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Patient costs and patient flow after implementation of S100B in Scandinavian head trauma guidelines

Jens-Kristian Bomholt-Riis, Thorbjørn Søren Rønn Jensen, Line Pedersen, Louise Fournais, Vagn Eskesen & Ramona Åstrand

Department of Neurosurgery, Copenhagen University Hospital – Rigshospitalet, Denmark

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ABSTRACT

INTRODUCTION. The serum biomarker S100B has been implemented in the Scandinavian Neurotrauma Committee (SNC) 2013 Head Injury Guidelines for patients classified with mild head injury (MHI). Patients with a serum S100B level < 0.10 µg/l sampled within six hours after trauma can be discharged without further observation or investigation. The aim of this study was to examine the influence of S100B implementation on patient costs and patient flow in an emergency department.

METHODS. In this retrospective study, we included MHI patients (≥ 18 years) admitted to Rigshospitalet, Copenhagen, Denmark, between 1 February 2013 and 31 January 2014. Medical records were examined for the time of trauma, time of S100B sampling, serum S100B level, the severity of the head injury, clinical symptoms, radiological examinations, hospitalisation, discharge, surgical intervention, readmission and mortality.

RESULTS. Among 2,033 patients screened for potential study candidates, 227 patients met the inclusion criteria and were enrolled in the study. Among these patients, 119 (52%) were not treated according to SNC 2013 Head Injury Guidelines, leaving 108 (48%) with full guideline adherence. Compared with MHI management without S100B, implementation of S100B produced an additional cost of €1.26 per patient. Overall, the addition of S100B did not affect the waiting time for examination with S100B sampling or CT.

CONCLUSION. The use of S100B in the SNC 2013 Head Injury Guidelines did not reduce patient costs, nor did it cause substantial additional patient costs or delayed patient flow.

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Head injuries are classified into different severity levels [1] of which 70-90% are mild head injuries (MHI) [2]. The risk of serious complications for patients suffering MHI is low, though not negligible [3], making MHI management challenging. Routine use of CT of the head is inadvisable due to its high cost, hampered patient management and a potential risk of radiation-induced malignancy [4]. To reduce the amount of head CT, use of the serum biomarker S100B as a screening tool in MHI patients has been studied [5, 6].

In 2013, the Scandinavian Neurotrauma Committee (SNC) published the revised Scandinavian head injury guidelines in which serum S100B was introduced into clinical use [1] (**Supplementary 1 https://ugeskriftet.dk/files/a09210697_-_supplementary.pdf**).

According to this guideline, patients classified as having a mild, low-risk head injury and a serum S100B level < 0.10 µg/l sampled within six hours after trauma may be discharged, provided no other circumstances demands admission [1]. It has been proposed that S100B may reduce the cost associated with treatment of patients with head injuries and improve patient flow in the emergency department (ED) [6-9]. A few studies have investigated the financial impact of S100B implementation to the Canadian CT Head Rule guidelines [10, 11]. Information about the financial benefit of S100B in the SNC 2013 Head Injury Guidelines in a Danish population is lacking, and no study has yet examined patient flow after implementation of S100B.

Thus, the aim of this study was to examine the influence of S100B implementation on patient costs and patient flow in a Danish ED.

METHODS

Study setting and study population

We conducted a retrospective study in collaboration between the Trauma Centre and the Department of Neurosurgery at Copenhagen University Hospital, Rigshospitalet, Denmark. The hospital has a level-1 trauma centre, with an uptake area for head trauma that varies according to trauma severity. For moderate to minimal head trauma, the Trauma Centre is a referred ED with an uptake area restricted to the Central Copenhagen Area (120,000 inhabitants). The Department of Neurosurgery serves 2.5 million inhabitants at all times. The revised SNC guidelines were implemented in January 2013.

