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Original Article

NT pro BNP: A Factor to Predict the Outcome of Head Trauma Patients

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Abstract

Background: Surveying serum markers can be valuable in predicting the outcome of patients with head trauma. The current study examined the diagnostic value of the serum level of Brain Natriuretic Peptide (BNP) to determine the hospital outcome of patients with head trauma.

Methods: This descriptive-analytical study was conducted on 40 patients with pure head trauma who had indications for brain CT scans and required hospitalization from July 2017 to May 2019 at Trauma Medical-Educational Center. The variables were age, gender, initial consciousness level based on Glasgow Coma Score (GCS), trauma mechanism, the time-lapse between trauma and admission to hospital, mortality, Glasgow Outcome Scale (GOS) during discharge, GOS at one and six months after discharge, initial serum level of NT-pro BNP (N Terminal-pro BNP), and results of brain CT scan.

Results: Concerning the reports of brain CT scans, from 40 patients, 26 patients had normal brain CT scans, and 14 patients had abnormal brain CT scans. Mean ± SD value of NT-pro BNP for normal group was 407.7 ± 190.25 pg/ml and for abnormal group was 631.43 ± 219.25 pg/ml (p = 0.009). Only five patients with abnormal CT scans died during the study. In predicting mortality of patients, the initial serum level of NT-pro BNP was 693 pg/ml with 80%sensitivity and 74% specificity.

Conclusion: assessing of the serum values of NT-pro BNP can help predict the mortality rate of patients with head trauma. Higher values of NT-pro BNP during hospitalization is a good indicator of a low survival rate in patients.

Keywords: Glasgow Coma Score, pro-brain natriuretic peptide, Mortality.

Introduction

According to medical terminology, trauma is any penetrating or blunt injury that is caused by external factors in the human body, intentionally or unintentionally. Trauma is the fourth cause of human death throughout the world and is the most prevalent cause of mortality in the first four decades of life.[1,2,3,4] It should be mentioned that the young population is the prominent group affected by trauma in most parts of the world.[5] Based on previous studies, the most prevalent cause of the trauma is an accident[6,7] and traumatic brain injuries are one of the primary causes of the mortality of the patients.[8] A traumatic brain injury could affect various organs, such as the cardiac system, that results in death.[9]

Brain Natriuretic Peptide (BNP) is a serum marker with a low half-life that is used in evaluating congestive heart failure, ischemic cardiomyopathy, and dysfunction of the left ventricle. This marker was also helpful in determining the prognosis of head trauma patients.[2,10,11,12] Some serum markers included Neuron-specific Enolase (NSE), S100B, tau protein, and Malondialdehyde increase in the brain of trauma patients.[10] Cevik et al. reported that a BNP level of more than ten pg/ml (without knowing the cause of the increase) helps find intracranial pathologies after trauma.[13] Demir et al. found that the BNP level as a marker is not enough for diagnosing intracranial pathologies in minor head trauma cases.[10] Additively, Costa et al. reported that BNP level does not increase in head trauma patients, and there is no correlation between them.[14]

Based on the above discussion, the results of studies on BNP value and its relationship with the outcome of head trauma patients are contradictory. The current study aimed to examine initial BNP serum levels in pure head trauma patients and determine its predictive value for the outcome of patients.

Methods

Study protocol

In a descriptive-analytical study at the emergency ward of Trauma Medical-Educational Center of Medical Sciences University from July 2017-May 2019, 40 head trauma patients were included.

The study sample included all patients older than 18 years who should be examined by CT scan and hospitalized based on available diagnostic methods. The sample size was considered 40 based on the limitations of previous reports on the sensitivity and specificity of NT-pro BNP in predicting acute head trauma.

Inclusion criteria were the lack of trauma history, age equal to or above 18, having head trauma, coming to this medical center, and need for CT scan and hospitalization. Exclusion criteria were the heart and chest trauma at the same time, congestive heart failure history, hypertension history, acute coronary syndrome, ischemic stroke, hysteria, syncope, coming to the center two hours after trauma, and not being satisfied to participate in the study.

