The Economic Impact of S-100B as a Pre-Head CT Screening Test on Emergency Department Management of Adult Patients with Mild Traumatic Brain Injury

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Abstract

Recent research suggests that serum S-100B may serve as a good pre-head computed tomography (CT) screening test because of its high sensitivity for abnormal head CT scans. The potential economic impact of using S-100B in the emergency department setting for management of adult patients with isolated mild traumatic brain injury (mTBI) has not been evaluated despite its clinical implementation in Europe. Using evidence from the literature, we constructed a decision tree to compare the average cost per patient of using S-100B as a pre-head CT screening test to the current practice of ordering CT scans based on patients' presenting symptoms without the aid of S-100B. When compared to scanning 45–77% of isolated mTBI patients based upon their presenting symptoms, using S-100B as a pre-head CT screen does not lower hospital costs (\$281 versus \$160), primarily due to its low specificity for abnormal head CT scans. Sensitivity analyses showed, however, that S-100B becomes cost-lowering when the proportion of mTBI patients being scanned exceeds 78%, or when final CT scan results require 96 min or more than the wait for blood test results. Generally speaking, if blood test results require less time than imaging, and if head CT scan rates for patients with isolated mTBI are relatively high, using S-100B will lower costs. Recommendations for using S-100B as a screening tool should account for setting-specific characteristics and their consequent economic impacts. Despite its high sensitivity and excellent negative predictive value, serum S-100B has low specificity and low positive predictive value, limiting its ability to reduce numbers of CT scans and hospital costs.

Key words: computed tomography; cost minimization; S-100B; mild traumatic brain injury

Introduction

RECENT YEARS HAVE SEEN A GROWING AWARENESS of mild traumatic brain injury (mTBI), including its recognition as a "serious public health problem" by the Centers for Disease Control and Prevention (CDC) (National Center for Injury Prevention and Control, 2003). The CDC mTBI Work Group defines mild traumatic brain injury as (National Center for Injury Prevention and Control, 2003):

An occurrence of injury to the head resulting from blunt trauma or acceleration or deceleration forces with one or more of the following conditions attributable to the head injury:

- (i) Any period of observed or self-reported transient confusion, disorientation, or impaired consciousness;
- (ii) Any period of observed or self-reported dysfunction of memory (amnesia) around the time of injury, but not longer than 24 hours;

- (iii) Observed signs of other neurological or neuropsychological dysfunction;
- (iv) Any period of observed or self-reported loss of consciousness lasting 30 minutes or less.

The CDC estimates that up to 75% of the more than 1.5 million traumatic brain injuries seen in the hospital setting are mild traumatic brain injuries (National Center for Injury Prevention and Control, 2003). As identified by the American College of Emergency Physicians (ACEP) in an update to the group's clinical policy for managing mTBI: "The challenge to the [emergency department] is identifying which patients with a head injury have an acute traumatic intracranial injury, and which patients can be safely sent home" (Jagoda et al., 2008).

Among an estimated 460,000 annual emergency department (ED) visits for isolated mTBI, the majority of patients (63.3–83.6%) have a Glasgow Coma Scale (GCS) score of 15

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(Jagoda et al., 2002) and would be considered neurologically intact. With the maturation of computed tomography (CT) technology, head CT has become the primary tool used to detect significant intracranial injuries including intracranial hemorrhage. In this group of neurologically intact patients, most will have a normal head CT scan. The prevalence of a positive CT revealing an acute intracranial lesion in patients with isolated mTBI and GCS score of 15 ranges from 3–19% (Jagoda et al., 2008; Bazarian et al., 2006; Borg et al., 2004). If the majority of ED patients with isolated mTBI have negative head CT scans and no clinical complications from other injuries, it may be feasible to screen for and reduce the number of unnecessary CT scans and discharge patients faster without compromising patient safety or quality of care.