We aimed to include all adult patients (≥ 18 years) admitted to the Trauma Centre between 1 February 2013 and 31 January 2014, with a mild, low-risk head injury within the preceding 24 hours. Patient records with at least one of the following diagnosis codes according to the International Classification of Diseases, 10 edition (ICD-10); DS01 (scalp wound), DS02 (cranial and facial fractures), DS06 (intracranial injury) and DS100 (alcohol intoxication) were screened for inclusion in our study population. Patients diagnosed with alcohol intoxication were screened to ensure inclusion of patients with head injuries but an ICD-10 misdiagnosis. We excluded non-Danish patients (due to follow-up limitations), patients with a serum S100B drawn for other reasons than head injury, patients with insufficient medical records, patients admitted to the ED later than 24 hours after their head injuries, and secondarily referred patients.

Medical records were examined for time of trauma, time of S100B sampling, serum S100B level, severity of head injury, clinical symptoms, radiological examinations, hospitalisation, discharge, surgical intervention, readmission and mortality. Waiting time was examined for the full study population and calculated from arrival at the ED to S100B sampling and from arrival at the ED to head CT. Examinations within ten minutes and after six hours from the time of trauma were considered outliers and were excluded.

All data were anonymised and stored in a project database (Microsoft Excel), as approved by the Danish Data Protection Agency (journal number 2012-58-0004 and I-suite number RH-2017-164).

S100B sampling and biochemical analysis

Volumes of 5 ml venous blood were sampled and collected in a microtainer tube without additives. Samples were allowed to clot for 30 minutes and were then centrifuged for ten minutes at 3,000 G before collecting the serum. The samples were analysed with an electrochemiluminescence assay (Elecsys S100 assay, Roche Diagnostics, Mannheim, Germany) performed on a Cobas 8000 modular analyser. The range of serum S100B detection was reported to be 0.02-39 µg/l. The laboratory results were available one hour after sampling.

Statistics

All analyses were done with SPSS, version 25.0 (Chicago, IL, USA). The statistical significance level was set to $p < 0.05$. All tests were two-sided. Data are presented as mean ± standard deviation (SD). Comparisons of means between groups were analysed using the independent samples t-test when data were normally distributed.

Cost analysis

Danish healthcare is state owned and tax financed. Hospital expenses are based on the annual hospital budget rather than on refunds per service. The latest Tariff Catalogue from 2017 from Rigshospitalet was used to provide updated patient costs. The costs of a serum S100B sample and a non-contrast head CT were €60 and €178, respectively. The costs for admission and observation for head injuries in the ED were calculated per initiated 24-hour period and were summed to €692. We restricted the costs for admission and observation to one day as our study only regards the initial patient management.

