Diagnostic accuracy of pre-operative NT-proBNP level in predicting short-term outcomes in coronary surgery: a pilot study

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Abstract

Background: B-type natriuretic peptides (BNP) are acknowledged markers of acute and chronic heart failure. Insufficient data exist, however, regarding their diagnostic usefulness in cardiac surgery, particularly in coronary patients.

Aim: To assess diagnostic accuracy of preoperative value of NT-proBNP level as a predictor of short-term postoperative complications in subjects undergoing coronary artery bypass grafting (CABG).

Methods: This pilot study included 100 consecutive patients scheduled for elective CABG, including 24 females and 76 males (mean age 65.9 ± 9.1 years). Exclusion criteria were: significant valvular disorders, off-pump procedure, renal failure (GFR < 60 mL/min/1.73 m²), low ejection fraction (< 30%), intra-aortic balloon pump counterpulsation (IABP), use of inotropic agents, atrial fibrillation (AF), and implanted pacemaker or defibrillator. The NT-proBNP level was measured on the day of the surgery before induction of anaesthesia. We investigated short-term postoperative complications, defined as those occurring within 30 days or before hospital discharge.

Results: Median NT-proBNP concentration was 526.0 pg/mL (IQR 156.0–1150.0). None of patients died postoperatively. Excessive drainage (> 850 mL) was found in 13 (13%) patients and 22 (22%) subjects required transfusions. Prolonged mechanical ventilation (> 12 h) was necessary in 15 (15%) patients and respiratory failure occurred in 2 (2%) of them. Postoperative AF was present in 34 (34%) subjects. Perioperative myocardial infarction was diagnosed in 2 (2%) persons. Low cardiac output was present in 9 (9%) patients. Haemodynamic support with the use of IABP was necessary in 7 (7%) patients and inotropic drugs were used in 61 (61%) subjects. Stroke or delirium was diagnosed in 1 (1%) subject. The NT-proBNP level correlated with the operative risk estimated by logistic and additive EuroSCORE: r = 0.558 (95% CI 0.406–0.680; p < 0.001) and r = 0.551 (95% CI 0.397–0.674; p < 0.001), respectively. The NT-proBNP level correlated significantly with the length of Intensive Care Unit (ICU) stay and hospital stay: r = 0.412 (95% CI 0.238–0.566; p < 0.001) and r = 0.547 (95% CI 0.393–0.672; p < 0.001), respectively. The NT-proBNP level was a predictor of postoperative prolonged mechanical ventilation, respiratory failure, AF, IABP use, inotropic support and postoperative platelet transfusions (p < 0.05 for all). However, good or very good diagnostic accuracy was found only in relation to mechanical ventilation (AUROC = 0.854), respiratory insufficiency (AUROC = 0.867), IABP use (AUROC = 0.889), and milrinone use (AUROC = 0.929).

Conclusions: Preoperative assessment of NT-proBNP level in CABG patients could be a valuable diagnostic method for predicting several postoperative complications, especially pulmonary outcomes and requirement for haemodynamic support, and it correlated with the length of ICU stay and hospital stay.

Key words: coronary artery bypass grafting, NT-proBNP, diagnostic accuracy, postoperative complications

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INTRODUCTION
B-type natriuretic peptides (BNP) and N-terminal BNP pro-peptide (NT-proBNP) are established markers of acute and chronic heart failure (HF) [1, 2]. Their level reflects the haemodynamic status and has a prognostic value, as it correlates with mortality and morbidity even in patients without overt HF [2–4]. The use of natriuretic peptides as a population screening tool to detect left ventricular (LV) dysfunction is, however, limited [5].

Monitoring BNP and NT-proBNP levels has been successfully used to evaluate cardiovascular (CV) status in patients acutely admitted to emergency departments [6], patients with cardiac arrhythmia and patients undergoing heart transplantation [7]. Still little is known, however, on their utility in patients undergoing cardiac surgery, including surgery for coronary artery disease. Monitoring BNP and NT-proBNP levels might help evaluate operative risk and predict post-operative complications.

Our study aimed to assess diagnostic accuracy of pre-operative value of NT-proBNP level as a predictor of short-term postoperative complications in subjects undergoing coronary artery bypass grafting (CABG).

