Note: This copy is for your personal non-commercial use only. To order presentation-ready copies for distribution to your colleagues or clients, contact us at www.rsna.org/rsnarights.

2. Cervellin G, Benatti M, Carbucicchio A, et al. Serum levels of protein S100B predict intracranial lesions in mild head injury. Clin Biochem 2012;45:408–411.

3. Topolovec-Vranic J, Pollmann-Mudryj MA, Ouchterlony D, et al. The value of serum biomarkers in prediction models of outcome after mild traumatic brain injury. J Trauma 2011;71(5 Suppl 1):S478–486.

4. Vos PE, Jacobs B, Andriessen TM, et al. GFAP and S100B are biomarkers of traumatic brain injury: an observational cohort study. Neurology 2010;75(20):1786–1793.

5. Snoey ER, Levitt MA. Delayed diagnosis of subdural hematoma following normal computed tomography scan. Ann Emerg Med 1994;23(5):1127–1131.

Response

From
Yvonne W. Lui, MD
New York University School of Medicine, 660 First Ave, 2nd Floor, New York, NY 10016
e-mail: *Yvonne.lui@nyumc.org*

My colleagues and I thank Drs Lippi and Cervellin for their comments regarding S100B as a biomarker of brain injury in response to our article (1). S100B is a protein expressed in astrocytes, and recent work has shown elevated serum levels acutely after brain injury owing to blood-brain barrier disruption and glial injury (2). We agree that data suggest S100B to be a promising marker for traumatic brain injury; however, several points should be noted, as follows: *(a)* There is no consensus on diagnostic criteria of MTBI, *(b)* S100B is nonspecific and may be elevated in other central nervous system disorders (3) and in systemic injury (4,5), *(c)* the clinical application of S100B in MTBI is still being established (6), and *(d)* the relevance of S100B is removed from our study (1), where we reported chronic regional brain atrophy after concussion by using magnetic resonance (MR) imaging.

MR imaging is a highly promising tool with which to evaluate MTBI not only for diagnosis but also for elucidating mechanisms and long-term effects. MR imaging does not use ionizing radiation and is generally not used to assess acute injury. Most patients with MTBI have no abnormalities at conventional imaging. Current interest is in studying novel imaging methods that reveal metabolic, microstructural, and functional brain alterations (7–10). Our study was important because it showed that chronic volume loss can occur after a single concussive episode. Early biomarkers of injury to identify individuals at risk for long-term sequelae are needed.

Several studies have shown that S100B may be promising to triage patients with head trauma for computed tomographic (CT) evaluation; however, other studies do not support S100B's clinical usefulness in the prediction of long-term symptoms (11). Although CT uses ionizing radiation, it remains the standard of care in the assessment of acute intracranial trauma—for which there are established appropriateness criteria (12). Our study did not involve the use of CT.

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References

1. Zhou Y, Kierans A, Kenul D, et al. Mild traumatic brain injury: longitudinal regional brain volume changes. Radiology 2013; 267(3):880–890.

2. Papa L, Ramia MM, Kelly JM, Burks SS, Pawlowicz A, Berger RP. Systematic review of clinical research on biomarkers for pediatric traumatic brain injury. J Neurotrauma 2013;30(5):324–338.

3. Astrand R, Unden J, Romner B. Clinical use of the calcium-binding S100B protein. Methods Mol Biol 2013;963:373–384.

4. Schulte S, Schiffer T, Sperlich B, Knicker A, Podlog LW, Struder HK. The impact of increased blood lactate on serum S100B and prolactin concentrations in male adult athletes. Eur J Appl Physiol 2013; 113(3):811–817.

5. Sorci G, Riuzzi F, Arcuri C, et al. S100B protein in tissue development, repair and regeneration. World J Biol Chem 2013; 4(1):1–12.

6. Schiavi P, Laccarino C, Servadei F. The value of the calcium binding protein S100 in the management of patients with traumatic brain injury. Acta Biomed 2012;83(1):5–20.

7. Kirov II, Tal A, Babb JS, Lui YW, Grossman RI, Gonen O. Diffuse axonal injury in mild traumatic brain injury: a 3D multivoxel proton MR spectroscopy study. J Neurol 2013;260(1):242–252.

8. Miles L, Grossman RI, Johnson G, Babb JS, Diller L, Inglese M. Short-term DTI predictors of cognitive dysfunction in mild traumatic brain injury. Brain Injury 2008;22(2):115–122.

9. Tang L, Ge Y, Sodickson DK, et al. Thalamic resting-state functional networks: disruption in patients with mild traumatic brain injury. Radiology 2011;260(3):831–840.

10. Zhou Y, Milham MP, Lui YW, et al. Default-mode network disruption in mild traumatic brain injury. Radiology 2012;265(3):882–892.

11. Babcock L, Byczkowski T, Wade SL, Ho M, Bazarian JJ. Inability of S100B to predict postconcussion syndrome in children who present to the emergency department with mild traumatic brain injury: a brief report. Pediatr Emerg Care 2013;29(4):458–461.

12. Papa L, Stiell IG, Clement CM, et al. Performance of the Canadian CT Head Rule and the New Orleans Criteria for predicting any traumatic intracranial injury on computed tomography in a United States level I trauma center. Acad Emerg Med 2012;19(1):2–10.