Serum S-100B has the potential to serve as a good screening test because of its high sensitivity for abnormal head CT scans. Current research suggests that this astrocyte protein is released after a traumatic brain injury, crosses the damaged blood–brain barrier, and is detectable in serum within minutes of injury (Borg et al., 2004). Studies from the United Kingdom, continental Europe, and Brazil have demonstrated sensitivities and specificities of S-100B as a marker of traumatic abnormalities on head CT to be in the ranges of 95–100% and 20–31%, respectively (Müller et al., 2007; Biberthaler et al., 2006; Townend and Ingebrigtsen, 2006; Poli-de-Figueiredo et al., 2006). While S-100B specificity is low, its high sensitivity makes the blood test attractive as a screening tool to potentially rule out the need for a head CT scan. Consequently, the updated ACEP clinical policy on neuroimaging after head injury includes a Level C recommendation, acknowledging evidence from the literature that S-100B may be used as a pre-head CT screen in the management of isolated mTBI (Jagoda et al., 2008).

Using S-100B may also help physicians arrive at a clinical decision faster without waiting for the patient to get a CT scan or waiting for the final radiology report. Serum S-100B levels can be assayed using an automated device in 18 minutes (Biberthaler et al., 2006). While most U.S. hospital laboratories can process automated analysis in 1–2 h, there may be wider variability in the time needed to obtain and interpret head CT scan results. Under optimal conditions, some institutions may obtain CT results in minutes. During times of ED crowding, or during mass casualties however, delays for CT are substantial (National Center for Injury Prevention and Control, 2007). In addition, smaller facilities (especially rural EDs) may not have a CT scanner on site and the transportation of patients from such a site to larger hospitals for a CT scan can take several hours.

Thus the primary economic advantage to S-100B screening lies in its potential to reduce unnecessary CT scans and in-hospital time, leading to reduced per-patient hospital costs. To date, however, no studies have examined what economic impacts may be associated with using the S-100B assay despite its current clinical use in Germany and Austria (S. Grueb, personal communication, 2009). The updated ACEP clinical policy highlights the need for evidence on the cost-effectiveness of S-100B as a pre-head CT screening tool (Jagoda et al., 2008). The objective of this study is to investigate the potential cost reductions, from a hospital perspective, associated with the use of serum S-100B levels to screen adult patients presenting with isolated mTBI and GCS score of 15 to determine if a CT scan is needed.

Methods

This investigation was reviewed by the institutional review board and considered exempt from full review.

We used a decision-tree model to compare costs associated with the current practice of ordering a head CT based on presenting symptoms to the costs associated with using S-100B to screen for those patients who would then receive a head CT only if S-100B is abnormal (Fig. 1). Current practice in the U.S. for ordering a CT is at the discretion of the ED physician depending on the patient's presenting symptoms. Several decision rules exist to aid in this decision, including the New Orleans Criteria (Haydel et al., 2000) and the Canadian CT Head Rule (Stiell et al., 2001). These decision rules use symptoms such as amnesia, vomiting, and signs of a skull fracture to guide CT ordering, and have been shown to be highly sensitive to clinically important CT findings (Stiell et al., 2005; Smits et al., 2005). The extent to which these rules are used by practicing clinicians, however, is unknown. In the intervention arm, patients with a serum S-100B level above $0.1 \mu\text{g/L}$ will receive a CT scan, while patients with serum S-100B below the cutoff will be discharged. We used the cutoff of $0.1 \mu\text{g/L}$ because this value has been shown to maximize the sensitivity of S-100B as a screen for abnormal head CT findings (Müller et al., 2007; Biberthaler et al., 2006; Romner et al., 2000).

Past studies have consistently recommended CT scans for all patients with a GCS score of 13–14, whereas evidence is equivocal for those with a GCS score of 15 (Borg et al., 2004; Jagoda et al., 2002). This decision model will, therefore, be restricted to mTBI with a presenting GCS score of 15.

