Trauma Mon. 2016 May; 21(2):e28012. doi: 10.5812/traumamon.28012.

Published online 2016 March 20. **Review Article**

Adaptation of Traumatic Brain Injury Guidelines in Iran

Shayan Abdollah Zadegan,[1,2] Seyed Mohammad Ghodsi,[3] Jalil Arabkheradmand,[4] Abbas Amirjamshidi,[5] Abdolreza Sheikhrezaei,[6] Masoud Khadivi,[3] Morteza Faghih Jouibari,[3] Seyed Mahmood Tabatabaeifar,[7] Guive Sharifi,[8] Jalal Abbaszadeh Ahranjani,[9] Farhad Motlagh Pirooz,[10] Seyed Fakhredin Tavakoli,[10] Parviz Mohit,[11] Yadollah Alimohammadi,[11] and Vafa Rahimi-Movaghar[1,2,3,*]

[1]Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences, Tehran, IR Iran
[2]Research Centre for Neural Repair, Tehran University, Tehran, IR Iran
[3]Department of Neurosurgery, Shariati Hospital, Tehran University of Medical Sciences, Tehran, IR Iran
[4]Ahya Neuroscience Research Center, Tehran, IR Iran
[5]Department of Neurosurgery, Sina Hospital, Tehran University of Medical Sciences, Tehran, IR Iran
[6]Department of Neurosurgery, Imam Hospital, Tehran University of Medical Sciences, Tehran, IR Iran
[7]Functional Neurosurgery Research Center, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[8]Department of Neurosurgery, Loghman Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[9]Department of Neurosurgery, Urmia University of Medical Sciences, Urmia, IR Iran
[10]Department of Neurosurgery, Islamic Azad University, Medical Branch, Mashhad, IR Iran
[11]Tehran University of Medical Sciences, Tehran, IR Iran

[*]*Corresponding author*: Vafa Rahimi-Movaghar, Sina Trauma and Surgery Research Center, Hassan-Abad Square, Imam Khomeini Ave, P. O. Box: 113653876, Tehran, IR Iran. Tel: +98-9153422682; +98-2166718311, Fax: +98-2166705140, E-mail: v_rahimi@sina.tums.ac.ir

Received 2015 March 02; **Accepted** 2015 May 09.

Abstract

Context: The National institute for health and care excellence (NICE) and scottish intercollegiate guidelines network (SIGN) are two well-known sources of clinical guideline development. In the past years, they have developed clinical guidelines for the management of head injury. In this report, we will highlight our modifications to these guidelines according to the domestic situation in a developing country.

Evidence Acquisition: The guidelines were appraised using the appraisal of guidelines for research and evaluation (AGREE) instrument. All key recommendations were reviewed by 14 prominent Iranian neurosurgeons; levels of evidence were evaluated and items with limited evidence were determined. Available evidence for selected items were reviewed and discussed.

Results: The following items were the most challenging when accounting for the domestic situation in Iran: age as a risk factor for referral, computed tomography scan, the impact of medical comorbidities, pregnancy, consultation, referral to a neurosurgical unit, and teleconsulting and observation before discharge.

Conclusions: The evidence in the discussed topics was limited and controversial. This report is important because it exposes the current knowledge gap in head trauma studies in Iran.

Keywords: Brain Injuries, Trauma, Practice Guideline, Referral and Consultation, Comorbidity, Age Factors, Patient Discharge, Telemedicine

1. Context

National institute for health and care excellence (NICE) and scottish intercollegiate guidelines network (SIGN) have developed many clinical guidelines in past years. In the topic of head injury, NICE published a guideline in 2003 which was revised in 2007 and 2014 (1). The SIGN head injury guideline was published in 2000 which was superseded by a revised version in 2009 (2). Since guidelines were designed in developed countries, they may need some modifications to be adopted in developing countries.

The traumatic brain injury (TBI) guidelines from two well-known sources (NICE and SIGN) were selected for adaptation in Iran. In this report, we will highlight the most important modifications made by the panel of Iranian neurosurgeons.

