Preoperative Brain Natriuretic Peptide Predicts Late Mortality and Functional Class but Not Hospital Readmission After Cardiac Surgery

Per Vikholm, MD, Petter Schiller, MD, and Laila Hellgren, MD, PhD

Objectives: N-terminal brain natriuretic peptide (NT-proBNP) is an established biomarker of heart failure and has been found to predict mortality and morbidity after cardiac surgery. The aim of this study was to investigate whether preoperative NT-proBNP can predict postoperative New York Heart Association (NYHA) functional class and hospital readmission in addition to morbidity and mortality.

Design: Retrospective.

Setting: University hospital.

Participants: All patients undergoing aortic valve replacement for aortic stenosis and coronary artery bypass grafting from January to December 2008 (n = 390).

Measurements and Main Results: Preoperative NT-proBNP was recorded prospectively. Five-year mortality was obtained through national registries. Postoperative functional class, morbidity, and hospital readmission were obtained through telephone interviews. Patients were divided into quartiles based on preoperative NT-proBNP; the medians of each quartile were 103 ng/L, 291 ng/L, 825 ng/L and 2,375 ng/L. Increased preoperative NT-proBNP was associated with reduced postoperative functional class. In the first quartile, 7% (7/97) were in NYHA functional class III-IV compared to 26% (25/97) in the fourth quartile ($p < 0.01$). Increased preoperative NT-proBNP was also associated with reduced long-term survival ($p < 0.01$). The covariate adjusted hazard ratio for mortality in the fourth quartile was 2.9 (1.61-5.08; $p < 0.01$) compared to the other quartiles. No association was found between preoperative NT-proBNP and postoperative hospital readmission.

Conclusions: Increased preoperative NT-proBNP is associated with reduced long-term survival and functional class but not hospital readmission post-cardiac surgery. Thus, NT-proBNP might have additive value to established risk factors in the preoperative assessment of patients undergoing cardiac surgery.

KEY WORDS: cardiac surgery, heart failure, mortality, morbidity, postoperative outcome, B-type natriuretic peptide

THE VALUE OF BOTH brain natriuretic peptide (BNP) and its N-terminal portion (NT-proBNP) as prognostic and diagnostic biomarkers has been studied extensively in patients with heart failure and acute coronary syndrome and, more recently, also in patients undergoing cardiac surgery.[1–3] In cardiac surgery, both markers have been found to predict short-term and long-term mortality as well as symptom-free survival.[4–8]

Several attempts have been made to further clarify the role of NT-proBNP, both as a sole predictor but also its additive value to established risk factors such as reduced left ventricular (LV) function in cardiac surgery patients. Preoperative BNP and NT-proBNP also have been shown to predict postoperative complications such as atrial fibrillation (AF), heart failure, need for inotropic drugs, renal failure, and prolonged hospital stay in patients undergoing both coronary artery bypass grafting (CABG) and aortic valve replacement (AVR).[4,6,7,9,10] Thus, there already is support for the use of preoperative BNP/NT-proBNP as a marker for an adverse outcome after cardiac surgery procedures.

To further investigate the relation of this biomarker to timing of cardiac surgery, more recent studies have searched for preoperative cut-off levels that could indicate increased postoperative morbidity and mortality.[3,7,8] However, to advocate earlier surgery in patients with increased NT-proBNP, preoperative levels must be associated with increased mortality as well as an adverse outcome in terms of postoperative function for the patient.

To the authors' knowledge, no study has focused on the utility of NT-proBNP in predicting postoperative functional class and morbidity, more specifically hospital readmission. Both reduced functional class and hospital readmission might reflect surgical correction too late in the disease process and morbidity related to the surgical procedure. Even though the patients survive the surgical procedure, the burden of morbidity can shadow the long-term result in terms of reduced physical capacity and quality of life.

In this study, the authors hypothesized that increased preoperative NT-proBNP could predict long-term mortality, reduced functional class, and hospital readmission after cardiac surgery.

METHODS

All patients (n = 390) undergoing CABG (n = 234), isolated AVR (n = 114) for aortic stenosis (AS) and isolated AVR for AS with concomitant CABG (n = 42) from January 1, 2008 through December 31, 2008 were included in this study. Exclusion criteria were significant aortic insufficiency and double-valve procedures. The study was performed after approval by the local human ethics committee. All patients were informed and agreed to participate in the followup of clinical variables that were entered into the analyses. All procedures were performed with standard technique on extracorporeal circulation (ECC).