Interpreting the Accuracy of Clinical Predictors of Head CT Abnormal Findings in Nontrauma Patients

From
Davi J. F. Solla, MD
Medical School of the Federal University of Bahia, Praça XV de novembro, s/n - Largo do Terreiro de Jesus, Salvador, Bahia, Brazil
e-mail: *davisolla@hotmail.com*

Editor:

We read with interest the article by Wang and You in the March 2013 issue of *Radiology* (1). They aimed to identify predictors of clinically important abnormal findings on computed tomographic (CT) images of the head among emergency department patients without a history of trauma.

The identification of clinical predictors of the ultimate utility of imaging examinations is an area of research

with the potential to refine medical reasoning leading to further imaging examinations and to affect the efficient investment of available financial resources. Because there is a scarcity of studies examining the utility of head CT in patients without trauma, this study deserves special attention.

However, important limitations of the study must be noted. The explicit ones were pointed out by the authors: The retrospective design may have introduced bias to the data, and the heterogeneity in CT requisitions (nonstandardized and nonuniversal but guided by previous physician's assumptions in face of the physical examination findings) possibly changed pretest probability and also overestimated the predictors' sensitivity and specificity.

We also need to draw attention to the omission of specificity and likelihood ratios. By analyzing the published data, notably those in Table 4 of their article, we can infer the following: *(a)* For the parameter "One or more of five clinical predictors, or age >70 y" (the independent predictors proposed in Table 3), the sensitivity was 96.0% but the specificity was 24.0%, resulting in a positive likelihood ratio of only 1.26 (95% confidence interval: 1.22, 1.31); and *(b)* for the parameter "One or more of five clinical predictors" or the one including "presentation with seizures," the specificity and positive likelihood ratio would be alike or even worse.

A positive likelihood ratio this low results in minimal or no change to the posttest probability (2–4). Considering the somewhat low prevalence of abnormal findings in this study sample, this is more worrisome. For example, application of the positive likelihood ratio of the proposed clinical predictors (1.26) to the pretest probability of 14.2% (the prevalence of abnormal CT findings in the article) would give us a similar posttest probability of 17.0% (5).

Identifying a set of predictors for abnormal findings in head CT images would require specificity to be as valued as sensitivity and the study design to preferably be prospective, including a universal CT requisition protocol, independent of a patient's previous signs or symptoms.

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References

1. Wang X, You JJ. Head CT for nontrauma patients in the emergency department: clinical predictors of abnormal findings. Radiology 2013;266(3):783–790.
2. Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. JAMA 1994;271(5):389–391.
3. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. BMJ 2004;329(7458):168–169.
4. Grimes DA, Schulz KF. Refining clinical diagnosis with likelihood ratios. Lancet 2005;365(9469):1500–1505.
5. Fagan TJ. Nomogram for Bayes theorem [letter]. New Engl J Med 1975;293(5):257.

Response

From
Xi Wang, MD,* and John J. You, MD, MSc[†‡]
Departments of Radiology,* Medicine,[†] and Clinical Epidemiology & Biostatistics,[‡] McMaster University, 1280 Main St West, Room HSC-2C8, Hamilton, ON, Canada L8S 4K1
e-mail: *jyou@mcmaster.ca*

We are grateful for Dr Solla's interest in and constructive comments about our work (1). We concur that the specificity and positive likelihood ratio derived from our data are low. However, as Dr Solla points out, clinical decision rules are valuable because of their ability to promote the more efficient use of resources. The principal opportunity for cost reduction therefore arises from the ability of a clinical decision rule to "rule out" the presence of a significant abnormality and thus enable physicians to safely avoid requesting a particular test, such as head CT. In other words, the utility of a clinical decision rule is largely determined by its sensitivity and negative likelihood ratio.

The negative likelihood ratio for patients with one or more of the five clinical predictors identified in our study (ie, focal neurologic deficit, altered mental status, history of malignancy, nausea or vomiting, derangements in coagulation profile) or those older than 70 years is as follows: (1 - sensitivity)/specificity = (1 - 0.96)/0.24 = 0.17. If we apply a negative likelihood ratio of 0.17 to a population where the pretest probability of having a significant abnormality at head CT is 14.3%, the posttest probability is reduced substantially to 2.8% (2). For the combination of "one or more of five clinical predictors, age >70 y, or presentation with seizures," the associated negative likelihood ratio is 0.09, reducing the posttest probability further to 1.5%.

As stressed in our article, the clinical predictors of abnormal head CT identified in our study require prospective validation before clinical application (3). Our findings represent the first step in the development of a clinical decision rule that has the potential to substantially reduce CT use in this patient population without missing clinically important neurologic abnormalities.

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References

1. Wang X, You JJ. Head CT for nontrauma patients in the emergency department: clinical predictors of abnormal findings. Radiology 2013;266(3):783–790.
2. Fagan TJ. Nomogram for Bayes theorem [letter]. N Engl J Med 1975;293(5):257.
3. Laupacis A, Sekar N, Stiell IG. Clinical prediction rules: a review and suggested modifications of methodological standards. JAMA 1997;277(6):488–494.