

ABCD2 Score and BNP Level in Patients with TIA and Cerebral Stroke

¹H.R. Mortezaeigi, ¹A. Taghizadeh, ¹M. Talebi, ¹K. Amini and ²M. Goldust

¹Neuro Science Research Center, Tabriz University of Medical sciences, Tabriz, Iran

²Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: Scoring systems have been designed to help physicians in early prediction of cerebral stroke following Transitional Ischemic Attack (TIA). ABCD2 system is one of these scoring systems. Considering increase of brain natriuretic peptide following cerebral ischemic stroke, BNP level may be associated with incidence of ischemic stroke following TIA. The present study evaluates ABCD2 score, BNP level in patients with TIA and incidence of cerebral stroke. This cross sectional-analytical study evaluated 78 patients with TIA. ABCD2 score was calculated for all patients based on some criteria including age, blood pressure, clinical manifestations (speech/motor disorder), symptoms duration and diabetes. BNP level was measured at the reference laboratory when the patient referred to the treatment center. The patients were followed up for 6 months considering incidence of cerebral stroke and TIA. Mean age of the patients was 66.53±13.08 years and the sample was consisted of 62.8% male and 37.2% female patients. Mean BNP level and mean ABCD2 score was 611.31±125.61 and 4.61±0.99 in all patients, respectively. During follow-up period, TIA recurrence and cerebral stroke were, respectively seen in 11.5 and 3.8% of cases. Mortality was reported in 5.1% of the patients. BNP was significantly higher in cases with recursive TIA ($p = 0.03$). But, there was not any difference considering ABCD2 score ($p = 0.38$). BNP is capable of predicting TIA recurrence following first TIA and it can be used in this case.

Key words: Transitional Ischemic Attack (TIA), stroke, ABCD2, Brain Natriuretic Peptide (BNP)

INTRODUCTION

Cerebral ischemic stroke is defined as every kind of vascular damage resulting in reduction of blood circulation to special area of the brain and is associated with neurologic symptoms (Goldust *et al.*, 2011; Sadeghpour *et al.*, 2011; Ssi-Yan-Kai *et al.*, 2012). The symptoms can be started suddenly or gradually. Ischemia constitutes about 80% of cerebral strokes and results in cerebral artery occlusion (Golfurushan *et al.*, 2011; Hotter *et al.*, 2012; Milan *et al.*, 2011). The rest cerebral strokes are of hemorrhagic type resulted from blood vessel rupture into cerebral parenchyma or inside of subarachnoid space (Goldust *et al.*, 2012; Navi *et al.*, 2012; Sadighi *et al.*, 2011). Ischemic strokes are initially often manifested with transient ischemic attack. Coherent studies have reported wide variety at 7-day risk of cerebral stroke following 0-12.8% TIA (Goldust *et al.*, 2013a; Vafae *et al.*, 2012; Walker *et al.*, 2012). Emergency management of TIA focuses on determining risk factors, anti-platelet treatment and management of treatable risk factors including atrium fibrillation and carotid artery stenosis (Goldust *et al.*, 2013b, c; Jickling *et al.*, 2012). There are some evidences indicating to efficiency of

emergency preventive treatment in reducing early risk of cerebral stroke following TIA (Purroy *et al.*, 2012). Patients with suspected to TIA are differently treated at the emergency department such that some offer quick hospitalization and care while others suggest outpatient visit by the specialists (Goldust *et al.*, 2013d; Mohebbipour *et al.*, 2012; Tari *et al.*, 2012). Scoring systems have been designed to help physicians in early prediction of cerebral stroke following transitional ischemic attack (TIA). ABCD is one of these scoring systems subsequently changed to ABCD2 system (Amarenco *et al.*, 2012; Goldust and Rezaee, 2013; Lotti *et al.*, 2013). ABCD2 score is based on five factors including age higher than 60 years (1 point), blood pressure more than 140/90 mmHg (1 point), clinical manifestations such as one-sided weakness (2 points) and speech disorder by itself (1 point), lasting of symptoms at least for 60 min (2 points) or varying between 10 to 59 min (1 point) and diabetes (1 point). The total score was calculated through summing up of the mentioned cases (Horer *et al.*, 2011). Brain Natriuretic Peptide (BNP) increases following cerebral ischemic stroke (Urabe, 2010). It has been proved that it is one of the independent determinants of mortality and heart infarction in patients