Data gathering

When patients arrived at the emergency ward, diagnostic and therapeutic actions were done for them. The blood sample was taken to determine the serum level of BNP at the laboratory evaluations. For evaluating NT-pro BNP level, 2cc of blood was needed. Samples were centrifuged and kept at -70 Celsius. Then, they were assessed by Cobas E411 device (Roche, Germany) using the luminance electrochemical method. Also, a brain CT scan was done by Siemens SOMATOM Emotion 6 device (Siemens, Germany) for hospitalized patients. CT scans were reported by a radiologist. During hospitalization, study variables were collected and their results were recorded. These variables were age, gender, the initial level of consciousness based on the Glasgow Coma Score (GCS), trauma mechanism, the time-lapse between trauma and coming to the hospital, mortality, Glasgow Outcome Scale (GOS) during discharge, GOS one month after discharge, GOS six month after discharge, NT-pro BNP level, and findings of CT scan. Patients were divided into normal, and abnormal groups based on CT-scan results and NT-pro BNP level was compared for both groups.

Head trauma patients' outcomes were evaluated based on Glasgow Outcome System (GOS), which includes five levels mortality score, vegetative state score, acute disability score (patient can understand information but can't live independently), medium disability score (patient can live independently but can't return to job or school), and good recovery score (patient can return to career or school).[15,16]

Statistical Analysis

Data were analyzed using SPSS software 17.0. First, the normality of the data distribution was examined by the Kolmogorov-Smirnov test. Then, descriptive statistics were utilized, including mean ± SD for quantitative variables and frequency (percent) for qualitative variables. Moreover, the Chi-square test and Independent Sample t-test were used to compare the two groups quantitatively and qualitatively. ROC curve, sensitivity, and specificity were employed to determine the diagnostic value of NT-pro BNP ($p<0.005$).

Ethical consideration

This study was confirmed by the Ethics Committee of Medical Sciences University with code 37858 on 7/24/2016. Written consent of all participants was taken before performing the research. This study did not have any additional costs for the patients.

Results

In this study, 40 patients were examined. The mean age of patients was 58.67 ± 18.71. In terms of gender, 29 patients were men (72.5%), and others were women. Based on brain CT-scan results, patients were divided into the normal (26 patients, 65%) and the abnormal CT-scan group (14 patients, 35%). Five patients died from the abnormal CT-scan group.

Table 1 compares the demographic characteristics, vital signs, and clinical status of two groups based on CT-scan results. Although both groups were in the medium intensity range based on GAP, there was a significant difference between the two groups in terms of trauma intensity (GAP score) ($p < 0.001$). Table 2 demonstrates demographic

characteristics and vital signs of two groups based on hospital outcome at the time of discharge (patient is alive or dead).

The ROC curve was used to calculate the prediction value of NT-pro BNP for determining hospital outcomes, (figure 1). Based on the results of this analysis, the area under curve was calculated at 0.869. The cut-off point for NT-pro BNP serum level topredict mortality of patients was 693 pg/ml with a sensitivity of 80% and specificity of 74%. Table 3 shows the initial serum level of NT-pro BNP for patients based on GOS during discharge and one month after discharge. According to the table, it is clear that lower initial serum levels of NT-pro BNP in patients increase their survival and recovery even one month after discharge.

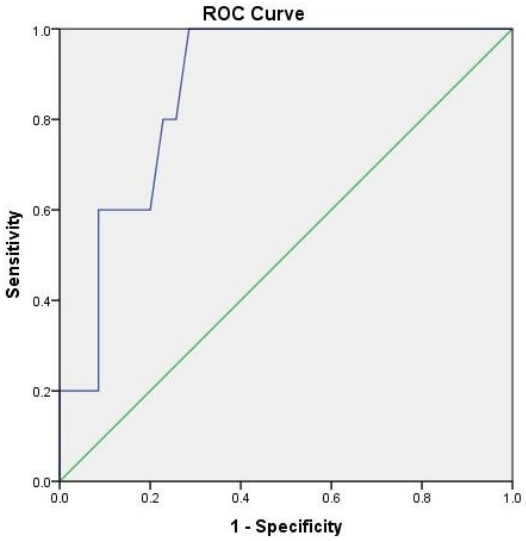

Figure 1: Value of NT pro BNP in predicting mortality of patients

Table 1. Comparison the demographic characteristics, vital signs, and clinical status of two groups based on CT-scan results