We further restricted the analysis to patients with isolated mTBI because studies have shown that additional traumatic injuries, such as fractures, increase serum S-100B levels, potentially leading to false-positives for head injury (Uden et al., 2005; Savola et al., 2004). In addition, multiply-injured patients typically require rapid imaging of the head, chest, and abdomen, and are not likely to be discharged without CT imaging. We also focused on adult patients because the decision-making process for CT imaging in adults differ from that for children. Unlike adults, the pediatric literature on the management of mTBI highlights considerations of sedation, parental concerns, and elevated relative radiation exposure and long-term cancer risks in the decision to order CT imaging in children (Atabaki et al., 2008; Thiessen and Woolridge, 2006). Thus, our analysis is intended for management of adult patients (>18 years old) with isolated mTBI who present with a GCS score of 15.

We conducted the analysis from the hospital perspective, accounting for the aggregated costs accumulated between ED presentation and disposition at 48 h. Previous studies have found that neurological deterioration after 7 days from initial injury is extremely rare (Borg et al., 2004) and 48 h captures, on average, the period within which deterioration might occur (Fabbri et al., 2005; af Geijerstam and Britton, 2005; af Geijerstam et al., 2004; Voss et al., 1995; Shackford et al., 1992; Livingston et al., 1991). We performed the analysis from the hospital perspective in order to estimate per-case costs within a 48-h time period.

Model assumptions

In order to create a workable model and construct the decision tree in Figure 1, several assumptions were made. We

FIG. 1. Decision tree model. Patients with isolated mTBI begin at left-most node. Each branch has a probability of occurrence, and terminal branches are associated with aggregated hospital costs (CT, computed tomography; ED, emergency department; Obs, emergency department observation).

assumed patients presenting to the ED with isolated mTBI who are assessed not to be in need of a head CT scan are discharged without further observation or evaluation. This assumption is consistent with the recommendations by the World Health Organization Collaborating Centre Task Force on mTBI (Borg et al., 2004).

Because of its high sensitivity, the advantage of S-100B is its ability to rule out patients for subsequent head CT scanning. Thus in the model, patients testing negative for S-100B are discharged, while patients with a positive S-100B receive a CT scan. Traumatic intracranial injury on head CT at any point may lead to admission for neurosurgery or a period of ED observation. If a patient receives an observation period prior to his or her final disposition during the 48 h, we assumed that a second CT is performed as part of the evaluation for observation stay.

A patient re-visiting the ED because of his or her initial isolated mTBI is assumed to receive the same full evaluation

as a patient initially presenting with an abnormal CT. Thus, a return to the ED within 48 h includes the cost of a CT to check for changes in old findings or new findings.

If a patient worsens during a period of ED observation, we assumed the patient requires admission for a neurosurgical intervention. If a patient dies, we assumed the death occurs after admission (with or without ED observation). Therefore, the death of the patient still incurs the costs of ED stay and admission.

Costs

We compared costs in the intervention arm to costs in the current practice arm using several possible clinical scenarios to determine expected average costs for the two decision arms. These relevant disposition events from the hospital perspective are hospital admission for neurosurgical procedure, admission for surgery after a period of observation,

TABLE 1. COST COMPONENTS

<i>Cost component</i>	<i>Amount (\$U.S.)</i>	<i>± 2 SD (\$U.S.)</i>
Time cost of 1-h wait time in ED (Falvo et al., 2007)	\$380	N/A
S-100B assay	\$20.00	\$15.00–\$25.00 ^a
CT scan (CPT 70450)	\$216.87	\$155.18–\$278.56
Standard ED visit (CPT 99284)	\$111.57	\$100.76–\$122.38
ED observation (CPT 99235)	\$162.56	\$144.06–\$181.06
Hospital admission with surgery (CPT 99222, 99233, 61322; DRG 2)	\$12,748.03	\$12,361.39–\$13,134.68
Re-visit ED = standard ED visit (CPT 99284) + CT scan (CPT 70450)	\$328.44	\$255.94–\$400.94

^aArbitrary range for S-100B cost.

Costs of disposition events used in analysis are sums of relevant components.

