# 2024 Vol. 7.3 Original-, udviklings-, og kvalitets artikler

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#### Keywords:

Head trauma; Mild brain injury; S100B; SNC; Guideline adherence; CT scan

Usage of biomarker S100B to avoid CT after low-risk, mild head trauma: a single center clinical review of the Scandinavian head trauma guideline and guideline adherence

Abstract

# **Background**

In 2013, the Scandinavian Neurotrauma Committee (SNC) published a new guideline for managing minimal, mild, and moderate head trauma. The SNC guideline included using biomarker S100B to identify patients needing a head computed tomography (CT).

Purpose: To explore the use of S100B and guideline adherence in relation to the SNC guideline

#### Methods

In this retrospective cohort study, data was collected for all consecutive S100B blood samples drawn in a Danish Emergency Department between March 1, 2022 and March 1, 2023. Patient data was extracted from "EPJ Syd". Patient records were screened to determine the head trauma category based on patient history, physical examination, and symptoms.

#### Results

A total of 236 patient cases were included and categorized according to SNC head trauma categories. Guideline adherence was achieved for 152 patient cases (64.4%). Non-adherence (35.6%) was mainly seen in the minimal and low-risk, mild head trauma categories. The reasons for non-adherence were excessive S100B blood sampling, late blood sampling, and missing and excessive head CTs.

# Conclusion

Guideline adherence was generally challenged, and non-adherence was a substantial part of the results. Further studies are needed to explore reasons for non-adherence and possible solutions for improving guideline adherence.

**Abbreviations:** Emergency Department (ED), Computed Tomography (CT), Scandinavian Neurotrauma Committee (SNC), Negative Predictive Value (NPV), Interquartile Ranges (IQR), Glasgow Coma Scale (GSC)

# Introduction

The majority (85%) of all head injuries are classified as mild head traumas, and annually, an estimated 20,000 patients are diagnosed with a mild head injury in Danish Emergency Departments (EDs) (1).

Computed tomography (CT) is often used to diagnose intracranial injuries in patients with head trauma, which has caused an increase in the use of head CTs (2). In Denmark, there has been a general increase in CT scans, including head CTs, over the past decades, with the overall number increasing from 230,000 to 990,000 from 2003 to 2017 (3).

In 2013, the Scandinavian Neurotrauma Committee (SNC) published a new guideline (SNC guideline) for managing head trauma, including the biomarker S100B (4). The SNC guideline's purpose was to diagnose patients needing neurosurgical or medical intervention and identify possible brain lesions. As a secondary purpose, the biomarker S100B was introduced (4). The biomarker is elevated in patients with intracranial injuries and, therefore, used to rule out the need for a head CT. S100B is a brain injury biomarker with a high sensitivity of 97% and a high negative predictive value (NPV) of 99% (5).

The SNC guideline identifies head trauma categories based on the severity of trauma. The categories are minimal, mild, and moderate, with the mild category subdivided into three subcategories based on risk factors (Fig. 1). According to the SNC guideline, S100B only applies to the low-risk, mild head trauma category (4). Recently, the use of S100B in a more diverse population of patients has been discussed (6).

Studies exploring guideline adherence revealed a lower adherence to the minimal and mild head trauma categories compared to the other head trauma categories, often resulting in unnecessary CT scans and longer admission times (7, 8).

To our knowledge, no studies have investigated guideline adherence based solely on consecutive S100B blood sample data. Therefore, this study aimed to explore the use of S100B and guideline adherence in relation to the SNC guideline. Our objective was to estimate the clinical use of S100B blood samples regarding the treatment of the correlating head trauma in a Danish ED.

Materials and methods

# Study design and setting

This retrospective, single-center cohort study included head trauma patients admitted to a Danish ED at a University Hospital. The ED had an intake of roughly 66,000 patients in 2022 (10).

This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline (11).

#### Patient selection and data collection

All included patients were 18 years old or above with head trauma and a correlating S100B blood sample. Head trauma was defined as any kind of blunt head trauma. All patients meeting these criteria were included consecutively between March 1, 2022, and March 1, 2023. All data collection was conducted in April 2023.

A list of serum S100B samples was obtained through the Department of Clinical Biochemistry. This only included patients with S100B blood samples from the ED and all other departments. This included a majority of blood samples for monitoring severe cerebral injury from the Neurological Intensive Care Unit. All blood samples drawn from departments other than the ED and for purposes other than head trauma were excluded from this study. The concentration ( $\mu$ g/L), date, and time of the S100B blood samples were extracted for all remaining patients. Patient data, including age, gender, use of blood thinners, Glasgow Coma Scale (GCS), cause of injury, time of trauma and blood sampling, and whether a head CT was performed, were extracted from the Danish patient record system called "EPJ Syd." Patients with incomplete records or patients who left against medical advice were excluded (Fig. 2). Incomplete records were defined as records in which any of the patient data listed above were missing.