METHODS

Study group
Upon approval of the Ethics Committee and obtaining written patient consent, the study group was recruited from consecutive 900 patients referred for elective CABG between September 2009 and June 2010. Exclusion criteria included significant valve disease (requiring surgical correction), off-pump procedure, preoperative chronic kidney disease (glomerular filtration rate — GFR < 60 mL/min/1.73 m²), severely decreased LV ejection fraction (LVEF < 30%), preoperative intra-aortic balloon pump counterpulsation (IABP) or use of inotropic agents, preoperative atrial fibrillation (AF), and implanted pacemaker or defibrillator. Overall, 100 patients fulfilling the above criteria were included into the study. We determined their exact clinical profile including demographic variables, concomitant disease, HF symptoms categorised using the New York Heart Association (NYHA) functional classification, and the operative risk determined by logistic and additive EuroSCORE.

The NT-proBNP level determination
The NT-proBNP level was measured on the day of the surgery before induction of anaesthesia. The ECLIA (Electrochemiluminescence, Elecsys 2010, Roche Diagnostics) was used to assess NT-proBNP concentration in venous blood.

Post-operative complications
We investigated postoperative complications including early deaths (within 30 days or before hospital discharge), excessive drainage (defined as exceeding the 90. percentile of the observed values), need for blood transfusion, respiratory failure, need for prolonged mechanical ventilation (> 12 h), AF, myocardial infarction (MI), low cardiac output syndrome, need for haemodynamic support using IABP or inotropic drugs, central nervous system ischaemia or delirium, acute renal failure, and splanchnic ischaemia. Acute respiratory distress syndrome was diagnosed in subjects requiring prolonged mechanical ventilation to combat or prevent hypoxaemia due to an inflammatory process, impaired perfusion or other forms of capillary transport disturbances.

Statistical analysis
Statistical analysis was performed using procedures of the MedCalc software. Quantitative variables are presented as mean values and standard deviations (normally distributed variables) or median values and interquartile ranges (IQR) (non-normally distributed variables), and qualitative variables as absolute numbers and percentages. Correlations between quantitative variables were evaluated using the Pearson linear correlation coefficient, if necessary after logarithmic transformation. Diagnostic accuracy was analysed on the basis of the area under the ROC curve (AUROC). A p value < 0.05 was considered statistically significant.

RESULTS
The study included 24 women and 76 men. The mean patient age was 65.9 ± 9.1 years. A detailed patient characteristics including comorbidities is shown in Table 1. The median baseline operative risk was 4 points (IQR 2–7) by additive EuroSCORE and 2.90% (IQR 1.75–8.40) by logistic EuroSCORE. Median NT-proBNP level was 526.0 pg/mL (IQR 156.0–1150.0).

The median time of cardiopulmonary bypass was 71 min (IQR 60–81), and the median time of aortic clamping was 48 min (IQR 46–54). Median of three bypass graft per patient were performed (IQR 3–3). The left anterior descending artery was grafted in 98 patients (including 96 arterial grafts), the left circumflex artery was grafted in 92 patients (all venous grafts), and the right coronary artery was grafted in 80 patients (all venous grafts); in addition, 13 grafts were performed to other coronary vessels (all venous grafts), resulting in complete revascularisation in all patients.

No postoperative deaths were noted. The median duration of stay in the postoperative Intensive Care Unit (ICU) was 2 days (IQR 2–2), and of total hospitalisation time was 7 days (IQR 6–8). Median postoperative drainage volume was 500 mL (IQR 400–735), and excessive drainage (> 850 mL) was noted in 13 (13%) patients. Blood product transfusions were necessary in 22 (22%) patients, including packed red cells in 22 (22%) patients, fresh frozen plasma in 16 (16%) patients, and platelets in 9 (9%) patients. Prolonged mechanical ventilation (> 12 h) was necessary in 15 (15%) patients, and respiratory failure was diagnosed in 2 (2%) patients. Postoperative AF was noted in 34 (34%) patients, and perioperative MI was diagnosed in 2 (2%) patients. Low cardiac out-

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NT-proBNP level in predicting outcome in CABG patients

Preoperative NT-proBNP level showed a significant correlation with baseline risk by logistic EuroSCORE (r = 0.558; 95% CI 0.406–0.680; p < 0.001) and additive EuroSCORE (r = 0.551; 95% CI 0.397–0.674; p < 0.001). The NT-proBNP level showed a negative correlation with baseline GFR (r = –0.211; 95% CI –0.391 to –0.015; p = 0.04) but was not related to cardiopulmonary bypass duration (r = 0.111; 95% CI –0.094 to 3.07; p = 0.3) and aortic clamping duration (r = –0.113; 95% CI –0.309 to 0.093; p = 0.3). Of note, LVEF showed a significant negative correlation with NT-proBNP level (r = –0.540; 95% CI –0.666 to –0.384; p < 0.01). The NT-proBNP levels were highest in patients with lowest LVEF (30–40%; median 1780.0 pg/mL; IQR 977.5–2861), lower in patients with LVEF of 41–50% (median 480 pg/mL; IQR 203.7–699.0), and lowest in patients with LVEF > 50% (median 306 pg/mL; IQR 99.8–999.0; p < 0.001).