2. Evidence Acquisition

Two TBI guidelines, NICE triage, assessment, investigation and early management of head injury (Guideline No. 176, Jan 2014) and SIGN early management of patients with a head injury (Guideline No. 110, May 2009) were selected using the appraisal of guidelines for research and evaluation (AGREE) instrument (related search keywords: brain, injury, trauma, clinical, and guideline) (1-3). In the first round, the panel reviewed the key recommendations of the guidelines, evaluated the evidence provided by the guidelines, and considered possible revisions. Then the panel collected the answers of the experts and determined

which items had limited evidence. In the second round, the panel reviewed and discussed the available evidence for determined items. In the absence of reliable evidence, the panel relied on the consensus of its members. Since pre-hospital telephone advice is unavailable in Iran, we excluded all of the recommendations related to that topic.

3. Results

The main recommendations were adopted considering the highest available level of evidence. Some modifications were applied after collecting the expert panel review.

3.1. Age

The NICE and SIGN guidelines had multiple recommendations that the high risk age is 65 years. These recommendations included: indications for referral to the hospital (NICE guideline), the criteria for CT head scan (NICE/SIGN guideline), and the criteria for immediate request for three-view radiographic imaging of the cervical spine (NICE guideline). The expert panel reduced the high risk age to 60 years according to evidence which support lower risk age (4-7).

3.2. Significant Medical Comorbidity and Pregnancy

The SIGN guideline discussed medical comorbidity as a practice point. The expert panel added this item as a recommendation for referral to the hospital.

3.3. Consultation and Referral to a Neurosurgical Unit

Both guidelines recommended that persistent coma (GCS score 8/15 or less) after initial resuscitation should result in referral to a neurosurgical unit. Another criterion was unexplained confusion (GCS < 14) that persists for more than 4 hours. Our panel preferred to consider GCS score 14/15 or less for immediate referral to a neurosurgeon.

3.4. Discharge

Considering CT imaging results, GCS = 15/15, without additional risk factors or other relevant adverse sociomedical factors, is sufficient for discharging the patient from the emergency department (ED) to be observed at home (SIGN/NICE). The panel recommended a 6-hour observation period during the daytime and 7 pm – 7 am observation at night in the ED after the patient is fully conscious.

3.5. Underlying Cause of the Injury

Exploring the basic cause of the injury (not simply the mechanism) is essential.

4. Conclusions

The panel reviewed and adopted the clinical recommendations in the SIGN and NICE guidelines for implementation in Iran. The different domestic situation compelled the expert panel to change some of the recommendations.

During the panel discussion, it was suggested to reduce the risk age from 65 to 60 years. According to previous studies, both 65 and 60 years were defined as a high-risk factor in patients with head injury. Arienta et al. (4) (1997), Haydel (5) (2000), Servadei et al. (7) (2001) and Ono et al. (6) (2007) reported that age over 60 years is associated with positive findings in the CT scan (4-7). In some other studies, age over 65 was a high-risk factor (8, 9). In Iran, Saadat and colleagues, in a study for developing a clinical decision rule for cranial CT scan, did not find any abnormality in the imaging of Iranian patients < 65 years old with mild TBI who did not have a warning sign or symptom (10). However, Saboori et al., in a prospective cohort study of 682 Iranian patients, showed that age > 60 years is significantly correlated to an abnormal cranial CT after TBI (11). Sharif-Alhoseini and colleagues in a prospective study on 642 patients found that a combination of age > 60 years and headache is associated with a significantly higher rate of abnormal brain CT scans in mild TBI (12). In light of the above studies' differing results and our limited knowledge of the effect of age on TBI in Iran, the panel decided to use the age > 60 years in recommendations. Further studies will be needed to determine the risk age for TBI patients in Iran.

Significant medical comorbidities were added as a recommendation for referral to the hospital. The importance of chronic disease in mortality rate after trauma have been previously documented (13). In a secondary analysis of discharge data of TBI patients, Scheetz found that certain chronic conditions, including congestive heart failure, coagulation disorder, hypertension and malignancies, increased the odds of short-term mortality (14). A study by Liao and colleagues on 1104 TBI patients with end-stage renal disease (ESRD) and 3312 TBI patients without ESRD showed an increased risk of mortality among TBI patients with a pre-existing end-stage renal disease (15). Diabetes mellitus is another risk factor which showed almost 1.5-fold increased mortality rate of TBI patients in 5-year study of Lustenberger et al. (16). Chou et al. in a retrospective cohort study of 7,622 patients with stroke, showed that they had a higher mortality after TBI (17).