CT, computed tomography; CPT, Current Procedural Terminology code; DRG, Diagnosis-Related Group; ED, emergency department; SD, standard deviation; N/A = not applicable.

re-visit to the ED, and discharge with no sequelae. Relevant cost components for the disposition events include costs of S-100B blood testing, CT scan, ED visit without observation, ED visit with ED observation, hospital admission with surgery, and the time cost associated with an occupied ED bed that could otherwise be used for another patient (Table 1). Specifically, it is those patients discharged as a result of a negative S-100B test who would lower time costs otherwise accrued from occupied ED beds. Also, from the hospital perspective, false-positive results (e.g., the cost of unnecessary treatment) and false-negative results (e.g., the cost of re-admission with avoidable complications) both incur real costs that would not be recovered.

In the current framework, the analysis of expected costs for each decision arm is predicated on test characteristics of S-100B, not CT scans. As the comparator, CT scan findings are viewed as the gold standard for detecting intracranial hemorrhage, thus patient flow through the decision tree is not impacted by false CT results. As S-100B would realistically be used in the clinical setting, its diagnostic test characteristics (i.e., sensitivity and specificity) directly impact expected outcomes, whereas CT scan characteristics do not. In other words, because we examine the cost impact of S-100B as an intervention to CT scans, CT sensitivity and specificity are not direct cost-calculation inputs.

Our analysis utilized 2007 national average Medicare reimbursement rates for relevant Current Procedural Terminology (CPT) codes and national base Diagnosis-Related Group (DRG) rates as proxies for costs to the hospital (Table 1). The cost of the S-100B assay (\$20.00) is approximated from Medicare reimbursement rates for similar immunoassay-based laboratory tests.

In order to account for the costs associated with throughput time, we needed an estimate of the hourly value of resources needed to keep a patient in the ED. There has been no published direct estimate of this figure. Two studies, however, have estimated total loss in potential hospital revenue as a result of having to provide care for admitted patients boarding in the ED when those resources could have been used to take care of additional patients (Falvo et al., 2007; Bayley et al., 2005). For our initial analysis, we used the valuation by Falvo and associates (2007), for which the time cost of an admitted

patient occupying an ED bed is \$380 per hour. In the sensitivity analyses (see below), we examined the relationship between time cost and the economic impact of S-100B.

Primary data analysis

For the base-case analysis, we employed a static decision analytic model to calculate expected incurred costs for S-100B-tested and S-100B-untreated ED patients over a 48-h time horizon (TreeAgePro 2008 Suite; TreeAge Software, Inc., Williamstown, MA). We estimated the probability of possible outcomes (i.e., base-case input probabilities) at each stage in the management of mTBI for both the intervention and current practice arm (Table 2) from the literature by using the mathematical average of values extractable from presented data. Sources were limited to studies with at least 50 patients (to exclude case reports or case series) published after 1989. We chose not to include earlier studies to focus on clinical practice after the establishment and maturation of CT technology.

A review of the literature on management of mTBI in the ED revealed that 45–77% of adult patients with suspected mTBI receive a head CT scan (Table 2). The variation in CT scan rates reflects variations in imaging use rather than prevalence of mTBI because we selected studies focusing on similar patient populations (e.g., adults with GCS score 13–15 and isolated head injury). Among those patients who receive a scan, 3–19% have an abnormality requiring further attention, and of these patients with relevant CT findings, 0.08–3.7% require admission for neurosurgery. Regarding the performance of S-100B as a screening test, at a cutoff of 0.1 µg/L, the published sensitivity ranges from 0.91–1.00 and specificity ranges from 0.2–0.31 (Müller et al., 2007; Biberthaler et al., 2006; Poli-de-Figueiredo et al., 2006; Biberthaler et al., 2001). The average of the values reported by the included studies was used in our model calculations (base-case values, Table 2). In addition, we assumed that clinical decision-making using head CT results takes, on average, 1 h longer than decision-making using laboratory test results. Various time differences between CT scan and laboratory test results were explored in the sensitivity analyses (see below). Thus, we compared the practice of scanning, on average, 61%