Variables	Alive (35 patients)	Dead (5 patients)	P value
Age	57.82±18.43	62.71±20.99	0.536
Gender (male/female)	24/9	5/2	0.636
MAP	90.30±8.22	96.43±7.61	0.078
Heart rate	76.27±10.78	78.28±7.65	0.643
O2 saturation	92.18±3.10	90.28±3.60	0.161
GCS	10.33±1.20	7.28±1.11	<0.001
GAP score	16.55±0.83	14.14±2.20	<0.001
Trauma to hospital time (minute)	88.63±22.02	100.00±23.62	0.379
Admission duration (days)	4.70±2.47	6.86±3.98	0.068
NT pro BNP levels (pg/mL)	407.70±190.25	631.43±219.25	0.009
Mortality • **Yes** • **No**	 0 33	 5 2	<0.001
GOS (Discharge time) • **Death** • **Vegetative state** • **Severe disability** • **Moderate disability** • **Recovery**	 0 0 0 19 (57.6%) 14 (42.4%)	 5 (71.4%) 0 0 1 (14.3%) 1 (14.3%)	<0.001
GOS (1 month after discharge) • **Death** • **Vegetative state** • **Severe disability** • **Moderate disability** • **Recovery**	 0 0 0 12 (36.4%) 21 (63.6%)	 5 (71.4%) 0 0 1 (14.3%) 1 (14.3%)	<0.001

Table 2. Comparison the demographic characteristics and vital signs of two groups based on hospital outcome

Variables	Alive (35 patients)	Dead (5 patients)	P value
Age	58.86±18.40	62.71±20.99	0.873
Gender (male/female)	26/9	3/2	0.422
MAP	90.48±8.10	97.67±8.22	0.072
Heart rate	75.54±10.53	77.20±9.07	0.895
O2 saturation	92.00±3.20	90.80±3.70	0.444
GCS	10.20±1.30	7.00±1.00	<0.001
GAP score	16.40±1.03	14.20±2.59	0.001
Trauma to hospital time (minute)	89.42±22.02	99.00±26.07	0.379
Admission duration (days)	4.74±2.41	7.40±4.72	0.050
NT pro BNP levels (pg/mL)	411.82±199.13	692.00±105.15	0.004

Table 3. Comparison the serum level of NT-pro BNP of patients based on GOS during discharge and one month later

GOS	Discharge time	One Month after discharge
• **Dead** • **Vegetative status** • **Severe disability** • **Moderate disability** • **Recovery**	716.33±133.50 - 610.00±00 561.28±140.55 216.86±43.36	716.33±133.50 610.00±00 701.00±00 595.00±137.60 303.59±142.60
P value	<0.001	<0.001

Discussion

In this study, 40 head trauma patients were studied in two groups (normal and abnormal) based on CT-scan results. Mortality in this study was five patients. Higher values of NT-pro BNP during discharge and one month after discharge showed higher mortality and lower outcome.

Recent studies have used the BNP marker for evaluating the increased fluid load in patients with acute burnings who receive a blood transfusion.[17,18,19,20] Friese et al. observed that BNP values in patients with liquid retention and pulmonary edema increase over time.[21] Moreover, Kirchhoff et al. reported a direct and significant relationship between serum level of NT-pro BNP and decreased amount of cardiac index in multi-trauma patients; the amount of this marker had a meaningful association with trauma intensity.[22]

In current study, mean ± SD of NT-pro BNP values was 407.7 ± 190.25 pg/ml for patients with normal CT-scan and was 631.43 ± 219.25 pg/ml for patients with abnormal CT-scan ($p < 0.009$). It is seen that NT-pro BNP is higher in patients with abnormal CT-scan. Consistent with the current study, Cevic et al. (2009) found that NT-pro BNP values are significantly higher in patients with abnormal CT-scan.[8] Five patients died during this study. These patients were in an abnormal CT-scan group. In predicting mortality rate, serum level of NT-pro BNP has obtained 693 pg/ml with a sensitivity of 80% and specificity of 74%. Zhang et al. (2012) showed that NT-pro BNP was higher in patients whose outcome was death.[12]

Surveying the relationship between NT-pro BNP and GOS at the time of discharge and GOS one month after discharge in the current study showed that higher values of NT-pro BNP were accompanied by a significantly low survival rate ($p < 0.001$). Qian et al. showed that serum level of NT-pro BNP was considerably higher in head trauma patients with low survival rates.[23] In the study of Sviri et al., the level of this peptide was also higher in head trauma patients.[24]