Pregnancy was considered to be a factor for referral to the hospital after TBI due to the lack of enough studies on TBI in pregnancy (18). In a number of studies that have investigated TBI, pregnancy was not evaluated as a

separate factor nor was it an exclusion criterion for participants' selection (9). Experimental and clinical studies suggest that estrogen and progesterone are neuro-protective in patients with moderate to severe TBI (19-24). Due to elevated levels of these hormones in pregnancy, the outcome of TBI during pregnancy might better; so it is not a risk factor, but a protective factor. To investigate this issue, Berry and colleagues, in a retrospective review of moderate to severe TBI patients, found 71 pregnant women among 18,800 female patients. After controlling for risk factors, there was a trend toward increased mortality in the pregnant TBI patients. However the trend was not significant (P = 0.07), so they concluded that there is no significant difference in mortality between pregnant and non-pregnant moderate to severe TBI patients (25). This study had some limitations. The most important limitation was that 71 pregnant women was compared with 8,854 non-pregnant women. In a response to the study, Wright and colleagues stated that any null hypothesis testing would be confirmed with such a "hugely unequal" number (26). The safety of the mother is one side of the story. The adverse effects of maternal head trauma and altered mental status for fetal viability have been shown previously (18, 27). Thus, the practice in this item should be cautious due to our knowledge gap.

In the two guidelines, a GCS score of 8/15 or less and unexplained confusion (GCS < 14) that persists for more than 4 hours were two items necessitating neurological referral and consultation. In our panel, a GCS score 14/15 or less meant that the patient should see a neurosurgeon immediately, even with a normal CT report. An inexperienced radiologist could miss a considerable number of abnormalities in the CT scan of an acute TBI (28). Moreover, even with a normal initial CT scan, there is a chance of delayed post-traumatic hemorrhage after a TBI (29). Recent studies have revealed that patients with moderate (GCS 9 - 12) and severe (GCS 8 or less) TBI should be managed in neuroscience centers, regardless of the need for neurosurgical intervention, and at the least the situation of these patients should be discussed with a neurosurgeon (30, 31). The panel did not accept a 4-hour wait and see period before consultation in the case of confused patients because of the importance of the first four hours and the fact that even patients with GCS of 13 - 14/15 (mild TBI) could develop a parenchymal contusion (12, 32). In a study to determine the impact of time on mortality of TBI patients, Kim et al., included 493 patients from seventeen Level I and II trauma centers (33). They found that surgery within four hours of arrival is associated with half the likelihood of mortality and a significantly shorter length of hospital stay (33). Although there are different views regarding the effect of timing on surgery outcomes, most authors believe in the importance of the timing of decompression surgery (34). Thus, until this discrepancy is resolved, it is reasonable to act more cautious.

In the case of consultation in medical centers without neurosurgery expert, teleconsulting was proposed as a solution. It was previously shown that using teleconsultation for neurosurgical patients can reduce costs and unnecessary transportation (35-37). In the study of Servadei and colleagues during January 1998 to December 2000, CT examinations were sent to a neurosurgical unit for head injury management and consultation. Out of 637 first examinations of acute trauma cases, only 23% (150 patients) were actually transferred to the neurosurgery unit (38). In 2013, the study of Migliaretti and colleagues on 519 patients with mild TBI confirmed the benefits of teleconsulting, especially in elderly patients (39).

For discharging TBI patients from ED, there was no recommended observation time in the guidelines. In developing countries, communication between patient and the health care system is weak and the family care is not sufficient, so the panel recommended an observation period in the ED after the patient is fully conscious. Also in many centers no standard advice leaflet is available to inform the patient for possible return. In suburban and rural road locations, long transport times cause a delay in a return to the hospital, which could result in mortality and morbidity (40).

