

Perioperative Prognostic Value of N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) Level in Patients Undergoing Open Heart Surgery

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Abstract

Background: In this article, we examined the relationship between the pre- and postoperative N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and occurrence of complications in patients undergoing open heart surgery.

Aim of Study: To find out the prognostic value of NT-proBNP as a valuable marker in predicting postoperative myocardial insult, short term outcome in patients undergoing open heart surgery and evaluate the independency of this biomarker.

Patients and Methods: It was carried out on 105 patients who had cardiac surgery in our department from April 2016 to August 2017. All patients had preoperative and postoperative ECG, Echocardiography and full investigations. Venous blood samples were drawn for estimation of serum level NT-proBNP by ELISA one hour prior to the operation and 24 hours after the operation. Intraoperative and postoperative data include cardiopulmonary bypass time, aortic cross clamping time, requirement for cardiac support immediately after the operation, ICU and hospital stay and occurrence of postoperative complications.

Results: There was highly statistically significant difference between preoperative and postoperative NT-proBNP ($p < 0.001$). Also, we found a significant relation between postoperative NT-proBNP and need of inotropes immediately after operation ($p = 0.035$). Patients who had prolonged ICU stay and hospitalization had significantly higher postoperative NT-proBNP levels with ($p < 0.001$) and ($p = 0.009$) respectively. Our results showed that there was a significant relationship between postoperative NT-proBNP and most of postoperative complications ($p < 0.001$).

Conclusion: NT-proBNP levels strongly correlated with postoperative complications, suggesting its value as a useful prognostic predictor after cardiac surgery which can predict early outcome after cardiac surgery. NT-proBNP levels may be an option when an echocardiogram is not feasible and inotropes may be needed, especially if these levels can be measured in the patient's bed. So, NT-proBNP may become

a clinical routine biomarker capable of predicting patients' perioperative and early postoperative risk because of it is convenient, quick and not expensive. The quantitative cut-off values may be used by physicians in their decision to delay heart surgery in order to further ameliorate the patient.

Key Words: NT-proBNP – Cardiac surgery – Inotropes – Complications.

Introduction

BRAIN natriuretic peptides (BNPs) are cardiac hormones released by ventricular myocytes in response to ventricular dysfunction and wall stress. It is named as such because it was originally identified in extracts of porcine brain, although in humans it is produced mainly in the cardiac ventricles and atria [1,2].

Brain naturetic peptides are finally cleaved into the biologically active mature BNP and the biologically inactive NT-proBNP, which are released into the blood stream, both are established as cardiovascular biomarkers, especially in heart failure, hypertension, acute coronary syndrome or stable ischemic cardiac disease having diagnostic and prognostic values. It was found that it is related to increase in intraventricular pressure and its level rises by the effect of cardiopulmonary bypass [3,4].

Theoretically it was found that NT-pro BNP have analytical advantages over mature BNP due to its longer half life furthermore, it could be analyzed 72 hours after the sample has been taken. [5,6].

Aim of the work: Is to find out the prognostic value of NT-proBNP as a valuable marker in predicting postoperative myocardial insult, short term outcome in patients undergoing open heart surgery and evaluate the independency of this biomarker.

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Patients and Methods

This study was carried out on a randomly selected 105 patients who had cardiac surgery in our department from April 2016 to August 2017.

Exclusion criteria were: Patients with acute renal failure, preoperative insertion of intra-aortic balloon, off-pump open heart surgery and ejection fraction less than 30%.

All patients were subjected to:

- A- Full history taking and thorough clinical examination.
 - B- *Investigations:* Complete blood count, liver function tests, urea, creatinine, LDH, Troponin and CK-MB.
 - C- Preoperative and postoperative ECG and Echocardiography.
 - D- Estimation of serum level NT-pro BNP by ELISA one hour prior to the operation and 24 hours after the operation: [7].
- NT-Pro BNP was analyzed using a commercial NT-pro BNP ELISA Kit (Biomedica, Vienna, Austria).
 - Venous blood was obtained by direct venipuncture and collected into serum separator tubes. Samples were centrifuged within 20min from sampling. Serum was stored frozen at -20°C and thawed only once at the time of analysis.

Results

Table (1): Shows that 12 patients had aortic valve replacement, 9 patients had mitral valve replacement, 3 patients had tricuspid valve replacement, 51 patients had CABG surgery, 3 patients had double valve replacement and 21 patients had combined surgery.

Table (2): Shows that the mean age of patients was 43.17 ± 12.79 (range 22-68 years) with female predominance of the patients.

Table (3): Show that there were 3 patients died after one week postoperative (2.9%).

Table (4): Shows significant difference between NT-proBNP with age, Duration of ventilation dependence, CPB time, Aortic cross clamp, ICU stay, hospital stay and postoperative creatinine when p -value was $<0.05^*$ while was non statistically significant difference with others items when p -value was >0.05 .