TABLE 2. DECISION MODEL CALCULATION INPUTS

Description		Base-case values	Range	Source
CT scan rate (i.e., probability of getting CT at presentation)		0.61	0.45–0.77	Shackford et al., 1992
Probability of initial CT+		0.11	0.03–0.19	Taheri et al., 1993
Probability of admission after initial CT+		0.0189	0.0008–0.037	Shackford et al., 1992
Probability of ED observation after initial CT–		0.093	0.0477–0.1397	Borg et al., 2004
Probability of admission after initial CT+ and ED observation		0.0014	—	Borg et al., 2004
Probability of admission after initial CT– and ED observation		0.00123	0.00056–0.0019	Livingston et al., 2000
Probability of ED re-visit after discharge without initial CT		0.0161	0.00053–0.0316	af Geijerstam and Britton, 2005
Probability of ED re-visit after discharge with initial CT–		0.0126	0.0031–0.022	Shackford et al., 1992
Probability of ED re-visit after initial CT+ and ED observation		0.0001	—	Fabbri et al., 2004
Probability of ED re-visit after initial CT– and ED observation		0.00005	—	Hemphill et al., 1999
Time advantage associated with using S-100B		1 hour	—	Authors' estimate
S-100B 0.1 $\mu\text{g/L}$ cutoff	Sensitivity	0.973	0.91–1	Poli-de-Figueiredo et al., 2006
	Specificity	0.302	0.2–0.31	Biberthaler et al., 2006
^a S-100B 0.14–0.2 $\mu\text{g/L}$ cutoff	Sensitivity	0.911	0.83–1	Biberthaler et al., 2001
	Specificity	0.663	0.65–0.68	Müller et al., 2007

^aNot used in base-case analysis.

Base-case probabilities and S-100B sensitivity and specificity used in the decision tree to calculate the expected cost per patient-case. CT, computed tomography; ED, emergency department.

of isolated mTBI patients with a presenting GCS score of 15, in whom 11% will have an abnormality on head CT, to the practice of using S-100B first and subsequently discharging stable patients 1 h earlier, with the hour valued at \$380 (Falvo et al., 2007), and scanning those patients who test positive for S-100B, for whom the average S-100B sensitivity and specificity are 0.973 and 0.302, respectively (Table 2).

Sensitivity analyses

Several aspects of ED care for mTBI vary from institution to institution. The sensitivity analyses focused on aspects of care with the greatest variation, or most uncertainty, as reported in the literature. Because the base-case average values may not represent many institutions, it is important to examine how variation in these factors would influence the ability of using S-100B to lower costs. The sensitivity analyses examined the CT scan rate for isolated mTBI, the time difference between obtaining results of head CT scan compared to results from blood testing, and the hourly cost of keeping a patient in the ED, that is, the time cost. One-way sensitivity analyses separately examined the impact of each of these factors on the cost impact of S-100B. Two-way sensitivity analyses examined the combined impact of variation in these cost-driver variables relative to each other.

Results

Base-case

The intervention of using S-100B as a screen would cost hospitals on average \$281 per patient-case, while the current practice strategy (selective CT scanning based on presenting symptoms and physician discretion) would cost on average \$160 per patient. This estimate assumes that head CT scanning results require, on average, 1 h more than laboratory test results, and that this hour is valued at \$380. Thus the current practice of imaging isolated mTBI patients without using serum S-100B leads to lower hospital costs.

One-way sensitivity analyses

While holding other variables constant at base-case values, in order for S-100B to result in lower costs, the proportion of isolated mTBI patients undergoing head CT scanning must be above 0.782. Alternatively, the wait for head CT results must be at least 96 min longer than the wait for blood test results at a CT scan rate of 77%, the maximum reported in our literature review, for S-100B to be cost-lowering. With a lower CT scan rate of 61%, our base-case value, no feasible time advantage allows S-100B to be the better alternative. Finally, at the maximum reported rate for head CT scans of 77%, the associated time cost

FIG. 2. Two-way sensitivity analysis: CT scan rate and time cost (per hour). As the CT scan rate increases, the amount of time cost savings needed for serum S-100B to be advantageous decreases; that is, the greater the CT scan rate, the easier it is for S-100B to lower costs.

must be $> \$600/\text{hour}$ for S-100B to perform better than current practice. Again, at our base-case scan rate of 61%, no reasonable value of time allows S-100B to be advantageous.