with cerebral stroke (Ghia *et al.*, 2012). Causes of BNP increase is still unknown considering acute stroke. Also, BNP is excreted by brain (Corso *et al.*, 2011). Although only trivial part of BNP is produced by the brain, it can be supposed that considerable volumes of BNP enter blood circulation following acute cerebral parenchyma destruction (Arsava *et al.*, 2011). Considering the mentioned cases, it can be assumed that BNP level may be related to incidence of ischemic stroke following TIA. The present study evaluates ABCD2 score and BNP level in patients with TIA and incidence of cerebral stroke.

MATERIALS AND METHODS

Subjects: This cross sectional-analytical study evaluated 78 patients referred to emergency department of Imam Reza hospital, Tabriz from July 2011 to July 2012. The sampling method was simple.

Exclusion criteria: History of previous stroke, convulsion, cerebral space occupant mass, subdural hematoma, hypoglycemia, classic migraine, cerebral hemorrhage and cavernous vein thrombosis.

Methods: All patients with TIA referred to emergency department of Imam Reza hospital within 12 months were selected and demographic findings and history of previous diseases were recorded in all patients. ABCD2 index was calculated for the patients. The score is based on age (older than 60 years: 1 point), blood pressure (more than 140/90 mmHg: 1 point), clinical manifestations (one-sided weakness: 2 points or speech disorder without one-sided weakness: 1 point), duration of symptoms (lasting for 10 to 59 min: 1 point or more than 60 min: 2 points) and diabetes (yes: 1 point and No: 0 point). A blood sample was taken and sent to central laboratory in order to determine BNP level. The understudy patients were followed up for one, three and 6 months. The results were evaluated. The understudy variables included age, gender, neurologic findings, background diseases, ABCD2 level, BNP level, paraclinical findings, TIA incidence, stroke and mortality rate.

Statistical analysis: All understudy data was analyzed using SPSS16 statistical software. Descriptive statistical methods (frequency, percentage, mean, standard deviation) were used to statistically evaluate the data. Chi-square and Independent t-test were used to compare qualitative and quantitative variables, respectively. In this study, $p < 0.05$ was regarded meaningful.

RESULTS

Mean age of the patients was 66.53 ± 13.08 years and the oldest and youngest patients were 92 and 30 years old, respectively. The patients were consisted of 49 (62.8%) males and 29 (37.2%) females. There were diabetes in 9 (11.5%), hypertension in 41 (52.6%), hyperlipidemia in 11 (14.1%), alcohol consumption in one (1.3%), smoking in 8 (10.3%) and OCP consumption in 2 (2.6%) of cases. Also, history of myocardial infarction and atrium fibrillation were seen in 6 (7.7%) and one (1.3%) of cases. There was speech disorder in about half of the patients which was mainly disartria. In this study, hemiparesia was the most prevalent finding observed in about half of the patients. Sensory symptoms was seen in 18 (23.1%) and cerebellar signs in 8 (10.3%) patients. There were vertigo and involvement of cranial nerve (all facial) in 17 (21.8%) and 7 (9%) patients. Abnormal results as cerebral atrophy were seen in 9 (11.5%) cases of the CT-scans. The findings were normal in the rest 69 (88.5%) cases. Mean BNP level was 611.31 ± 125.16 with the average of 213.75 in all understudy patients. The lowest and highest BNP level was 8.25 and 5800, respectively. Mean ABCD2 score was 4.61 ± 0.99 with the average of 5 in all understudy patients and the lowest and highest score was 2 and 6, respectively. Recurrence of TIA was observed in 9 (11.5%) cases during the follow-up period. All recursive cases occurred before two months, e.g. one case was seen the next day, 4 cases within one month, one case after 45 days and one case after two months. Also, one case was repeated both in the first and third months. During the follow-up period, stroke was seen in 3 (3.8%) patients. In all cases, it occurred during the first week, i.e., two cases after one day and 1 case within the first week. Out of all patients, there was mortality in 4 (5.1%) cases. Considering the patients conditions, 50 ones (64.1%) were hospitalized for more studies. mean age of the patients with and without recursive TIA was respectively 69.88 ± 10.8 and 66.08 ± 13.38 years. As observed, mean age was higher in the patients with recursive TIA. However, the difference was not meaningful between two groups ($p = 0.41$). There was not statistically significant difference between these two groups considering gender distribution in cases with and without recursive TIA ($p = 0.47$). The study revealed that BNP level was significantly higher in cases with recursive TIA ($p = 0.03$). Mean ABCD2 score in cases with and without TIA was 4.88 ± 1.16 and 4.57 ± 0.97 , respectively. There was not any statistically meaningful difference between these two groups ($p = 0.38$). Out of 9 recursive cases, ABCD2 score equaled 2, 5 and 6 in one, six and two cases. It is observed that ABCD2 score was more than 5 in most recursive