Clinical data were recorded prospectively. The following variables were entered into the database preoperatively: Age, sex, left ventricular (LV) function, New York Heart Association (NYHA) functional class, rhythm, hypertension, diabetes, positive inotropic medications, preoperative stroke, hemoglobin, and creatinine. Operative variables were recorded postoperatively: ECC-time, intra-aortic balloon pump (IABP), ventricular assist device (VAD), positive inotropic medications, postoperative rhythm, dialysis, blood transfusion, intensive care unit (ICU) stay, hospital stay, postoperative stroke, infections, and early mortality (ie, 30-days mortality).

From the Department of Cardiothoracic Surgery, Uppsala University Hospital, Uppsala, Sweden.

Address reprint requests to Peter Vikholm, MD, Uppsala University Hospital, Department of Cardiothoracic Surgery, SE75185 Uppsala, Sweden. E-mail: per.vikholm@akademiska.se

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Plasma NT-proBNP was sampled 1 day preoperatively in addition to routine blood analysis, and values were available for all patients. The blood samples were analyzed at the laboratory for clinical biochemistry by immunoassay using a Modular Analytics E170 (Roche Diagnostics, Indianapolis, IN).

Patient followup regarding NYHA functional class, postoperative stroke, anticoagulation, postoperative rhythm, hemorrhage, and hospital readmission was carried out through telephone interviews with the patients. Hospital readmission was defined as admission to the hospital due to any cause. The time to readmission after surgery was divided into less than 1 month, 1-3 months, 3-6 months, or more than 6 months. The number of admissions was classified into 1 time, 2-5 times, or more than 5 times. If patients had been readmitted to the hospital, hospital discharge data were obtained to verify diagnosis. The median followup for telephone interviews was 32 months, with a response rate of 90%.

Survival data were obtained through a continuously updated population register; thus, all patients could be assigned a date of death or identified as being alive. The followup was performed on July 1, 2013, with a median followup of 60 months (ie, 5 years) since surgery.

Statistical analysis was performed in SPSS version 20.0 (SPPS Inc. Chicago, IL). Patients were divided into quartiles based on preoperative NT-proBNP value for analysis and comparison. Categoric variables were expressed as percentages and continuous variables as mean ± standard deviation. Categoric variables were compared using X^2-test and continuous variables using analysis of variance (ANOVA). P-values < 0.05 were considered statistically significant.

Kaplan-Meier plots for each quartile were used for survival analysis; comparison of significant differences in survival among the quartiles was done with a log-rank test (Mantel-Cox). Stepwise Cox proportional hazard analysis was used for risk adjustment and to identify independent preoperative risk factors for overall mortality. The inclusion limit for stepwise backward elimination was a p value < 0.05. The following variables were included in the analysis: Age, sex, diabetes, hypertension, LV ejection fraction, hemoglobin, creatinine, and NT-proBNP. Among these variables, age, hemoglobin, creatinine, and NT-proBNP were found to be significant predictors.

A receiver operator characteristics (ROC) curve also was plotted to identify sensitivity and specificity for NT-proBNP values to predict mortality.

RESULTS

All patients were divided into quartiles based on preoperative NT-proBNP values. The median value of NT-proBNP in the quartiles were: 103 ng/L, 291 ng/L, 825 ng/L and 2,375 ng/L (Table 1).

Increased preoperative NT-proBNP was associated with older age, female sex, reduced LV function, diabetes, preoperative AF, need for preoperative inotropic support, IABP, low hemoglobin concentration and increased creatinine (Table 1). There was also

Table 1. Patient Characteristics Divided by Preoperative NT-proBNP-Quartile, n = 390