Two-way sensitivity analyses

With our base-case assumption that CT results take 1 h longer than blood test results, two-way analysis demonstrates that increasing the time costs slightly reduces the proportion of patients needing to be scanned to make S-100B cost-advantageous (Fig. 2). Increasing the time to wait for CT results (compared to laboratory results) has a greater impact on reducing the proportion of patients needing to be scanned to make S-100B advantageous (Fig. 3). Viewed another way, the greater the CT scan rate, the lower the time-differential and time cost thresholds for preferring S-100B as a pre-CT screen.

Discussion

Our decision model reveals that the economic impact of an ED management strategy that screens all isolated mTBI patients with serum S-100B is highly dependent on hospital-specific characteristics. Screening patients for subsequent

head CT with serum S-100B can lower hospital costs when scan rates exceed 78% of isolated mTBI patients, if final CT results require 1 h longer than blood test results, and with this hour difference valued at \$380. As time becomes increasingly valuable, the threshold CT scan rate at which S-100B becomes advantageous lowers (Fig. 2). Similarly, as the serum assay saves more time relative to waiting for CT scan results, lower rates of scanning patients allow S-100B to be cost-lowering (Fig. 3). Generally speaking, if obtaining S-100B test results requires less time than imaging results, and if head CT scan rates for such patients are relatively high, using S-100B will lower costs compared to current practice. Despite its high sensitivity and excellent negative predictive value, S-100B assay has low specificity and low positive predictive value, limiting its ability to reduce hospital costs.

No other assessments of the economic impact of S-100B as a pre-CT screen have been performed, though the assay is currently used clinically in several European countries. The need for better evidence of the cost-effectiveness of the assay has been noted by the ACEP in its evaluation of the evidence for the ability of S-100B to reduce potentially unnecessary head CT scans. This idea of reducing unnecessary CTs is not

FIG. 3. Two-way sensitivity analysis: CT scan rate and time advantage (hours) associated with S-100B. As CT scan rate increases, the less time advantage needed when using a blood test instead of waiting for CT imaging for S-100B to lower costs. In other words, the more patients scanned, the easier it is for S-100B to offer an advantage and lower costs.

new in ED management of patients. Indeed, a recent *New England Journal of Medicine* review of clinical practice for acute pulmonary embolisms (PEs) recommended using the D-dimer assay to screen patients with low or moderate prior probability for need of CT imaging of the lung vasculature (Konstantinides, 2008). The use of D-dimer in clinical algorithms for acute PE has differing economic implications depending on the setting. A study using European data found the test to be cost-lowering, but a study using U.S. data found the test to have little economic advantage (Righini et al., 2007; Duriseti et al., 2006). While our study demonstrates that S-100B does not lead to lower short-term ED costs, we provide more detailed evidence for specific settings in which S-100B could reduce costs.

While current literature seems to reflect clinical management of isolated adult mTBI as being relatively conservative with respect to ordering CT scans, there are several circumstances in which using S-100B as a pre-CT screen can lower short-term costs in the acute setting. Hospitals with a relatively high baseline rate of scanning adult isolated mTBI patients (i.e., scanning over 78% of this group) may find S-100B to be helpful in safely ruling out patients who do not need a

head CT scan. Alternatively, if there is a high time cost associated with obtaining CT results compared to laboratory test results, either in terms of hours delayed or occupied ED resources that could be used to take care of other acutely ill patients, using S-100B could be advantageous. The National Center for Injury Prevention and Control (2007) has reported that surge situations or times of ED crowding present a triaging challenge to any hospital in deciding which patients must receive diagnostic imaging immediately and which patients may safely await imaging (if needed at all).