cases. Out of 3 patients with stroke during the follow-up period, one patient was older than 65 and two cases older than 85 years. Additionally, BNP levels were 8.52, 334.90 and 3300.00, respectively. ABCD score was 5 and 6 in one and two cases, respectively. Comparison was not possible due to low volume of the affected cases.

DISCUSSION

Out of every 100,000 patients, 100 cases are visited for TIA at the emergency departments. Although it often seems benign, there is high risk of cerebral stroke following TIA. Cerebral stroke constitutes main cause of disability in adult patients (Meng *et al.*, 2011). Coherent studies have reported wide variety of 7-day risk of cerebral stroke following 0-12.8% TIA (Weitzel-Mudersbach *et al.*, 2011). Identifying patients with TIA who are at high risk of cerebral stroke is regarded as an opportunity to prevent cerebral stroke (Olivot *et al.*, 2011). However, emergency evaluation of all TIA cases requires high expenses. For this purpose, researchers have introduced methods such as ABCD2 scoring system to determine high risk patients. (Engelter *et al.*, 2012). The present study deals with the relationship found between ABCD2 and BNP index and TIA and incidence of cerebral stroke. Out of 78 patients of this study, cerebral stroke and TIA recurrence were seen in 3.8 and 11.5% of the cases. However, there was not any significant relationship between TIA and ABCD2. (Sheehan *et al.*, 2009) reported a meaningful relation between ABCD2 score at recurrence rate of TIA following initial TIA. However, they stated that ABCD2 score in TIA patients is not a predictive factor of TIA recurrence Sheehan *et al.* (2009). The contradictory results can be attributed to the fact that efficiency of ABCD2 system is still controversial since there are some evidences that patients with ABCD2 score <4 (as seen in the present study) have suffered from TIA and other criteria should be used in this case. There are contradictory results on efficiency of the system in identifying at risk patients (Galvin *et al.*, 2011). In multifocal study of Carpenter *et al.* (2009) including those patients with TIA referred to the emergency departments, it was suggested that ABCD2 score does not have sufficient accuracy at any cut off point as an predictor of imminent cerebral stroke (Carpenter *et al.*, 2009). In two different studies conducted by Sheehan *et al.* (2010) they once reported a significant relation between ABCD2 score and incidence of cerebral stroke and, then, lack of any relationship between the mentioned cases (Sheehan *et al.*, 2010;