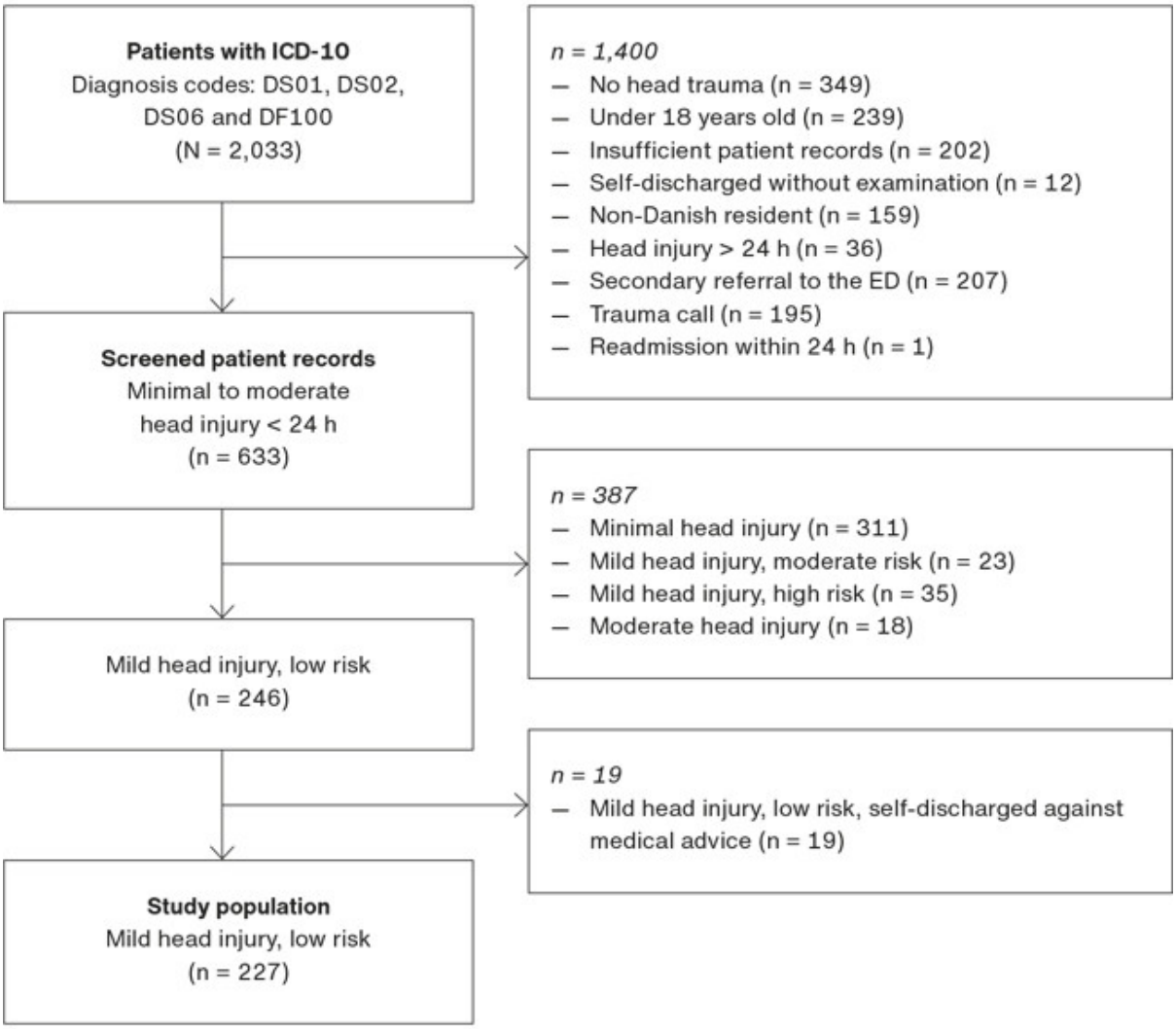
Trial registration: The Danish Data Protection Agency (journal number 2012-58-0004 and I-suite number RH-2017-164).

RESULTS

Patient inclusion

A total of 2,033 patient records were screened for potential study candidates (**Figure 1**). We excluded 1,400 patients who failed to meet the inclusion criteria. An additional 406 patients were excluded as they had another severity classification than mild, low-risk head injury (n = 387) or were self-discharged against medical advice (n = 19). We enrolled 227 patients meeting the inclusion criteria; 155 (68%) were male (median age 29 years) and 72 (32%) were female (median age 43 years) (**Table 1**).

FIGURE 1 Study inclusion/exclusion process.



DF100 = acute alcohol intoxication; DS01 = scalp wound; DS02 = fracture of skull and facial bones; DS06 = intracranial injury; ED = emergency department; ICD-10 = International Classification of Diseases, tenth edition.

TABLE 1 Baseline characteristics and management of study patients.

		S-S100B candidates	
	Total	yes	no
Patients, total /female/male, n	227/72/155	189	38
Age, median/female/male, yrs	30/41/29	-	-
Level of consciousness and symptoms, n			
GCS 14	86	73	13
GCS 15 + LOC, no repeated vomiting	128	103	25
GCS 15 + repeated vomiting, no LOC	6	6	0
GCS 15 + repeated vomiting + LOC	7	7	0
Fractures, any[a], n			
With potential S100B release	38	-	-
Without potential S100B release	3	-	-
No fractures	186	-	-
Early discharge, w/o observation, S-S100B or head CT, n	49	41	8
Admission to observation, all, n	56	48	8
Initial admission to observation, n	14	12	2
Initial S-S100B test, n	144	121	23
S-S100B < 0.10 µg/l:	43	40	3
Then discharge/admission	34/6	32/5	2/1
Then head CT/normal CT	3/3	3/3	0/0
Then discharge/admission	2/1	2/1	0/0
S-S100B ≥ 0.10 µg/l:	101	81	20
Then admission/discharge	6/10	6/9	0/1
Then CT	85	66	19
Normal CT	74	60	14
Then discharge/admission	60/14	46/14	14/0
Abnormal CT	11	6	5
Then admission/discharge	10/1	6/0	4/1
Head CT, all, n	108	84	24
Normal/abnormal[b]	95/13	77/7	18/6
Initial head CT:	20	15	5
Normal, then discharge/admission	18, 15/3	14, 11/3	4, 4/0
Abnormal[b], then admission	2, 2	1, 1	1, 1
Compliance, n			
Compliance to guidelines	97	90	7
Noncompliance, overtriage	49	49	0
Noncompliance, undertriage	81	50	31