Cevic et al. reported that a BNP level of more than 10 pg/ml (without knowing the cause) might be valuable. In finding intracranial pathologies after trauma. Moreover, measuring BNP can be beneficial in

determining the use of CT scans [8]. In two studies conducted by Demir and Costa, the BNP level was not suitable as a marker for diagnosing intracranial pathologies.[10,11,12,13,14] Akgun et al. found a significant relationship between NT-pro BNP and the size of ischemic and hemorrhagic lesions. They reported that NT-pro BNP levels increased in patients whose cerebral lesions increased during the time.[25] Tsentsiper et al. on determining NT-pro BNP in head trauma patients concluded that BNP level increases in head trauma cases.[26]

Limitations

Due to the limitation of budget and cost of the NT-pro BNP test, a low size sample was examined, which is a limitation of the current study. Evaluating outcomes of patients based on GOS and one-month follow-up after discharge are strengths of the present study.

Conclusion

Concerning results obtained in the current study, examining serum amounts of NT-pro BNP can help predict the mortality of head trauma patients. Higher amounts of NT-pro BNP during discharge can be a good indicator of a low survival rate in patients. It is recommended to conduct studies with a bigger sample size to examine the diagnostic value of NT-pro BNP in patients with acute head traumas. Moreover, conducting a meta-analysis on NT-pro BNP or BNP value in the outcome of head trauma patients is proper for previous studies.

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Authors' contributions

All authors have read and approved the manuscript. MHS, ZP and HEB performed the data collection, literature review, and drafting of the manuscript. FR undertook the main parts of the study design and performed the statistical analysis.

Conflict of interest

The authors declare that they have no competing interests.

Financial disclosure

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Ethical consideration

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References

1. Rahmani F, Ebrahimi Bakhtavar H, Shams Vahdati S, Hosseini M, Mehdizadeh Esfanjani R. Evaluation of MGAP and GAP Trauma Scores to Predict Prognosis of Multiple-trauma Patients. *Trauma Monthly*. 2017;22(3): e33249.

2. Gregorio T, Albuquerque I, Neves V, Reinas R, Pipa S, Azevedo L, et al. NT-pro-BNP correlates with disease severity and predicts outcome in cerebral haemorrhage patients: Cohort study. *J Neurol Sci*. 2019; 399:51-6.

3. Amini K, Abolghasemi Fakhri S, Salehi H, Ebrahimi Bakhtavar H, Rahmani F. Mortality Prediction in Multiple Trauma Patients Using GAP, RTS and NTS Models. *Trauma Monthly*. 2021;26(5): 252-57.

4. Khajoei R, Abadi MZ, Dehesh T, Heydarpour N, Shokohian S, Rahmani F. Predictive value of the glasgow coma scale, age, and arterial blood pressure and the new trauma score indicators to determine the hospital mortality of multiple trauma patients. *Archive of Trauma Research*. 2021; 10:86-91.

5. Global status report on road safety 2018 Geneva: World Health Organization, 2018.

6. Shams Vahdati S, GhafarZad A, Rahmani F, Panahi F, Omrani Rad A. Patterns of Road Traffic Accidents in North West of Iran during 2013 New Year Holidays: Complications and Casualties. *Bull Emerg Trauma*. 2014;2(2):82-5.

7. Mousazadeh Y, Sadeghi-Bazargani H, Janati A, Pouraghaei M, Rahmani F. Prediction of mortality risk in patients with traffic injury: A case study in tabriz hospitals, Iran. *Archives of Trauma Research*. 2019;8(2):104-9.

8. Bunevicius A, Deltuva V, Laws ER, Iervasi G, Tamsauskas A, Bunevicius R. Preoperative N-terminal pro-B-type natriuretic peptide concertation and prognosis of brain tumor patients: a 5-year follow up study. Sci Rep. 2017;7(1):14775.

9. Prathep S, Sharma D, Hallman M, Joffe A, Krishnamoorthy V, Mackensen GB, et al. Preliminary report on cardiac dysfunction after isolated traumatic brain injury. *Crit Care Med*. 2014;42(1):142-7.

10. Demir A, Kavalci C, Yilmaz MS, Yilmaz F, Durdu T, Ceyhan MA, et al. The value of Serum BNP for diagnosis of intracranial injury in minor head trauma. *World J Emerg Surg*. 2014;9(1):16.