Sheehan *et al.*, 2009; Ong *et al.*, 2010) demonstrated that ABCD2 score has well sensitivity and negative informative value in predicting cerebral stroke following TIA (Ong *et al.*, 2010). In the present study, ABCD2 score was higher than 4 in all three cases of cerebral stroke (6 in two and 5 in one case). It was not possible to evaluate the relationship found between ABCD2 and incidence of cerebral stroke due to low prevalence of cerebral stroke in the understudy patients. Considering the above-mentioned cases, another criterion with high accuracy should be used. Brain natriuretic peptide increases following cerebral ischemic stroke and it has been proved that it is one of the independent determinants of mortality and heart infarction in patients with cerebral stroke. According to the reports, BNP levels increase 24 h after cerebral ischemic stroke (Chandratheva *et al.*, 2011). Some studies have stated that BNP levels are associated with neurologic inadequacies (Price *et al.*, 2010). Although, only trivial part of BNP is produced by the brain, it can be supposed that considerable volumes of BNP enter blood circulation following acute cerebral parenchyma destruction (Kim *et al.*, 2011). Considering the mentioned cases, it is possible that increase of BNP level serve as determinant of incidence of cerebral stroke following TIA. There are few studies about the relationship between BNP level and TIA recurrence or incidence of cerebral stroke (Wijnhoud *et al.*, 2010). In their study, (Chandratheva *et al.*, 2011) demonstrated that BNP in combination with some other biomarkers is capable to identify acute cerebral ischemia. Also, it was observed that BNP was somehow capable to identify TIA in association with other markers (Chandratheva *et al.*, 2010). Nguyen *et al.* (2010) stated that BNP can predict mortality incidence following cerebral stroke (Nguyen *et al.*, 2010). All these findings refer to efficiency of BNP in preventing problems after initial TIA. The present study reveals that BNP level in cases with recursive TIA is about three times more than those cases without any recursion. BNP level was 8.52, 334.90 and 3300.00 in three cases of cerebral stroke. However, it was not possible to evaluate the mentioned relationship due to low prevalence of cerebral stroke in the understudy patients. More evaluations with higher sample volumes are required.

CONCLUSION

BNP is capable to predict TIA recurrence following first TIA. It can be used in this case, too. Further studies are recommended to determine exact role of BNP in TIA recurrence and incidence of cerebral stroke following TIA.