The underlying cause of the injury should be questioned and explored. The importance of the mechanism of injury and dangerous mechanisms were previously explained as a part of the CCHR (Canadian CT head rule) decision-making tool (9). We are focusing on underlying medical and psychological conditions and the predisposing factors which can cause the injury, so it is important to determine if the injury is a primary event or secondary to another medical/psychological condition. For example, falling could be secondary to other clinical conditions like seizure, vertigo, arrhythmia, suicide, etc. The patient's condition should be thoroughly analyzed to find and treat the underlying factors, because missing these factors may result in repeated future injuries.

In conclusion, although we had to modify some recommendations according to the domestic conditions but the evidences in the discussed topics were limited and sometimes controversial. This report is important because it exposes the current knowledge gap in head trauma studies in Iran.

Footnotes

Authors' Contribution: Study supervision: Vafa Rahimi-Movaghar; study concept and design, data collection and

interpretation, drafting of the manuscript: Shayan Abdollah Zadegan and Vafa Rahimi-Movaghar; critical revision of the manuscript for important intellectual content: Seyed Mohammad Ghodsi, Jalil Arabkheradmand, Abbas Amirjamshidi, Abdolreza Sheikhrezaei, Masoud Khadivi, Morteza Faghih Jouibari, Seyed Mahmood Tabatabaeifar, Guive Sharifi, Jalal Abbaszadeh Ahranjani, Farhad Motlagh Pirooz, Seyed Fakhredin Tavakoli, Parviz Mohit and Yadollah Alimohammadi.

Funding/Support: This research was supported by Sina trauma and surgery research center (Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran) and ministry of health and medical education (Iran).