Variable*	First Quartile (n = 97)	Second Quartile (n = 98)	Third Quartile (n = 98)	Fourth Quartile (n = 97)	p Value
NT-proBNP, ng/L (Median)	103	291	825	2375	
NT-proBNP, ng/L, (IQR)	60 - 140	238 - 379	598 - 1055	1770 - 4360	
NT-proBNP, ng/L (Range)	5 - 195	196 - 470	486 - 1325	1326 - 45931	
Diagnosis					<0.01
CABG	76 (78)	70 (71)	47 (48)	41 (42)	
AVR	16 (17)	26 (27)	34 (35)	38 (39)	
AVR + CABG	5 (5)	2 (2)	17 (17)	18 (19)	
Age, mean (SD), years	63 (9)	68 (9)	71 (9)	73 (9)	<0.01
Sex					0.01
Male	85 (88)	70 (71)	67 (68)	69 (71)	
Female	12 (12)	28 (29)	31 (32)	28 (29)	
LVEF					<0.01
≥50%	94 (97)	87 (89)	75 (77)	46 (47)	
30-50%	2 (2)	10 (10)	19 (19)	32 (33)	
<30%	1 (1)	1 (1)	4 (4)	19 (20)	
Rhythm					<0.01
Sinus/PM	92 (95)	92 (94)	84 (86)	74 (76)	
AF	5 (5)	6 (6)	14 (14)	23 (24)	
NYHA-class					0.33
I	4 (4)	2 (2)	1 (1)	1 (1)	
II	18 (19)	12 (12)	18 (18)	11 (11)	
III	73 (75)	81 (83)	73 (75)	76 (78)	
IV	2 (2)	3 (3)	6 (6)	9 (9)	
Hypertension	88 (91)	89 (91)	86 (88)	91 (94)	0.55
Diabetes	18 (19)	23 (24)	16 (16)	33 (34)	0.02
Inotropes/IABP	0 (0)	0 (0)	0 (0)	4 (4)	0.01
CVL					0.21
Stroke	6 (6)	3 (3)	5 (5)	12 (12)	
TIA	2 (2)	3 (3)	2 (2)	1 (1)	
Hemoglobin, mean (SD), g/L	148 (12)	139 (14)	139 (12)	136 (16)	<0.01
Creatinine, mean (SD), mmol/L	79 (15)	80 (21)	82 (25)	93 (42)	<0.01

NOTE: The p values represent comparison among quartiles 1-4.

Abbreviations: AF, atrial fibrillation; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CVL, cerebral vascular lesion; IABP, intra-aortic balloon pump; IQR, interquartile range; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal brain natriuretic peptide; NYHA, New York Heart Association; PM, pacemaker; SD, standard deviation; TIA, transient ischemic attack.

*Values are presented as number and percentage of patients unless specified otherwise.

an increased proportion of patients with AS in higher quartiles ($p < 0.01$) (Table 1). The prevalence of hypertension and stroke, however, had no association with increased preoperative NT-proBNP. Further, there was no difference in the distribution of preoperative NYHA functional classes among the preoperative NT-proBNP quartiles ($p = 0.33$) as depicted in Figure 1A.

Early mortality was 1.7% (7/390) and had no association with increased values of preoperative NT-proBNP, ($p = 0.27$) (Table 2). Patients in the highest quartile had more complicated surgery with longer ECC time ($p < 0.01$) and more blood transfusions ($p < 0.01$) (Table 2). On the other hand, postoperative complications such as sternal infection, need for dialysis, and stroke did not differ among quartiles (Table 2).

Patients in the first quartile had the lowest risk to develop postoperative AF (Table 2). Among these patients, 71 % (73/97) maintained sinus rhythm postoperatively compared to 44% (45/97) of the patients in the fourth quartile ($p < 0.01$) (Table 2). The mean time spent in the ICU was 4.4 days in the fourth quartile and 3.8 days in the third quartile compared to 2.6 and 2.7 days in the first and second quartiles ($p < 0.01$) (Table 2).

Patients who had died at the 5-year followup had a mean preoperative NT-proBNP of 2,882 ng/L (1144-4620, 95%