Additionally, for community emergency clinics or rural hospitals without a CT scanner on-site, the added transportation resources and costs avoidable by using S-100B to rule out patients who do not need a CT scan would be valuable for patients and health care providers. In situations of potentially long hours of delay and/or hundreds of dollars in occupied ED resources, the high sensitivity of S-100B would allow emergency physicians to safely rule out adult patients with isolated mTBI who do not require CT scans.

Serum S-100B would ideally provide a uniform, objective criterion for assessing the need for head CT, instead of the

uncertainty and subjectivity associated with individual clinician practice style in response to non-specific patient symptoms, especially for a patient population with a relatively low likelihood of having clinically significant CT findings. The ultimate reason S-100B would not be more widely helpful to U.S. emergency departments and hospitals in lowering costs, however, is the low specificity of the assay. High false-positive rates mean relatively few patients would be ruled out for subsequent CT scans. Should S-100B be adopted as a clinical decision-making tool, it would be most advantageous in certain settings or situations as described above.

Limitations

Many of the studies providing probability values for our decision model did not stratify results by GCS scores, while our analysis was designed specifically for patients with a GCS score of 15. Whenever possible, we extracted values specific to patients with a GCS score of 15. Otherwise, we derived probabilities from patients with GCS scores ranging from 14–15, and even 13–15. Additionally, the studies providing data for this analysis were not limited to patients with isolated mTBI. The effect of using data from a “sicker” patient population is an overestimation of S-100B sensitivity and underestimation of S-100B specificity. As a result, our study overestimates the time-difference and time-cost thresholds needed for S-100B screening to become cost-saving. In other words, we underestimate the economic advantage associated with serum S-100B use.

Another limitation may result from using simple averages of value ranges found in the literature as our base-case input values, because studies of varying quality are not differentially weighted. While weighing studies of varying quality may alter our findings, sensitivity analyses allowed us to explore all possible variations in our model input probability and cost values. Furthermore, the sensitivity analyses demonstrated that the CT scan rate, time difference between obtaining head CT scan results compared to blood test results, and the hourly time cost of a keeping a patient in the ED were principal cost drivers. We duly explored variation in these three variables and arrived at a consistent scenario for the cost-lowering advantage that S-100B presents when patient scan rates are high, or when the blood test offers a significant time (in hours and dollar value) advantage.

Finally, it must be noted that this study explicitly excludes some possible long-term benefits that would not be realized within the 48-h time horizon. In particular, we have not factored in the potential long-term benefit to society in reducing unnecessary radiation exposure. Radiation from over the 63 million CT scans obtained each year in the U.S. contributes to about 2% of all cancers (Brenner and Hall, 2007). The adult brain receives a higher organ dose of radiation (20 mGy) during a head CT than any abdominal organ during an abdominal CT scan (stomach and liver, 13 mGy; colon and bone marrow, 4 mGy; Brenner and Hall, 2007). The radiation exposure delivered to a rapidly increasing number of patients in the U.S. poses a public health concern in the future. The short time horizon of our analysis excludes the potential long-term cost to society from CT radiation exposure, and thus underestimates the potential advantage the use of S-100B might offer as a pre-CT screening test.

Conclusion

Adding S-100B as a pre-CT screen would result in lower hospital costs if over 78% of isolated mTBI patients are receiving head CT scans. Alternatively, when the CT scan rate is lower, the test must be associated with a substantial time advantage (i.e., each hour spent waiting for CT results must represent a large time cost, or waiting for CT would increase ED length-of-stay by over 1.5 hours). It appears that current practice as reflected by the literature shows, on average, that physicians are conservative in ordering head CT scans for mTBI patients, and adding S-100B as a screening tool does not present a clear economic advantage in further reducing the number of CT scans. While evidence in the literature and our model demonstrate the advantage of current practice over S-100B, we have sought to characterize practice conditions in which pre-head CT screening would be cost-lowering. When a relatively high percentage of patients with isolated mTBI receive head CT scans, or when there are significant time costs or time delay associated with waiting for CT scan results, using S-100B will help lower hospital costs.

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