References

1. Head Injury: Triage, Assessment, Investigation and Early Management of Head Injury in Children, Young People and Adults. ; 2014.
2. Early management of patients with a head injury 2009. Available from: http://www.sign.ac.uk.
3. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting, and evaluation in health care. *Prev Med.* 2010;**51**(5):421–4. doi: 10.1016/j.ypmed.2010.08.005. [PubMed: 20728466].
4. Arienta C, Caroli M, Balbi S. Management of head-injured patients in the emergency department: a practical protocol. *Surg Neurol.* 1997;**48**(3):213–9. [PubMed: 9290706].
5. Haydel MJ, Preston CA, Mills TJ, Luber S, Blaudeau E, DeBlieux PM. Indications for computed tomography in patients with minor head injury. *N Engl J Med.* 2000;**343**(2):100–5. doi: 10.1056/NEJM200007133430204. [PubMed: 10891517].
6. Ono K, Wada K, Takahara T, Shirotani T. Indications for computed tomography in patients with mild head injury. *Neurol Med Chir (Tokyo).* 2007;**47**(7):291–7. [PubMed: 17652914] discussion 297-8.
7. Servadei F, Teasdale G, Merry G, Neurotraumatology Committee of the World Federation of Neurosurgical S. Defining acute mild head injury in adults: a proposal based on prognostic factors, diagnosis, and management. *J Neurotrauma.* 2001;**18**(7):657–64. doi: 10.1089/089771501750357609. [PubMed: 11497092].
8. Mower WR, Hoffman JR, Herbert M, Wolfson AB, Pollack CJ, Zucker MI, et al. Developing a clinical decision instrument to rule out intracranial injuries in patients with minor head trauma: methodology of the NEXUS II investigation. *Ann Emerg Med.* 2002;**40**(5):505–14. [PubMed: 12399794].
9. Stiell IG, Wells GA, Vandemheen K, Clement C, Lesiuk H, Laupacis A, et al. The Canadian CT Head Rule for patients with minor head injury. *Lancet.* 2001;**357**(9266):1391–6. [PubMed: 11356436].
10. Saadat S, Ghodsi SM, Naieni KH, Firouznia K, Hosseini M, Kadkhodaie HR, et al. Prediction of intracranial computed tomography findings in patients with minor head injury by using logistic regression. *J Neurosurg.* 2009;**111**(4):688–94. doi: 10.3171/2009.2.JNS08909. [PubMed: 19284234].
11. Saboori M, Ahmadi J, Farajzadegan Z. Indications for brain CT scan in patients with minor head injury. *Clin Neurol Neurosurg.* 2007;**109**(5):399–405. doi: 10.1016/j.clineuro.2007.01.013. [PubMed: 17350162].
12. Sharif-Alhoseini M, Khodadadi H, Chardoli M, Rahimi-Movaghar V. Indications for brain computed tomography scan after minor head injury. *J Emerg Trauma Shock.* 2011;**4**(4):472–6. doi: 10.4103/0974-2700.86631. [PubMed: 22090740].
13. Morris JJ, MacKenzie EJ, Edelstein SL. The effect of preexisting conditions on mortality in trauma patients. *JAMA.* 1990;**263**(14):1942–6. [PubMed: 2313871].
14. Scheetz LJ. Injury patterns, severity and outcomes among older adults who sustained brain injury following a same level fall: a retrospective analysis. *Int Emerg Nurs.* 2015;**23**(2):162–7. doi: 10.1016/j.ienj.2014.09.003. [PubMed: 25281285].
15. Liao JC, Ho CH, Liang FW, Wang JJ, Lin KC, Chio CC, et al. One-year mortality associations in hemodialysis patients after traumatic brain injury–an eight-year population-based study. *PLoS One.* 2014;**9**(4):eee93956. doi: 10.1371/journal.pone.0093956. [PubMed: 24714730].
16. Lustenberger T, Talving P, Lam L, Inaba K, Bass M, Plurad D, et al. Effect of diabetes mellitus on outcome in patients with traumatic brain injury: a national trauma databank analysis. *Brain Inj.* 2013;**27**(3):281–5. doi: 10.3109/02699052.2012.743178. [PubMed: 23252407].
17. Chou YC, Yeh CC, Hu CJ, Meng NH, Chiu WT, Chou WH, et al. Risk and mortality of traumatic brain injury in stroke patients: two nationwide cohort studies. *J Head Trauma Rehabil.* 2014;**29**(6):514–21. doi: 10.1097/HTR.0000000000000007. [PubMed: 24263175].
18. Grossman NB. Blunt trauma in pregnancy. *Am Fam Physician.* 2004;**70**(7):1303–10. [PubMed: 15508541].
19. Asl SZ, Khaksari M, Khachki AS, Shahrokhi N, Nourizade S. Contribution of estrogen receptors alpha and beta in the brain response to traumatic brain injury. *J Neurosurg.* 2013;**119**(2):353–61. doi: 10.3171/2013.4.JNS121636. [PubMed: 23724987].
20. Dubal DB, Zhu H, Yu J, Rau SW, Shughrue PJ, Merchenthaler I, et al. Estrogen receptor alpha, not beta, is a critical link in estradiol-mediated protection against brain injury. *Proc Natl Acad Sci U S A.* 2001;**98**(4):1952–7. doi: 10.1073/pnas.041483198. [PubMed: 11172057].
21. Roof RL, Hall ED. Estrogen-related gender difference in survival rate and cortical blood flow after impact-acceleration head injury in rats. *J Neurotrauma.* 2000;**17**(12):1155–69. doi: 10.1089/neu.2000.17.1155. [PubMed: 11186229].
22. Wei J, Xiao GM. The neuroprotective effects of progesterone on traumatic brain injury: current status and future prospects. *Acta Pharmacol Sin.* 2013;**34**(12):1485–90. doi: 10.1038/aps.2013.160. [PubMed: 24241345].
23. Wright DW, Kellermann AL, Hertzberg VS, Clark PL, Frankel M, Goldstein FC, et al. ProTECT: a randomized clinical trial of progesterone for acute traumatic brain injury. *Ann Emerg Med.* 2007;**49**(4):391–402. doi: 10.1016/j.annemergmed.2006.07.932. [PubMed: 17011666] 402.e1-2.
24. Xiao G, Wei J, Yan W, Wang W, Lu Z. Improved outcomes from the administration of progesterone for patients with acute severe traumatic brain injury: a randomized controlled trial. *Crit Care.* 2008;**12**(2):R61. doi: 10.1186/cc6887. [PubMed: 18447940].
25. Berry C, Ley EJ, Mirocha J, Margulies DR, Tillou A, Salim A. Do pregnant women have improved outcomes after traumatic brain injury?. *Am J Surg.* 2011;**201**(4):429–32. doi: 10.1016/j.amjsurg.2010.10.008. [PubMed: 21421094].
26. Wright DW, Stein DG, Sayeed I, Hua F, Atif F, Yousf S, et al. Response to: Do pregnant women have improved outcomes after traumatic brain injury?. *Am J Surg.* 2012;**204**(5):803–4. doi: 10.1016/j.amjsurg.2011.05.002. [PubMed: 21880296].
27. Kissinger DP, Rozycki GS, Morris JJ, Knudson MM, Copes WS, Bass SM, et al. Trauma in pregnancy. Predicting pregnancy outcome. *Arch Surg.* 1991;**126**(9):1079–86. [PubMed: 1929837].
28. Laalo JP, Kurki TJ, Sonninen PH, Tenovuo OS. Reliability of diagnosis of traumatic brain injury by computed tomography in the acute phase. *J Neurotrauma.* 2009;**26**(12):2169–78. doi: 10.1089/neu.2009.1011. [PubMed: 19691423].
29. Alvarez-Sabin J, Turon A, Lozano-Sanchez M, Vazquez J, Codina A. Delayed posttraumatic hemorrhage. "Spat-apoplexie". *Stroke.* 1995;**26**(9):1531–5. [PubMed: 7660393].
30. Kolias AG, Guilfoyle MR, Helmy A, Allanson J, Hutchinson PJ. Traumatic brain injury in adults. *Pract Neurol.* 2013;**13**(4):228–35. doi: 10.1136/practneurol-2012-000268. [PubMed: 23487823].