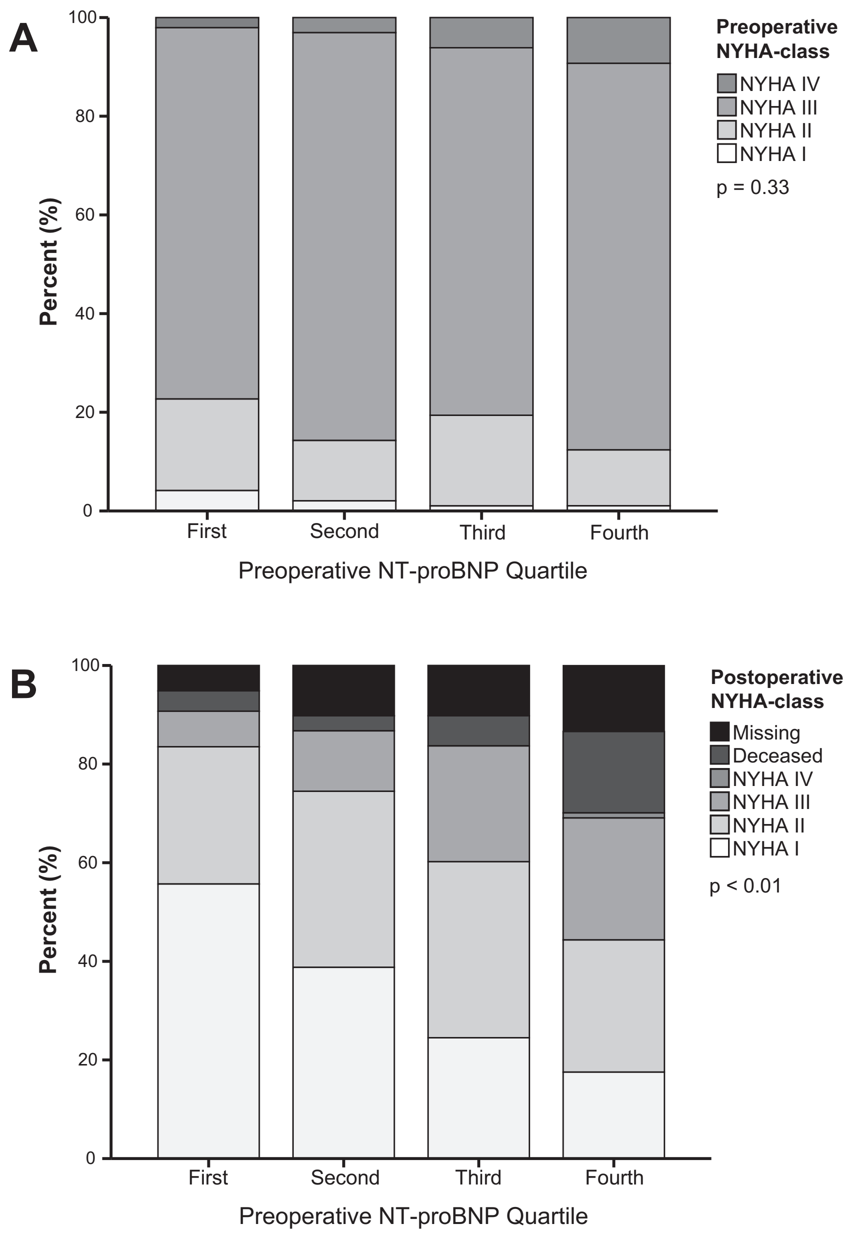

Fig 1. (A) Preoperative New York Heart Association functional class categorized by preoperative NT-proBNP quartiles, n = 390. (B) Postoperative New York Heart Association functional class, mortality, and patients lost to followup categorized by preoperative NT-proBNP quartiles, median followup time 32 months, n = 390.

Table 2. Operative Characteristics Divided by Preoperative NT-proBNP-Quartile, n = 390.

Variable*	First Quartile (n = 97)	Second Quartile (n = 98)	Third Quartile (n = 98)	Fourth Quartile (n = 97)	p Value
ECC-time, mean (SD), min	95 (35)	97 (34)	112 (39)	124 (45)	<0.01
IABP	0 (0)	0 (0)	2 (2)	4 (4)	0.06
VAD/ECMO	0 (0)	0 (0)	1 (1)	0 (0)	0.39
Inotropes†	2 (2)	6 (6)	5 (5)	10 (10)	0.11
Rhythm					<0.01
Sinus/PM	71 (73)	54 (55)	36 (37)	44 (45)	
AF	26 (27)	44 (45)	62 (63)	53 (55)	
Dialysis	0 (0)	0 (0)	1 (1)	2 (2)	0.29
Transfusion, mean (SD), units	2.1 (2.8)	2.3 (2.4)	3.6 (4.8)	4.1 (3.8)	<0.01
ICU, mean (SD), days	2.6 (1.5)	2.7 (1.4)	3.8 (4.1)	4.4 (4.7)	<0.01
CVL	3 (3)	3 (3)	4 (4)	6 (6)	0.66
Infections					0.44
Superficial sternal	2 (2)	2 (2)	5 (5)	3 (3)	
Deep sternal	4 (4)	0 (0)	4 (4)	4 (4)	
Other	7 (7)	7 (7)	7 (7)	12 (12)	
30-days mortality	0 (0)	1 (1)	3 (3)	3 (3)	0.27

NOTE: The p values represent comparison among quartiles 1-4.

Abbreviations: AF, atrial fibrillation; CVL, cerebral vascular lesion; ECC, extracorporeal circulation; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; NT-proBNP, N-terminal brain natriuretic peptide; PM, pacemaker; SD, standard deviation; VAD, ventricular assist device.

*Values are presented as number and percentage of patients unless specified otherwise.