GCS = Glasgow Coma Scale; LOC = loss of consciousness; S100B: a serum biomarker.
a) Potential S100B-releasing fractures included facial, spinal, clavicle, scapular, rib, humerus, radius, ulnar, tibial, fibula, femoral and pelvic fracture; nose fractures were not included in facial fractures as this fracture type has not shown a potential S-S100B increase [9].
b) Abnormal head CT included epidural haematoma, subdural haematoma, subarachnoid haemorrhage, cerebral contusion, basilar skull fracture and cranial vault fractures.

Guideline adherence

Among the 227 patients with mild, low-risk head injuries, 119 patients (52%) were not treated according to the SNC 2013 guidelines, leaving 108 patients with full guideline adherence.

A total of 189 patients (83%) were eligible for S100B sampling. Among these, 121 patients (64%) had a S100B drawn, 41 patients (22%) were discharged from the ED without further investigation, 12 patients (6%) were admitted for neurological observation and 15 patients (8%) were referred directly for head CT.

Due to potential S100B-releasing fractures, 38 patients (17%) were not eligible for S100B analysis. A total of 31 of

these patients (82%) were either overtriaged or undertriaged: 23 patients had a serum S100B sample drawn nonetheless and eight patients were discharged without further investigation. Two patients were admitted for observation without serum S100B or head CT and five patients were referred directly for head CT; all seven patients were managed in accordance with the guidelines. A triage overview is presented in **Supplementary Tables 2 and 3**.