31. Mendelow AD, Timothy J, Steers JW, Lecky F, Yates D, Bouamra O, et al. Management of patients with head injury. *Lancet.* 2008;**372**(9639):685–7. doi: 10.1016/s0140-6736(08)61280-5.
32. Zare MA, Ahmadi K, Zadegan SA, Farsi D, Rahimi-Movaghar V. Effects of brain contusion on mild traumatic brain-injured patients. *Int J Neurosci.* 2013;**123**(1):65–9. doi: 10.3109/00207454.2012.728653. [PubMed: 23005920].
33. Kim YJ. The impact of time from ED arrival to surgery on mortality and hospital length of stay in patients with traumatic brain injury. *J Emerg Nurs.* 2011;**37**(4):328–33. doi: 10.1016/j.jen.2010.04.017. [PubMed: 21741566].
34. Kim YJ. The impact of time to surgery on outcomes in patients with traumatic brain injury: a literature review. *Int Emerg Nurs.* 2014;**22**(4):214–9. doi: 10.1016/j.ienj.2014.02.005. [PubMed: 24680689].
35. Hassan R, Siregar JA, Rahman Mohd NAA. The implementation of teleneurosurgery in the management of referrals to a neurosurgical department in hospital sultanah amninah johor bahru. *Malays J Med Sci.* 2014;**21**(2):54–62. [PubMed: 24876808].
36. Rudinsky B, Gubric J, Gubricova M, Rudinska L. Telemedicine in urgent neurosurgery. *Bratisl Lek Listy.* 2001;**102**(6):294–7. [PubMed: 11725395].
37. Sinha VD, Tiwari RN, Kataria R. Telemedicine in neurosurgical emergency: Indian perspective. *Asian J Neurosurg.* 2012;**7**(2):75–7. doi: 10.4103/1793-5482.98648. [PubMed: 22870155].
38. Servadei F, Antonelli V, Mastrilli A, Cultrera F, Giuffrida M, Staffa G. Integration of image transmission into a protocol for head injury management: a preliminary report. *Br J Neurosurg.* 2002;**16**(1):36–42. [PubMed: 11926463].
39. Migliaretti G, Ciaramitaro P, Berchialla P, Scarinzi C, Andrini R, Orlando A, et al. Teleconsulting for minor head injury: the Piedmont experience. *J Telemed Telecare.* 2013;**19**(1):33–5. doi: 10.1177/1357633x12474738. [PubMed: 23454822].
40. Paravar M, Hosseinpour M, Mohammadzadeh M, Mirzadeh AS. Prehospital Care and In-hospital Mortality of Trauma Patients in Iran. *Prehosp Disaster Med.* 2014;**29**(5):473–7. doi: 10.1017/s1049023x14000879. [PubMed: 25196346].