Relation between the number of grafts and NT-proBNP level approached statistical significance (r = 0.203; 95% CI 0.006–0.384; p = 0.05). The NT-proBNP levels were highest in patients with 4 grafts (median 908.5 pg/mL; IQR 260.5–999.0), lower in patients with 3 grafts (median 559.0 pg/mL; IQR 151.5–1335.0), and lowest in patients with 2 grafts (median 290.0 pg/mL; IQR 92.8–554.75). A weak, albeit statistically significant correlation was found between baseline NT-proBNP level and postoperative drainage volume (r = 0.244; 95% CI 0.050–0.421; p = 0.01).

Preoperative NT-proBNP level was a significant predictor of the need for prolonged ventilation, respiratory failure, AF, need for IABP, need for inotropic drugs (dopamine, adrenaline, and milrinone), and platelet transfusion. Good or very good diagnostic accuracy (AUROC > 0.8) in predicting postoperative complications was found only for the need for prolonged ventilation (AUROC = 0.854), respiratory failure (AUROC = 0.867), need for IABP (AUROC = 0.889), and need for milrinone (AUROC = 0.929). For the remaining complications, the diagnostic accuracy was moderate (AUROC 0.7 to 0.8) or weak (AUROC 0.6 to 0.7). These findings are summarised in Table 2 and Figures 1–4.

DISCUSSION

The purpose of our study was to assess the usefulness of preoperative NT-proBNP measurements in predicting most common postoperative complications in patients undergoing CABG. We found that NT-proBNP measurements are particularly useful in predicting pulmonary outcomes and requirement for haemodynamic support with IABP. We also found that NT-proBNP level correlated with the length of ICU stay and total hospitalisation length. Of note, NT-proBNP
level was related to the extent of the surgery, with higher levels in patients with more grafts. The NT-proBNP level also correlated with the drainage volume.

These findings are mostly consistent with the current state of knowledge, although so far only few authors evaluated diagnostic accuracy of NT-proBNP measurements and reported potential cut-off values for predicting specific complications. In a study by Schachner et al. [8], preoperative level of > 502 ng/mL was significantly related to prolonged ventilation time, length of ICU stay, the need for IABP and haemofiltration, and the incidence of AF (p = 0.03) in patients undergoing CABG. In another study in a similar group of patients, NT-proBNP level was a predictor of an ICU stay lasting longer than one day (OR 1.03 for each increase in NT-proBNP level by 250 ng/L) and total hospitalisation length above one week (OR 1.07 for each increase in NT-proBNP level by