11. Rahmani F. Diagnostic value of brain natriuretic peptide in head trauma. *Journal of Analytical Research in Clinical Medicine*. 2016; 4:75-6.

12. Zhang Z, Zhang Z, Xue Y, Xu X, Ni H. Prognostic value of B-type natriuretic peptide (BNP) and its potential role in guiding fluid

therapy in critically ill septic patients. *Scand J Trauma Resusc Emerg Med.* 2012; 20:86.

13. 3evik Y, Durukan P, Erol FS, Yıldız M, İlhan N, Serhatlioğlu S. Diagnostic Value of Bedside Brain Natriuretic Peptide Measurement in Patients with Head Trauma. *Journal of Academic Emergency Medicine/Akademik Acil Tip Olgu Sunumlari Dergisi*. 2010;9(1):21-5.

14. Costa KN, Nakamura HM, Cruz LR, Miranda LS, Santos-Neto RC, Cosme Sde L, et al. Hyponatremia and brain injury: absence of alterations of serum brain natriuretic peptide and vasopressin. *Arq Neuropsiquiatr.* 2009;67(4):1037-44.

15. Bunevicius A, Kazlauskas H, Raskauskiene N, Mickuviene N, Ndreu R, Corsano E, et al. Role of N-terminal pro-B-type natriuretic peptide, high-sensitivity C-reactive protein, and inteleukin-6 in predicting a poor outcome after a stroke. *Neuroimmunomodulation*. 2015;22(6):365-72.

16. Rizoli S, Petersen A, Bulger E, Coimbra R, Kerby JD, Minei J, et al. Early prediction of outcome after severe traumatic brain injury: a simple and practical model. *BMC Emerg Med*. 2016;16(1):32.

17. Papp A, Uusaro A, Parviainen I, Hartikainen J, Ruokonen E. Myocardial function and haemodynamics in extensive burn trauma: evaluation by clinical signs, invasive monitoring, echocardiography and cytokine concentrations. A prospective clinical study. *Acta Anaesthesiol Scand*. 2003;47(10):1257-63.

18. Tobian AA, Sokoll LJ, Tisch DJ, Ness PM, Shan H. N-terminal pro-brain natriuretic peptide is a useful diagnostic marker for transfusion-associated circulatory overload. *Transfusion*. 2008;48(6):1143-50.

19. Zhou L, Giacherio D, Cooling L, Davenport RD. Use of B-natriuretic peptide as a diagnostic marker in the differential diagnosis of transfusion-associated circulatory overload. *Transfusion*. 2005;45(7):1056-63.

20. Wu X, Sha H, Sun Y, Gao L, Liu H, Yuan Q, et al. N-terminal pro-B-type natriuretic peptide in patients with isolated traumatic brain injury: a prospective cohort study. *J Trauma*. 2011;71(4):820-5; discussion 5.

21. Friese RS, Dineen S, Jennings A, Pruitt J, McBride D, Shafi S, et al. Serum B-type natriuretic peptide: a marker of fluid resuscitation after injury? *J Trauma*. 2007;62(6):1346-50; discussion 50-1.

22. Kirchhoff C, Leidel BA, Kirchhoff S, Braunstein V, Bogner V, Kreimeier U, et al. Analysis of N-terminal pro-B-type natriuretic peptide and cardiac index in multiple injured patients: a prospective cohort study. *Crit Care*. 2008;12(5): R118.

23. Qian A, Zhang M, Zhao G. Dynamic detection of N-terminal pro-B-type natriuretic peptide helps to predict the outcome of patients with major trauma. *Eur J Trauma Emerg Surg*. 2015;41(1):57-64.

24. Sviri GE, Soustiel JF, Zaaroor M. Alteration in brain natriuretic peptide (BNP) plasma concentration following severe traumatic brain injury. *Acta Neurochir (Wien).* 2006;148(5):529-33; discussion 33.

25. Akgun B, Erol FS, Yildirim H, Ilhan N, Kaplan M. The correlation of serum NT-proBNP levels of hemorrhagic and ischemic lesions detected with diffusion MRI in head traumas. *Turk Neurosurg*. 2013;23(3):336-43.

26. Tsentsiper L, Kondratyeva E, Kondratyev S, Dryagina N. Levels of N-terminal pro-brain natriuretic peptide in brain injury patients. *Critical Care*. 2015;19(Suppl 1): P458-P.