REFERENCES

- Amarenco, P., J. Labreuche and P.C. Lavalley, 2012. Patients with transient ischemic attack with ABCD² <4 can have similar 90-day stroke risk as patients with transient ischemic attack with ABCD² ≥4. *Stroke*, 43: 863-865.
- Arsava, E.M., K.L. Furie, L.H. Schwamm, A.G. Sorensen and H. Ay, 2011. Prediction of early stroke risk in transient symptoms with infarction: Relevance to the new tissue-based definition. *Stroke*, 42: 2186-2190.
- Carpenter, C.R., S.M. Keim, J. Crossley and J.J. Perry, 2009. Post-transient ischemic attack early stroke stratification: The ABCD² prognostic aid. *J. Emergency Med.*, 36: 194-200.
- Chandratheva, A., D.S. Lasserson, O.C. Geraghty and P.M. Rothwell, 2010. Population-based study of behavior immediately after transient ischemic attack and minor stroke in 1000 consecutive patients: Lessons for public education. *Stroke*, 41: 1108-1114.
- Chandratheva, A., O.C. Geraghty and P.M. Rothwell, 2011. Poor performance of current prognostic scores for early risk of recurrence after minor stroke. *Stroke*, 42: 632-637.
- Corso, G., E. Bottacchi, A. Brusa, C. Lia and S. Cordera *et al.*, 2011. Blood C-reactive protein concentration with ABCD² is a better prognostic tool than ABCD² alone. *Cerebrovasc Dis.*, 32: 97-105.
- Engelter, S.T., M. Amort, F. Jax, F. Weisskopf and M. Katan *et al.*, 2012. Optimizing the risk estimation after a transient ischaemic attack-the ABCDE plus sign in circle score. *Eur. J. Neurol.*, 19: 55-61.
- Galvin, R., C. Geraghty, N. Motterlini, B.D. Dimitrov and T. Fahey, 2011. Prognostic value of the ABCD² clinical prediction rule: A systematic review and meta-analysis. *Family Pract.*, 28: 366-376.
- Ghia, D., P. Thomas, D. Cordato, D. Epstein and R.G. Beran *et al.*, 2012. Low positive predictive value of the ABCD² score in emergency department transient ischaemic attack diagnoses: the South Western Sydney tRansient Ischaemic Attack study. *Inter. Med. J.*, 42: 913-918.
- Goldust, M., F. Golphoroushan and E. Rezaee, 2011. Treatment of solar lentigines with trichloroacetic acid 40% vs. cryotherapy. *Eur. J. Dermatol.*, 21: 426-427.
- Goldust, M., E. Rezaee and S. Hemayat, 2012. Treatment of scabies: Comparison of permethrin 5% versus ivermectin. *J. Dermatol.*, 39: 545-547.
- Goldust, M. and E. Rezaee, 2013. The efficacy of topical ivermectin vs. malation 0.5% lotion for the treatment of scabies. *J. Dermatol. Treat.*, (In Press).
- Goldust, M., E. Rezaee and R. Raghifar, 2013a. Comparison of oral ivermectin versus crotamiton 10% cream in the treatment of scabies. *Cutaneousv Ocul. Toxicol.*
- Goldust, M., M. Talebi, J. Majidi, M.A.R. Saatlou and E. Rezaee, 2013b. Evaluation of antiphospholipid antibodies in youths suffering from cerebral ischemia. *Int. J. Neurosci.*, 123: 209-212.
- Goldust, M., M.R. Ranjkesh, M. Amirinia, F. Golphoroushan, E. Rezaee and M.A.R. Saatlou, 2013c. Sertaconazole 2% cream vs. hydrocortisone 1% cream in the treatment of seborrheic dermatitis. *J. Dermatol. Treat.*, (In Press).
- Goldust, M., S.B. Nejad, E. Rezaee and R. Raghifar, 2013d. Comparative trial of permethrin 5% vs. lindane 1% for the treatment of scabies. *J. Dermatol. Treat.*, (In Press). 10.3109/09546634.2012.723122
- Golfurushan, F., M. Sadeghi, M. Goldust and N. Yosefi, 2011. Leprosy in Iran: An analysis of 195 cases from 1994-2009. *J. Pak. Med. Assoc.*, 61: 558-561.
- Horer, S., G. Schulte-Altdorneburg and R.L. Haberl, 2011. Management of patients with transient ischemic attack is safe in an outpatient clinic based on rapid diagnosis and risk stratification. *Cerebrovasc Dis.*, 32: 504-510.
- Hotter, B.A., J.M. Lechner, C.H. Nolte, H.J. Audebert and U. Malzahn *et al.*, 2012. ABCD² as a screening tool for cerebral infarction on stroke MRI? *Eur. Neurol.*, 67: 315-320.
- Jickling, G.C., X. Zhan, B. Stamova, B.P. Ander and Y. Tian *et al.*, 2012. Ischemic transient neurological events identified by immune response to cerebral ischemia. *Stroke*, 43: 1006-1012.
- Kim, A.S., S. Sidney, A.L. Bernstein, V.C. Douglas and S.C. Johnston, 2011. Urgent neurology consultation from the ED for transient ischemic attack. *Am. J. Emergency Med.*, 29: 601-608.
- Lotti, T., M. Goldust and E. Rezaee, 2013. Treatment of seborrheic dermatitis, Comparison of sertaconazole 2% cream vs. ketoconazole 2% cream. *J. Dermatol. Treat.*, 10.3109/09546634.2013.777154
- Meng, X., Y. Wang, L. Liu, Y. Pu and X. Zhao *et al.*, 2011. Validation of the ABCD²-I score to predict stroke risk after transient ischemic attack. *Neurol. Res.*, 33: 482-486.
- Milan, P.B., D.M. Nejad, A.A. Ghanbari, J.S. Rad and H.T. Nasrabadi *et al.*, 2011. Effects of *Polygonum aviculare* herbal extract on sperm parameters after EMF exposure in mouse. *Pak. J. Biol. Sci.*, 14: 720-724.