†Three or more inotropic drugs at the same time.

confidence interval [CI]), while survivors had a lower mean value of 1,046 ng/L (808-1284, 95% CI). Long-term survival was lower in the fourth quartile compared to the other quartiles ($p < 0.01$) (Fig 2A). With the other quartiles combined as 1 reference, the hazard ratio for mortality in the fourth quartile was 4.3 (2.54-7.39; $p < 0.01$) in univariate analysis. In multivariate Cox-regression analysis, age, hemoglobin and creatinine were found to be significant risk factors for reduced survival in addition to preoperative NT-proBNP. Survival adjusted for these risk factors revealed that the patients in the fourth quartile still had a lower survival than the patients in the other quartiles with a hazard ratio of 2.9 (1.6-5.1; $p < 0.01$) (Fig 2B).

The predictive value of NT-proBNP regarding long-term mortality was considered to be fair, with an area under curve of 0.72 (0.64-0.79) in the ROC analysis (Fig 3). A preoperative value of >850 ng/L had a sensitivity and specificity of 69% and 68%, respectively; while a preoperative value of >1300 ng/L had a sensitivity of 56% and a specificity of 80%.

There was no difference in patient response rate among the quartiles ($p = 0.13$) (Table 3). Increased preoperative NT-proBNP was associated with reduced postoperative NYHA functional class ($p < 0.01$) (Fig 1B). At followup, 7% (7/97) of patients in the first quartile were in NYHA-class III-IV; the proportion of patients in NYHA-class III-IV then gradually increased with each quartile, resulting in the largest proportion, 26% (25/97), in the fourth quartile (Table 3).

Increased preoperative NT-proBNP did not predict hospital readmission or time to readmission ($p = 0.11$) (Table 3). Further, the number of postoperative readmissions to the hospital was not higher in patients with increased preoperative NT-proBNP ($p = 0.75$). The diagnosis associated with hospital readmission (eg, arrhythmia, ischemia, and heart failure) was similar among all quartiles ($p = 0.27$) (Table 3).

DISCUSSION

This study demonstrated that increased preoperative NT-proBNP predicts reduced long-term survival and reduced NYHA functional class after cardiac surgery. On the contrary, early mortality was not affected by an increased value of preoperative NT-proBNP. Moreover, the study also revealed that the rate of hospital readmission and the number of admissions postoperatively were not increased in patients with increased preoperative NT-proBNP.

The predictive value of preoperative NT-proBNP has been evaluated in several studies with cardiac surgery populations.[4–8] However, the vast majority of these studies included series of patients with relatively small sample sizes, and the followup mainly has been focused on mortality and postoperative complications. The authors' study was based on consecutive patients within a defined geographic area; selection was thereby minimized, and the results should be representative and valid. In addition to mortality, they also assessed the relation of preoperative NT-proBNP to postoperative NYHA class and hospital readmission, which extended current available information on the predictive value of preoperative NT-proBNP and therefore motivated their study.

The increase in long-term mortality associated with elevated preoperative NT-proBNP is consistent with previous studies.[4,7,8,11,12] For example, Schachner et al studied NT-proBNP in 819 patients undergoing isolated CABG and found that a preoperative NT-proBNP $\geq$ 502 ng/L best predicted overall mortality.[7] This value corresponded well with the value of the patients in the third and fourth quartiles in the present study. Schachner et al also reported a 3-year survival rate for patients with preoperative NT-proBNP $\geq$ 502 ng/L at 87%,[7] also corresponding well to the survival rate in the authors' study for patients in the third and fourth quartiles. However,