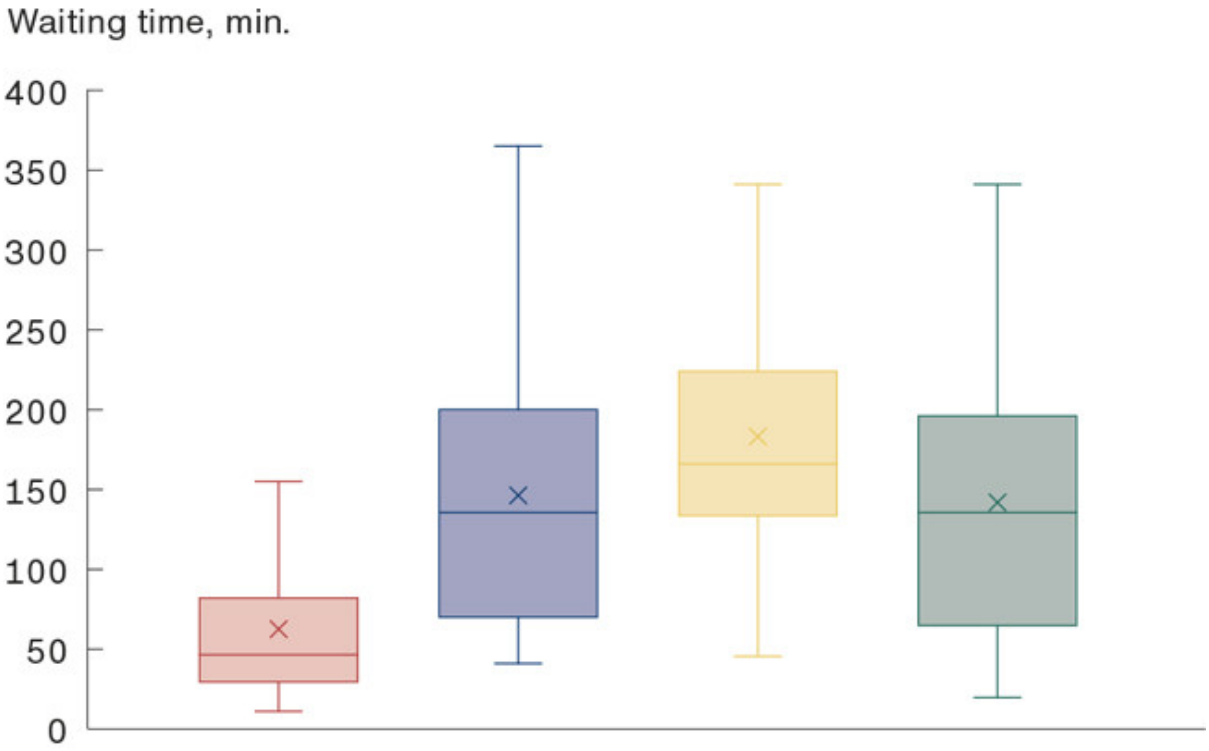
Cost analysis

Among the 121 serum S100B samples drawn on correct indication, 81 (67%) were abnormal, thus leading to a head CT according to the guideline recommendation. Based on these findings, in a theoretical scenario, with the use of serum S100B and initial triage of 121 patients with mild, low-risk head injuries, the cost would be €21,690 (121 patients × €60 per S100B + 0.67 × 121 patients × €178 per head CT). Without the use of serum S100B and a direct referral to head CT, the cost of the 121 patients would be €21,538 (121 patients × €178 per head CT). Accordingly, inclusion of S100B in MHI guidelines increased costs by €1.26 per patient.

Patient flow

Patient flow is measured as mean waiting time until their final examination. For patients examined with S100B only, the mean waiting time was 63 minutes. Patients examined with head CT only waited for an average of 146 minutes, whereas patients with S100B followed by head CT waited 183 minutes on average. The mean waiting time for a fused group of patients with S100B only and patients with S100B followed by a head CT was 141 minutes (**Figure 2**).

FIGURE 2 Box plot showing patients' waiting time for examination with the serum biomarker S-S100B alone (), head CT alone (), S-S100B followed by head CT () and accumulation of patients with S-S100B alone and S-S100B followed by a head CT ().



S100B = a serum biomarker.

Waiting time differed between patients examined with S100B only and those with head CT only ($p < 0.001$), and between patients examined with S100B only and those examined with S100B followed by head CT ($p < 0.001$). Waiting time for patients examined with head CT only and patients examined with S100B followed by head CT also differed ($p < 0.05$). No significant difference was observed between waiting time for those examined with head CT only and for the sum of patients examined with S100B only and patients examined with S100B followed by head CT (**Table 2**).

TABLE 2 Comparison of waiting time for different examinations after mild, low-risk head injury.

Comparison of examinations S100B only vs head CT only	Waiting time until final examination, mean, min. ± SD	p-value
S100B only vs head CT only	74 ± 56 versus 146 ± 91	< 0.001
S100B only vs S100B followed by head CT	74 ± 56 versus 183 ± 66	< 0.001
Head CT only vs S100B followed by head CT	146 ± 91 versus 183 ± 66	0.03
Head CT only vs sum of patients with S100B only + patients with S100B followed by head CT	146 ± 91 versus 141 ± 82	0.77

S100B: a serum biomarker; SD = standard deviation.

DISCUSSION

The management of MHI patients is challenging, but biomarkers may help [12]. So far, serum S100B has been the best brain biomarker [9, 13, 14] for ruling out patients without a risk of serious intracranial complications after MHI. We investigated the impact of serum S100B on patient flow and patient costs and found that the use of S100B in the SNC 2013 Head Injury Guidelines neither reduced nor caused substantial additional patient costs or delayed patient flow.