- Mohebbipour, A., P. Saleh, M. Goldust, M. Amirnia, Y.J. Zadeh, R.M. Mohamadi and E. Rezaee, 2012. Treatment of scabies: Comparison of ivermectin vs. lindane lotion 1%. *Acta Dermatovenerol. Croat*, 20: 251-255.
- Navi, B.B., H. Kamel, M.P. Shah, A.W. Grossman and C. Wong *et al.*, 2012. Application of the ABCD² score to identify cerebrovascular causes of dizziness in the emergency department. *Stroke*, 43: 1484-1489.
- Nguyen, H., D. Kerr and A.M. Kelly, 2010. Comparison of prognostic performance of scores to predict risk of stroke in ED patients with transient ischaemic attack. *Eur. J. Emergency Med.*, 17: 346-348.
- Olivot, J.M., C. Wolford, J. Castle, M. Mlynash and N.E. Schwartz *et al.*, 2011. Transient ischemic attack work-up as outpatient assessment of clinical evaluation and safety. *Stroke*, 42: 1839-1843.
- Ong, M.E., Y.H. Chan, W.P. Lin and W.L. Chung, 2010. Validating the ABCD² score for predicting stroke risk after transient ischemic attack in the ED. *Am. J. Emergency Med.*, 28: 44-48.
- Price, C.J., J.T. Crinion, A.P. Leff, F.M. Richardson and T.M. Schofield *et al.*, 2010. Lesion sites that predict the ability to gesture how an object is used. *Arch. Ital Biol.*, 148: 243-258.
- Purroy, F., P.E.J. Caballero, A. Gorospe, M.J. Torres and J. Alvarez-Sabin *et al.*, 2012. Prediction of early stroke recurrence in transient ischemic attack patients from the PROMAPA study: A comparison of prognostic risk scores. *Cerebrovasc Dis.*, 33: 182-189.
- Sadeghpour, A., R. Mansour, H.A. Aghdam and M. Goldust, 2011. Comparison of trans patellar approach and medial parapatellar tendon approach in tibial intramedullary nailing for treatment of tibial fractures. *J. Pak. Med. Assoc.*, 61: 530-533.
- Sadighi, A., A. Elmi, M.A. Jafari, V. Sadeghifard and M. Goldust, 2011. Comparison study of therapeutic results of closed tibial shaft fracture with intramedullary nails inserted with and without reaming. *Pak. J. Biol. Sci.*, 14: 950-953.
- Sheehan, O.C., A. Merwick, L.A. Kelly, N. Hannon and M. Marnane *et al.*, 2009. Diagnostic usefulness of the ABCD² score to distinguish transient ischemic attack and minor ischemic stroke from noncerebrovascular events: The North Dublin TIA Study. *Stroke*, 40: 3449-3454.
- Sheehan, O.C., L. Kyne, L.A. Kelly, N. Hannon and M. Marnane *et al.*, 2010. Population-based study of ABCD² score, carotid stenosis and atrial fibrillation for early stroke prediction after transient ischemic attack: The north Dublin TIA study. *Stroke*, 41: 844-850.
- Ssi-Yan-Kai, G., N. Nasr, A. Faury, I. Catalaa, C. Cognard, V. Larrue and F. Bonneville, 2012. Intracranial artery stenosis or occlusion predicts ischemic recurrence after transient ischemic attack. *Am. J. Neuroradiol.* 10.3174/ajnr.A3144
- Tari, C.F., M. Cavallari, B. Casolla, G. Caselli and A. Pieroni *et al.*, 2012. Stroke prediction after transient ischemic attacks in patients admitted to a stroke unit. *Eur. Neurol.*, 67: 34-38.
- Urabe, T., 2010. New clinical concept and therapeutic strategy for TIA. *Rinsho Shinkeigaku*, 50: 910-912.
- Vafaei, I., M.B. Rahbani Nobar and M. Goldust, 2012. Etiology of ocular trauma: A two years cross sectional study in Tabriz, Iran. *J. Coll. Physicians Surg. Pak.*, 22: 344-344.
- Walker, J., J. Isherwood, D. Eveson and A.R. Naylor, 2012. Triaging TIA/minor stroke patients using the ABCD² score does not predict those with significant carotid disease. *Eur. J. Vasc. Endovasc. Surg.*, 43: 495-498.
- Weitzel-Mudersbach, P.V., S.P. Johnsen and G. Andersen, 2011. Low risk of vascular events following urgent treatment of transient ischaemic attack: The Aarhus TIA study. *Eur. J. Neurol.*, 18: 1285-1290.
- Wijnhoud, A.D., L. Maasland, H.F. Lingsma, E.W. Steyerberg, P.J. Koudstaal and D.W. Dippel, 2010. Prediction of major vascular events in patients with transient ischemic attack or ischemic stroke: A comparison of 7 models. *Stroke*, 41: 2178-2185.