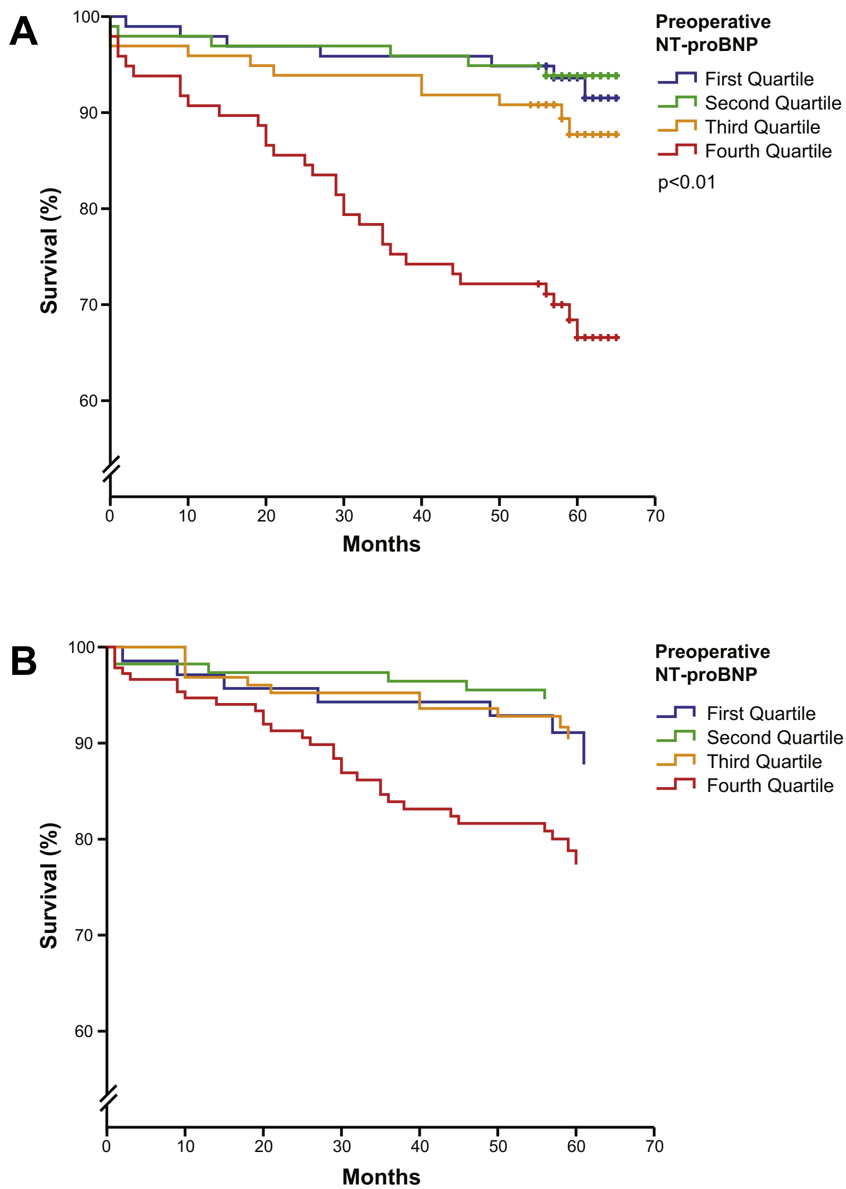

Fig 2. (A) Kaplan-Meier of overall survival categorized by preoperative NT-proBNP quartiles, n = 390. (B) Adjusted survival at mean of risk factors for reduced survival (age [69 years], hemoglobin [140 g/L], and creatinine [84 mmol/L]) categorized by preoperative NT-proBNP quartiles, n = 390.

when adjusting survival for age, hemoglobin, and creatinine, only patients in the fourth quartile (ie, NT-proBNP ≥1,326 ng/L) had increased long-term mortality. This suggested that only values of relatively high levels might have additive value to other risk score models in the preoperative evaluation of the patient. There was also an association between increased preoperative NT-proBNP and reduced NYHA functional class postoperatively. However, these data were not age-adjusted, and, therefore, it could be speculated whether these results might have been influenced by the increased mean age associated with each preoperative NT-proBNP quartile. On the other hand, studies on older patients undergoing cardiac surgery show that they are not necessarily in worse functional classification simply due to older age. In fact, older patients accepted for cardiac surgery are selected with respect to their better overall medical condition concerning non-cardiac diseases at the time of surgery.[13]

Several previous studies demonstrated conflicting results regarding early mortality and its relation to NT-proBNP.[4,6,14] The majority of studies that had found an association between NT-proBNP and early mortality had higher rates of early mortality than studies that found no association.[4,6,14] The studies reporting an association included more complex cases such as aortic root surgery, ventricular septal defects, and mitral valve surgery. For example. in one of the larger studies,[6] the use of preoperative IABP was above 10%. This indicated a high proportion of patients at increased risk for early mortality. The early mortality rate in the present study was low (ie, 1.7%),