**Table 2. Diagnostic accuracy of preoperative NT-proBNP level in predicting postoperative complications**

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>AUROC (95% CI)</th>
<th>Cut-off value for the given diagnosis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Value [pg/mL]</td>
<td>Sensitivity [%]</td>
</tr>
<tr>
<td>Prolonged mechanical ventilation (&gt; 12 h)</td>
<td>0.854 (0.769–0.917)</td>
<td>&gt; 1032</td>
<td>86.7</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>0.867 (0.785–0.927)</td>
<td>&gt; 1443</td>
<td>100.0</td>
</tr>
<tr>
<td>Excessive drainage (&gt; 850 mL)</td>
<td>0.625 (0.523–0.720)</td>
<td>&gt; 1335</td>
<td>53.8</td>
</tr>
<tr>
<td>Any blood product transfusion</td>
<td>0.538 (0.436–0.639)</td>
<td>&gt; 1335</td>
<td>31.8</td>
</tr>
<tr>
<td>Packed red cells transfusion</td>
<td>0.538 (0.436–0.639)</td>
<td>&gt; 1335</td>
<td>31.8</td>
</tr>
<tr>
<td>Fresh frozen plasma transfusion</td>
<td>0.496 (0.395–0.598)</td>
<td>≤ 71</td>
<td>31.2</td>
</tr>
<tr>
<td>Platelet transfusion</td>
<td>0.683 (0.582–0.772)</td>
<td>≤ 71</td>
<td>55.6</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0.650 (0.548–0.743)</td>
<td>&gt; 513</td>
<td>73.5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.571 (0.469–0.670)</td>
<td>&gt; 324</td>
<td>100.0</td>
</tr>
<tr>
<td>Low cardiac output syndrome</td>
<td>0.642 (0.540–0.736)</td>
<td>&gt; 1150</td>
<td>66.7</td>
</tr>
<tr>
<td>IABP</td>
<td>0.889 (0.811–0.943)</td>
<td>&gt; 1032</td>
<td>100.0</td>
</tr>
<tr>
<td>Any inotropic drug</td>
<td>0.730 (0.632–0.814)</td>
<td>&gt; 684</td>
<td>55.7</td>
</tr>
<tr>
<td>Dopamine</td>
<td>0.748 (0.651–0.829)</td>
<td>&gt; 559</td>
<td>61.7</td>
</tr>
<tr>
<td>Adrenaline</td>
<td>0.697 (0.597–0.785)</td>
<td>&gt; 1032</td>
<td>70.0</td>
</tr>
<tr>
<td>Milrinone</td>
<td>0.929 (0.859–0.970)</td>
<td>&gt; 1340</td>
<td>100.0</td>
</tr>
</tbody>
</table>

AUROC — area under ROC curve; CI — confidence interval; IABP — intra-aortic balloon pump counterpulsation
NT-proBNP level in predicting outcome in CABG patients

Importantly, findings were reported in a meta-analysis of studies evaluating the utility of preoperative NT-proBNP measurements in predicting early complications in patients undergoing vascular surgery [10]. In this study, BNP or NT-proBNP level was a significant predictor of the 30-day risk of a cardiac death (OR 7.6; 95% CI 1.33–43.4), non-fatal MI (OR 6.24; 95% CI 1.82–21.4), and a combined endpoint of major adverse cerebral and CV events (MACCE) (OR 17.37; 95% CI 3.31–91.15).

In turn, BNP level > 190 pg/mL was a predictor of an ICU stay lasting > 5 days (AUROC 0.712), and a level of > 20.5 pg/mL predicted the need for dobutamine use (AUROC 0.842). The BNP level significantly correlated with the duration of ventilation support, the length of ICU stay, and the duration of dobutamine administration [11]. In another study [12] patients with highest preoperative BNP levels required significantly longer ventilation, more frequently required inotropic support, and were at a higher risk of one-year mortality. Similar findings were reported in other studies [13], including patients undergoing off-pump CABG [14]. In the study by Hutless et al. [15], diagnostic accuracy of preoperative BNP level of > 385 pg/mL in predicting postoperative IABP use, the length of hospital stay ≥ 10 days, and one-year mortality was 86%, 79%, and 85%, respectively. These observations may also explain another quite interesting finding of our study, i.e. a relation between NT-proBNP level and postoperative drainage. Perhaps the latter is affected by baseline co-morbidities and low EF, as indicated by a correlation between NT-proBNP level and the EuroSCORE risk. These results, however, require confirmation in larger patient populations.

The ability to predict postoperative AF based on preoperative BNP or NT-proBNP levels has not been clearly confirmed yet, although more studies support it [16–19] than refute it [13]. In regard to the diagnostic accuracy of natriuretic peptides in predicting pulmonary complications, a study by Kolditz et al. [20] should be mentioned, as it has documented a high diagnostic accuracy (> 90%) of NT-proBNP level of > 4000 ng/L in predicting pleural effusion due to cardiac causes. Similar findings have been reported for a cut-off BNP level of 2201 ng/L [21], and other data indicate an ability to predict obstructive sleep apnea [22].

It has also been shown that perioperative variability of NT-proBNP is a strong and independent predictor of complications (HR 3.06; 95% CI 1.36–6.91) in patients undergoing vascular surgery [23]. Similar data regarding the ability to predict LV function following cardiac surgery have been reported by Chello et al. [24]. It has also been documented that preoperative levels correlated better than postoperative values with the duration of hospitalisation and long-term mortality risk in patients undergoing coronary surgery [25].

Figure 3. The ROC curve for the diagnostic accuracy of NT-proBNP level in predicting the need for postoperative intra-aortic balloon pump counterpulsation use.

Figure 4. The ROC curve for the diagnostic accuracy of NT-proBNP level in predicting the need for postoperative milrinone use.

