4 5] It may be, therefore, that a combination of biomarkers and clinical assessment will prove the most useful means to determine risk, though this remains untested.

Clinical implications and position in evaluation framework

There has been a move to developing evaluation frameworks for diagnostic tests in clinical practice. A widely used one is the ACCE framework describing analytic validity, clinical validity, clinical usefulness, and ethical, social, and economic implications.[18 19] Regarding NT-proBNP as a prognostic test before cardiac surgery, we would suggest that it has a high analytic validity as there are highly sensitive and specific assays for NT-proBNP. Its clinical validity is moderate due to the modest sensitivity and specificity it demonstrates for the outcome of 30 day mortality in this situation. Its clinical usefulness remains unproven. It does, however, provide additional prognostic information to that derived from existing clinical tools and assessments. Its clinical utility might be maximized when used in combination with other methods of risk stratification. Economically, it is relatively inexpensive at approximately £25 per test, but more data are required on its cost-effectiveness. Validation work will be required in other cardiac surgical groups.

Preoperative measurements of NT-proBNP may assist in the counselling of patients and relatives. They might also aid the planning of surgical lists. Where clinically appropriate, a stable patient who was identified to be at high risk of prolonged ICU care and mechanical cardiovascular support might be scheduled when other demands on these services are likely to be lower. This would facilitate the efficient use of resources.

BNP levels have been used to guide the therapy of patients with heart failure and this approach may reduce adverse events.[20 21] Patients awaiting cardiac surgery who have elevated levels of NT-proBNP may benefit from increased vasodilatation, diuresis, or both. Although one might speculate that this could reduce their risk of perioperative complications, further work would be necessary to test this hypothesis.

Limitations

This is a single-centre study with the inherent limitations. Although we studied a relatively large cohort, the small number of early deaths limits the ability to develop comprehensive multivariable models or perform subgroup analysis. Despite a lower than expected mortality, NT-proBNP levels conveyed statistically significant prognostic utility (even after adjustment for other scores)—so the question of power is arguably less of an issue. Reliance on a single level of NT-proBNP precludes any assessment of the stability of the measurements and we have no data regarding any recent changes to medical therapy. The study cohort consisted, however, of stable patients, the majority of whom would be expected to be taking an established medication regimen. Likewise, if preoperative NT-proBNP testing were to be used clinically for risk stratification, it seems unlikely that serial measures would be practical.

Although visual assessment of LV systolic function correlates well with more complex methods,[22] it is possible that more objective measures might convey superior prognostic information. A further limitation is the absence of data regarding diastolic function, in particular, parameters that reflect LV filling pressure. However, in both these regards, our study reflects standard clinical practice.

Conclusions

The current study demonstrates that NT-proBNP levels predict early outcome after cardiac surgery. Although the predictive utility is modest, it appears to be independent of other widely utilized methods of risk stratification in this setting. Potentially, natriuretic peptide levels might be combined with clinical scoring systems to better quantify the risk of individuals in this setting, used to identify patients who require further haemodynamic optimization

before surgery, or both. These putative roles require further investigation in large studies.

Acknowledgements

We are grateful to the staff on the Cardiothoracic Surgical and Intensive Care Units in Aberdeen Royal Infirmary for their help and support.

Funding

This study was funded by The British Heart Foundation. The funding organization approved the study design, but had no role in data collection, analysis, or interpretation. Likewise, it had no role in preparation or approval of the current manuscript.

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