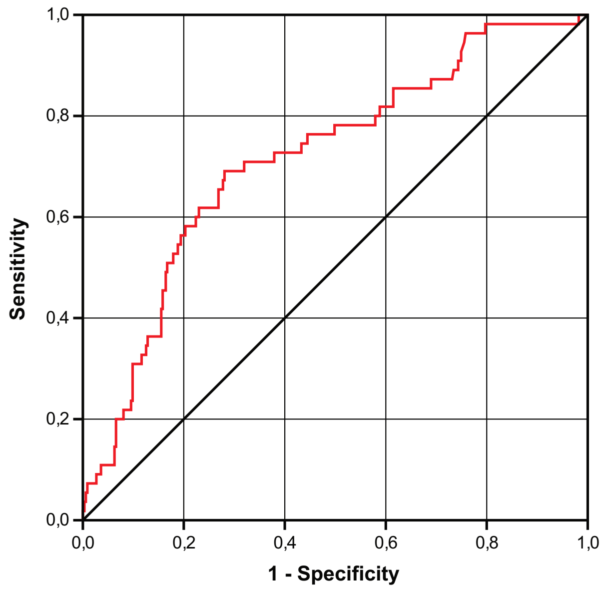

Fig 3. Receiver operating characteristic (ROC) curve for the sensitivity (the ability to correctly identify deceased patients at followup) and specificity (the ability to correctly identify patients who are alive at followup) of preoperative NT-proBNP, ie, diagnostic utility of NT-proBNP on long-term mortality after cardiac surgery, n = 390.

including only 7 cases in a population of CABG and AVR patients since the more complex cases were excluded. Thus, the few cases of early mortality and the more favorable population in the present study might explain the lack of association between NT-proBNP and early mortality.

An intriguing finding of this study was that despite the increased mortality and reduced postoperative NYHA functional class in the fourth quartile, there was no difference among quartiles in rate of hospital readmission, neither in time to first readmission nor in frequency of readmission. There was, however, a trend towards more frequent readmission due to heart failure in higher quartiles. In a study regarding hospital readmission of 7,493 cardiac surgery patients,[15] the risk of readmission increased with more advanced preoperative NYHA functional class and reduced LV function preoperatively. In that study, NT-proBNP was not reported, but both advanced NYHA functional class and reduced LV function which reflected clinical heart failure and, thereby, also increased levels of NT-proBNP. This correlation was illustrated in the authors' study in which there was an increase in the proportion of patients with reduced LV function with increasing quartile.

The association between LV function and NT-proBNP was further illustrated by Gonzales et al, who found that NT-proBNP values $\geq$ 1,604 ng/L have 67% sensitivity and 50% specificity for elevated LV filling pressures,[16] which is a reflection of diastolic heart failure. This suggests that NT-proBNP adds information in patients with normal systolic function and that preserved systolic LV function alone is not sufficient to identify preoperative heart failure.[17] In the cardiac surgery population, patients with heart failure with preserved ejection fraction (HFpEF) are not detected easily by routine echocardiography. Therefore, a high value of NT-proBNP can add useful information in the preoperative assessment of these patients. Interestingly, 50% of patients with highest values (ie, fourth quartile) of the present study had a preserved LV function on preoperative echocardiography.

Previous studies have demonstrated the predictive value of increased preoperative NT-proBNP for complications such as postoperative need for positive inotropic support, IABP, postoperative AF, renal failure, and longer ICU stay.[2,4,9–11] These endpoints were more specifically analyzed in a recent meta-analysis on the use of preoperative BNP and NT-proBNP that identified 819 studies.[18] In that meta-analysis, only 12 studies were shown to have a sufficient number of comparable end points (mortality, AF, IABP) to be properly evaluated. These endpoints were assessed in the present study and revealed that high preoperative NT-proBNP predicted increased prevalence of postoperative AF and long-term mortality. Furthermore, the authors found a trend towards increased use of inotropic support, IABP, and dialysis in the higher preoperative NT-proBNP quartiles; however, these findings did not reach statistical significance.

The findings of the present study support previous studies suggesting that elevated preoperative NT-proBNP is associated with adverse events post-cardiac surgery. However, a clinical cut-off value is difficult to define. The value of 850 ng/L maximizes sensitivity and specificity for long-term mortality according to the ROC analysis. However, for guidance of intervention, the authors advocate a higher value with higher specificity. In terms of prediction, a preoperative value of 1,300 ng/L has a positive predictive value of 31% and a negative predictive value of 92% for long-term mortality. Accordingly, 8% of the patients with NT-pro BNP less than 1300 ng/L were predicted to be deceased at long-term followup while 31% of the patients with a value of greater than 1300 ng/L would be deceased.

The earlier suggested cut-off value for increased left-sided filling pressures ($>$1604 ng/L) by Gonzales et al in combination with the cut-off value for adverse events suggested by Weber et al (640 ng/L),[3,16] suggested that patients in the highest quartile (median 2,375 ng/L) in the present study might have been operated too late in the disease process. Therefore, NT-proBNP levels above 1,300 ng/L might be a valuable addition to the preoperative assessment for the clinician and should probably encourage optimizing of the heart failure status of the patient preoperatively. This might be through optimization of volume status and medications; levels of NT-proBNP can then be measured repeatedly until the patient has reached a more favorable clinical condition. However, the full utility of preoperative NT-proBNP for postoperative risk stratification is yet to be more clearly defined.