Guideline adherence

Achieving full guideline adherence after implementation of MHI guidelines has been proven difficult [15]. This is confirmed by our results, as only about half of the MHI patients were treated according to the SNC 2013 Head Injury Guidelines. Taking into account that the SNC 2013 Head Injury Guidelines were published almost concurrently with the inclusion start date of the present study [1], and as compliance with guidelines has been shown to improve over time, an improved guideline adherence would be expected with a later study start date [16]. In general, high educational effort is needed and may be achieved by encouraging education and training when guidelines are implemented [15]. A multidisciplinary approach in which both nursing staff and medical doctors take a proactive role in guideline research has been proven effective when translating guidelines into clinical practice [17].

Effect of S100B on patient costs

As the cost of S100B analysis varies between centres, it is relevant to consider the price of a serum S100B sample versus that of a head CT [8, 18]. In our study, S100B was increased in 67% of patients with mild, low-risk head injury. The patient cost of following the guidelines with S100B testing would be equal to the patient cost of following the guidelines without S100B testing if the price of an S100B sample was 33% of the price of a head CT. If the price of a S100B sample was lower than 33% of the cost of a head CT, it would lower costs to add S100B to the head injury guidelines.

In a previous study by Calcagnile et al., which adopted a socioeconomic focus on the SNC 2013 Head Injury Quidelines, the authors found a reduced patient management cost of €39 per patient [8] using S100B. We were unable to present the same optimistic results in our study cohort as implementation of S100B increased patient costs by €1.26 per patient. Head injury patients are numerus in the ED. Thus, this extra cost should be considered insignificant, especially owing to CT reduction and avoidance of radiation, as shown in other studies [4, 19]. Although the present study solely assessed the influence of S100B implementation on patient costs at a theoretical level, we emphasise that comparable studies have reported a similar level of normal S100B samples

among patients with MHI, thus supporting the methodology applied in the present study [8, 18].

The cost analysis was based on the 121 patients with S100B drawn on correct indication and not on the 109 patients following the guidelines, as it was performed in a theoretical setting and calculated based on the percentage of abnormal S100B analysis only.

Effect of using serum S100B on patient flow

One bottleneck in patient flow is the waiting time for a head CT. As implementation of S100B has been shown to reduce the number head CTs in an ED [6], the addition of S100B to the MHI guidelines may potentially improve patient flow. We found no improved patient flow with the use of S100B. A serum S100B test only had a significantly shorter waiting time than head CT only and S100B followed by head CT. These findings support the general perception that waiting time for head CT in an ED contributes to the longest total waiting times. Waiting time for the sum of patients with S100B only and for patients with S100B followed by a head CT was similar to the waiting time for head CT only (Figure 2). This may be explained by S100B both prolonging the flow of patients with head CT following a positive S100B and shortening the flow of patients when head CT can be omitted due to a negative S100B. Thus, implementing the SNC 2013 Head Injury Guidelines did not slow down the patient flow.

Limitations

This study was of a retrospective character and the cohort was collected from February 2013 and one year forward. The SNC 2013 Head Injury Guidelines were published in February 2013 and were implemented by the beginning of the inclusion period. Thus, we expect that complete guideline implementation may be lacking, causing pessimistic results regarding guideline adherence and patient flow. An important follow-up study would be a comparison of guideline adherence and patient flow directly after implementation and in the following years.

Another study limitation is that the uptake area for MHI patients at the Trauma Centre at Rigshospitalet is relatively small, limiting the patient load and inclusion size. Finally, serum S100B may be analysed by few commercially available methods, though the most commonly used method in the Scandinavian countries is the one provided by Roche, as other biomarkers can be analysed on the same machine. This study did not consider the one-time cost of purchase of laboratory equipment. Furthermore, educating personnel in the use of a novel method requires time. These costs should be considered when implementing serum S100B.

An interesting aspect of the use of S100B isthe possible reduction of head CT in patients with MHI. Discussing this aspect is not within the scope of the present study and cannot be answered by the methodology applied.

CONCLUSION

Implementation of serum S100B under the SNC 2013 Head Injury Guideline neither reduces patient cost nor causes substantial additional patient costs. Patient flow is not delayed when following the SNC 2013 Head Injury Guidelines.

Correspondence *Ramona Åstrand*. E-mail: ramona.alice.aastrand.01@regionh.dk

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