Table (5): Shows that non significant relation between postoperative NT-proBNP and bradycardia when when p -value was >0.05 while was significant relation with other complications when p -value was <0.05 .

Table (1): Type of operation.

| Type of operation | N | % |
|-------------------|----|------|
| AVR | 12 | 11.4 |
| CABG | 51 | 20.0 |
| DVR | 3 | 8.6 |
| MVR | 9 | 37.1 |
| TVR | 3 | 2.9 |
| <i>Combined:</i> | | |
| AVR & CABG | 3 | 2.9 |
| MVR & CABG | 3 | 2.9 |
| MVR & Devaga | 12 | 11.4 |
| MVR & AVR& Devaga | 3 | 2.9 |

Table (2): Demographic data (age and sex).

| | N. (%) |
|---------------------|-------------------|
| <i>Age (years):</i> | |
| Range | 22-68 |
| Mean \pm SD | 43.17 \pm 12.79 |
| <i>Sex:</i> | |
| Female | 63 (60%) |
| Male | 42 (40%) |
| Total | 105 (100%) |

Table (3): Death within 30 days of surgery

| Death within 30 days of surgery | N | % |
|---------------------------------|-----|-------|
| Alive | 102 | 97.1 |
| Died | 3 | 2.9 |
| Total | 105 | 100.0 |

Table (4): Correlation between postoperative NT-proBNP and other items.

| | Post NT-proBNP | |
|------------------------------------|----------------|-------------|
| | r | p -value |
| Age | 0.327 | 0.002* |
| Duration of ventilation dependence | 0.508 | <0.001 ** |
| ICU stay | 0.674 | <0.001 ** |
| Hospital stay | 0.434 | 0.009* |
| EF % post | 0.062 | 0.529 |
| CPB time | 0.658 | <0.001 ** |
| Aortic cross clamp | 0.601 | <0.001 ** |
| Creatinine post | 0.433 | <0.001 ** |

Table (5): Relation between postoperative NT-proBNP and postoperative complication.

| Complication | Post NT-proBNP | | | | | |
|----------------------|----------------|----------------------|-----|----------------------|----------------|-----------------|
| | No | | Yes | | <i>t</i> -test | |
| | N | Mean \pm SD | N | Mean \pm SD | <i>t</i> | <i>p</i> -value |
| Neurological | 96 | 2540.47 \pm 493.17 | 9 | 3436.67 \pm 363.35 | 5.308 | <0.001 ** |
| Renal | 90 | 2663.27 \pm 723.39 | 15 | 3621.40 \pm 806.59 | 4.673 | <0.001 ** |
| Pulmonary | 99 | 2445.30 \pm 780.33 | 6 | 3705.00 \pm 700.04 | 3.858 | <0.001 ** |
| Wound infection | 78 | 2676.00 \pm 781.42 | 27 | 3158.78 \pm 781.71 | 2.767 | 0.007* |
| AF | 87 | 2091.06 \pm 806.60 | 18 | 2950.00 \pm 919.24 | 4.015 | <0.001 ** |
| Bradycardia | 99 | 2791.97 \pm 820.88 | 6 | 2935.00 \pm 332.34 | 0.423 | 0.673 |
| Pericardial effusion | 102 | 2773.68 \pm 795.42 | 3 | 3700.00 \pm 462.37 | 2.001 | 0.048* |

Discussion

In the present study we found a great variability in NT-proBNP levels. Our study design was restricted to adult cardiac surgery and occasionally we found female predominance of the patients.

In this study, there was highly statistically significant difference between preoperative and postoperative NT-proBNP with *p*-value<0.001. This is in agreement with Chen T et al and Liu H et al., who reported that NT-proBNP levels increase 24 hours after the operation. This may be attributed to that BNP is synthesized and secreted from cardiomyocytes in response to atrial or ventricular wall stretch [1,8].

Our results showed that there was a significant relation between postoperative NT-proBNP and need of inotropes immediately after operation. This is in accordance with Reyes G et al who showed that NT-proBNP levels were much higher in those patients that required inotropes in theatre or immediately after operation during their stay in the intensive unit care [9].

We also found a significant relationship between NT-proBNP and age. This is in agreement with Attaran S et al who said that NT- proBNP levels increase with age because there is a reduction in the natriuretic peptide clearance with aging [10].

There was a significant relationship between NT-proBNP and duration of ventilation dependence. Similarly, Shih C et al., showed that high NT-proBNP levels predicted longer ventilation time [11].

In our study, there was a significant relationship between NT-proBNP and both CPB time and aortic cross clamp. This is in agreement with Junior J et al., due to the ischemia caused by prolonged cross-clamp time. On the contrary, Reyes G et al., report-

ed that NT-proBNP levels were unrelated to both bypass and cross clamp time [9,12].