A limitation of this study was that the number of patients became smaller when subdividing into quartiles, which reduced the statistical power to predict rare events (eg, postoperative use of IABP and postoperative dialysis). Further, postoperative data of NYHA functional class and hospital readmission frequency were gathered through telephone interviews and, therefore, based on the subjective evaluation of patient history, which added some degree of uncertainty.

Table 3. Postoperative Followup and Mortality Divided by Preoperative NT-proBNP-value, n = 390

Variable*	First Quartile (n = 97)	Second Quartile (n = 98)	Third Quartile (n = 98)	Fourth Quartile (n = 97)	p Value
Response rate, interviews	88/93 (95)	85/95 (89)	82/92 (89)	68/81 (84)	0.13
NYHA-class*					<0.01
I	54 (56)	38 (39)	24 (25)	17 (18)	
II	27 (28)	35 (36)	35 (36)	26 (27)	
III	7 (7)	12 (12)	23 (24)	24 (25)	
IV	0 (0)	0 (0)	0 (0)	1 (1)	
Desceased	4 (4)	3 (3)	6 (6)	16 (17)	
Missing	5 (5)	10 (10)	10 (10)	13 (13)	
CVL*					0.44
Stroke	3 (3)	3 (3)	3 (3)	5 (5)	
TIA	0 (0)	4 (4)	3 (3)	2 (2)	
Anticoagulation*					0.19
Warfarin	12 (13)	12 (12)	18 (18)	19 (20)	
ASA	65 (67)	64 (65)	58 (59)	46 (47)	
Other	7 (7)	3 (3)	2 (2)	1 (1)	
Rhythm*					0.05
Sinus/PM	78 (80)	72 (73)	66 (67)	49 (51)	
AF	10 (11)	13 (14)	17 (17)	19 (20)	
Hemorrhage*					0.93
Minor	8 (8)	7 (7)	8 (8)	5 (5)	
Major	2 (2)	2 (2)	1 (1)	3 (3)	
Readmission to hospital*‡					0.27
Heart failure	0 (0)	0 (0)	3 (4)	4 (6)	
Arrhythmia	4 (5)	4 (5)	4 (5)	3 (4)	
Ischemia	6 (7)	4 (5)	1 (1)	1 (2)	
Other	23 (26)	23 (27)	26 (31)	21 (31)	
First readmission*					0.11
<1 month	6 (7)	5 (6)	9 (11)	3 (4)	
1-3 months	4 (5)	0 (0)	4 (5)	3 (4)	
3-6 months	1 (1)	0 (0)	1 (1)	4 (6)	
>6 months	22 (23)	25 (29)	19 (23)	19 (28)	
Occasions of readmission*					0.75
1 time	22 (25)	22 (26)	19 (23)	16 (24)	
2-5 times	10 (11)	9 (11)	12 (15)	10 (15)	
>5 times	1 (1)	0 (0)	2 (2)	2 (3)	
Survival, register study†					
1-year	95 (98)	96 (98)	94 (96)	88 (91)	
2-year	94 (97)	95 (97)	92 (94)	83 (86)	
3-year	93 (96)	95 (97)	92 (94)	74 (76)	
4-year	93 (96)	93 (95)	90 (92)	70 (72)	
Last follow-up (July 1, 2013)§	90 (93)	92 (94)	87 (89)	66 (68)	<0.01

NOTE: The p values represent comparison between quartiles 1 and 4. Values are presented as number and percentage of patients.

Abbreviations: AF, atrial fibrillation; ASA, acetylsalicylic acid; CVL, cerebral vascular lesion; NT-proBNP, N-terminal brain natriuretic peptide; NYHA, New York Heart Association; PM, pacemaker; TIA, transient ischemic attack.

*Data acquired through patient interviews.

†Data acquired through register studies, ie, no patient lost to followup.

‡Dominating cause for readmission to hospital.

§Median followup time since surgery 60 months (ie, 5 years).

In conclusion, this study confirmed that increased preoperative NT-proBNP is associated with reduced long-term survival and reduced NYHA functional class after cardiac surgery. On the contrary, early mortality and hospital readmission showed no association with increased preoperative NT-proBNP. The authors' study suggested that this biomarker can be of additive value in preoperative risk assessment in patients undergoing cardiac surgery.

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