Limitations of the study

Our work had some potential limitations, mostly due to a limited number of patients in this pilot study. Only when our observations are confirmed in a larger group of patients, it will allow more precise estimation of cut-off values for predicting particular postoperative complications. In addition, some complications occur relatively rarely and thus we were unable to analyse the predictive value in regard to the risk of mortality, renal, neurological, and psychiatric complications, or a combined endpoint of MACCE. Duration of follow-up was also a limitation, as in-hospital data do not allow for evaluation of a long-term predictive ability. Finally, a more precise analysis should take into account other factors that influence...
enience natriuretic peptide levels, such as age, gender and severity of atherosclerosis, and thus are potential confounding factors [26–29], and also the issue of appropriate reporting of diagnostic accuracy in the published studies [30].

CONCLUSIONS

1. Preoperative assessment of NT-proBNP level in CABG patients could be a valuable diagnostic method for predicting several postoperative complications, especially prolonged mechanical ventilation, respiratory failure, requirement for haemodynamic support using IABP or inotropic drugs, as well as the length of hospital stay.

2. Precise estimation of cut-off points for predicting the above-mentioned complications requires further research.

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Conflict of interest: none declared

References


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Trafność diagnostyczna przedoperacyjnego pomiaru stężenia NT-proBNP w przewidywaniu wczesnych powikłań w chirurgii wieńcowej: badanie pilotowe

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Streszczenie

Wstęp:
Peptydy natriuretyczne typu B (BNP) są uznanymi markerami ostrej i przewlekłej niewydolności serca. Wartość ich stężenia koreluje z chorobowością i umieralnością, również osób bez jawnych cech niewydolności serca. Wciąż niewystarczająca jest wiedza na temat użyteczności oznaczania stężenia BNP u pacjentów poddawanych operacjom kardiochirurgicznym, w tym chirurgii wieńcowej.

Cel:
Celem pracy była ocena trafności diagnostycznej przedoperacyjnego pomiaru stężenia NT-proBNP w przewidywaniu wczesnych powikłań pooperacyjnych u chorych poddanych pomostowaniu aortalno-wieńcowemu (CABG).

Metody:
Badanie miało charakter pilotowy; włączono do niego 100 kolejnych chorych zakwalifikowanych do CABG w trybie planowym; NT-proBNP oznaczano w dniu operacji, przed indukcją znieczulenia. Analizowano częstość występowania wczesnych powikłań pooperacyjnych (30 dni po operacji lub do wypisu ze szpitala).

Wyniki:
W badaniu uczestniczyło 24 (24%) kobiet i 76 (76%) mężczyzn. Średni wiek badanych wynosił 65,9 ± 9,1 roku. Wyjątkowo ryzyko operacyjne wzmacnialo w poprzednim EuroSCORE wynosiło: M = 4 punkty (IQR 2–7) wg modelu addytywnego oraz M = 2,90% (IQR 1,75–8,40) wg modelu logistycznego. Median NT-proBNP wynosiło 526,0 pg/ml (IQR 156,0–1150,0). Nikt z badanych nie zmarł w okresie pooperacyjnym. Transfuzje krwi i jej preparatów były konieczne u 22 (22%) pacjentów. Przedłużona wentylacja mechaniczna (> 12 h) była konieczna u 15 (15%) chorych, a niewydolność oddechową rozpoznano u 2 (2%) osób. Pooperacyjne AF wystąpiło u 34 (34%) badanych. Okołooperacyjny zawał serca stwierdzono u 2 (2%) chorych, a zespół małego rzutu — u 9 (9%). Wspomaganie hemodynamiczne za pomocą IABP było konieczne u 7 (7%) osób, a za pomocą leków inotropowych — u 61 (61%). Najczęście stosowano dopaminę: 60 (60%) przypadków, rzadziej adrenalinę (10 chorych) i milrinon (2 osoby). Stężenie NT-proBNP istotnie dodatnio korelowało z czasem pobytu na oddziale pooperacyjnym (r = 0,412; 95% CI 0,238–0,566; p < 0,001) i całkowitym czasem hospitalizacji (r = 0,547; 95% CI 0,393–0,672; p < 0,001). Wnioski: Przedoperacyjna ocena stężenia NT-proBNP u chorych poddawanych CABG może być cenną wskazówką ułatwiającą przewidywanie niektórych powikłań pooperacyjnych.

Słowa kluczowe: NT-proBNP, pomostowanie aortalno-wieńcowe, trafność diagnostyczna, powikłania pooperacyjne

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