In our study, we demonstrated that there was a significant relation between NT-proBNP and both prolonged ICU stay and hospitalization. This is in agreement with Chen T et al., who reported that the postoperative Day 1 NT-proBNP was significantly higher in patients with prolonged ICU stay and hospitalization. We also found that there was a significant relation between NT-proBNP and postoperative creatinine. This is in accordance with Bucholz E et al who reported that high NT-proBNP level was associated with impaired renal function. [8,13].

We found that there was no significant relation between NT-proBNP and ejection fraction. This is in agreement with Salustri A et al., [14]. But, on the contrary Kabukçu H et al reported that there was a significant relation between NT-proBNP and ejection fraction [15]. One reason for this finding could be the optimal treatment of our patients before surgery, as it is well known that NT-proBNP levels may vary depending on the quality of medical treatment [16].

Finally, in the present study we found that postoperative NT-pro BNP predicted most of post-operative complications. This is in agreement with many studies like Lara T et al., and Tavakol M et al., whereas Reyes G et al., reported that there was no any significant relation between NT-proBNP and the appearance of complications after surgery. [9,17,18].

Conclusion:

NT-proBNP levels strongly correlated with postoperative complications, suggesting its value as a useful prognostic predictor after cardiac surgery which can predict early outcome after cardiac surgery.

NT-proBNP levels may be an option when an echocardiogram is not feasible and inotropes may be needed, especially if these levels can be measured in the patient's bed. So, NT-proBNP may become a clinical routine biomarker capable of predicting patients'perioperative and early postoperative risk because of it is convenient, quick and not expensive.

Acknowledgments: This research was carried out without funding.

Conflicts of interest: No conflicts of interest declared.

Authors' Contributions: All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

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القيمة التنبؤية لمستوى (أن تي- برو بي أن بي) قبل وبعد الجراحة للمرضى الذين يخضعون لعمليات القلب المفتوح

وجد أن المضاعفات الرئيسية ما بعد جراحة القلب يمكن أن تؤثر بشكل كبير على النتائج.

لذلك فإن التشخيص المبكر والتصنيف الدقيق للمخاطر هما من المسائل المهمة لتطوير أهداف علاجية يمكن أن تحسن رعاية المرضى.

لذلك استخدام دلالات القلب كمنبؤات على حدوث مضاعفات القلب على المدى القصير والطويل سيكون مفيداً في الممارسة السريرية الروتينية.

البيبتيدات المخية المدرة للصوديوم (بي أن بي) هي هرمونات قلب يتم إفرازها أساساً من البطينين رداً على التحفيز المناسب ومن ثم تنقسم البيبتيدات إلى (بي أن بي) و (أن تي- برو بي أن بي) الذي يعد أكثر استقراراً وقياسه أكثر موضوعية.

حيث وجد أنه من الناحية النظرية قد يكون قياس (أن تي- برو بي أن بي) له مزايا تحليلية على (بي أن بي) نتيجة لطول عمر النصف بالإضافة إلى أنه ببئيد مستقر حيث يمكن تحليل العينة بعد أخذها بثلاثة أيام.

الهدف من الدراسة: معرفة القيمة التنبؤية الخاصة ب (أن تي- برو بي أن بي) كدلالة على مضاعفات عضلة القلب بعد العملية الجراحية والنتائج على المدى القصير وتقييم أستيقلالية هذا المؤشر الحيوي.

المرضى وطرق البحث: تم إجراء هذا البحث على عدد (١٠٥) مريض من الذين يخضعون لجراحات القلب المفتوح بقسم جراحة القلب والصدر جامعة طنطا وتم الحصول على الموافقة الخطية من جميع المرضى الذين سملتهم الدراسة حيث أنه تمت الموافقة على الدراسة من قبل لجنة الأخلاقيات بكلية الطب جامعة طنطا.

النتائج:

- وجود ارتباطاً إيجابياً بين مستويات (أن تي- برو بي أن بي) وكل من عمر المريض وأحتياجه لمنشطات القلب وزمن إغلاق الشريان الأورطي ومدة إقامة المريض في العناية المركزة والمستشفى.

- زيادة ملحوظة في مستوى (أن تي- برو بي أن بي) بعد جراحات القلب المفتوح.

- وجود ارتباطاً إيجابياً بين مستويات (أن تي- برو بي أن بي) ومدة أعتماذ المريض على جهاز التنفس الصناعي وظهور مضاعفات ما بعد جراحات القلب المفتوح.

الاستنتاج: ارتباط مستوى (أن تي- برو بي أن بي) ارتباطاً قوياً مع ظهور مضاعفات ما بعد جراحة، مما يشير إلى قيمته كمؤشر في التنبؤ بالنتائج في وقت مبكر بعد جراحة القلب.