A codebook was constructed between the two primary investigators with instructions for data collection to ensure high-quality data and a systematic approach to screening patient records. In case of ambiguity regarding patient records, the two primary investigators conferred these cases and came to an agreement. Data was stored in a secure SharePoint platform that was only accessible to the authors of this article.

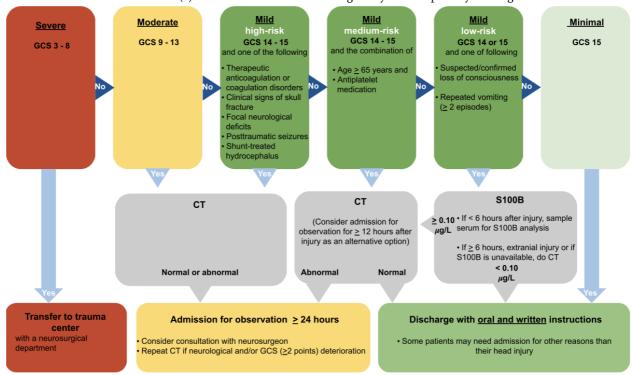
#### Variables of interest

The primary outcome variable was guideline adherence (yes/no) based on head trauma category, S100B blood sampling, and head CT evaluation.

# Head trauma categories

Patient records were screened for the different head trauma categories according to the modified SNC flowchart used in the ED (Fig. 1).

**Figure 1**. The SNC guideline as used in the Danish ED. This version has been modified from the original SNC flowchart to include instructions for severe head trauma (9). Translated from Danish to English by the two primary investigators.



Accepteret til publikation: 21.11.2024

Jensen et al.: Usage of biomarker S100B to avoid CT after low-risk, mild head trauma: a single center clinical review of the Scandinavian head trauma guideline and guideline adherence Dansk Tidsskrift for Akutmedicin, 2024, Vol. 7, s. 15-24 PUBLICERET AF DET KGL. BIBLIOTEK FOR DANSK TIDSSKRIFT FOR AKUTMEDICIN

Patient history, physical examination, and symptoms were combined in the assessment of the head trauma category. Causes of head trauma were categorized as incidental falls, traffic accidents, violent assaults, and others. If patients were treated for a new head trauma with  $\geq 72$  hours between each incident, they were defined as two individual patients. The included patients are referred to as patient cases.

# S100B blood sampling and assay

According to the SNC guideline, blood sampling should occur within six hours from the time of head trauma. Therefore, the head trauma and blood sampling times were noted and then subtracted to calculate the time in between. If the blood sample was drawn  $\geq 6$  hours after the trauma, it was registered as late blood sampling. The time of head trauma was defined as the time noted by the ED staff or the paramedics in the patient records.

Serum S100B analysis was performed on Cobas e801 instruments (Roche Diagnostics®, Mannheim, Germany) using Roche reagents.

# Hvad ved vi?

 SNCs guideline fra 2013 bliver brugt i danske akutmodtagelser til kategorisering af patienter med hovedtraumer, hvor biomarkøren S100B bruges til at identificere patienter med mildt hovedtraume som har behov for yderligere tiltag

# Hvad tilføjer denne artikel til vores viden?

 Der ses generelle udfordringer med korrekt brug af SNCs guideline, hvilket bl.a. fører til unødvendige S100B blodprøver og CT-C'er

#### Head CT indication

S100B serum concentration dictated whether a head CT was indicated. If the concentration was below the threshold of  $0.10\,\mu g/L$ , the patient should be discharged without a head CT. If the concentration was above the threshold, it should result in a head CT. If this was not the case, the patient records were checked for information regarding admission for a 12-hour observational regimen. The SNC guideline suggests observation as an alternative to head CTs (4), and therefore, a 12-hour observational regimen is categorized as guideline adherent. If the patient had a head CT without indication for S100B blood sampling, it was reported as an excessive CT. If the patient was discharged without an indicated head CT, it was reported as a missing CT, provided the patient was not admitted for observation as an alternative.

# Statistical analysis

For continuous variables, the normal distribution was tested with histograms and qq-plots. The variables were presented as median with interquartile ranges (IQR) in cases of not normally distributed variables. Descriptive statistics for categorical variables comprised of frequencies and respective percentages. All data was analyzed using STATA/BE 17.0 (StataCorp, College Station, Texas).

#### **Ethical considerations**

The present study was approved by the National Data Protection Agency (23/16197). Due to its retrospective nature, the need for informed consent from the study population was waived.

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All S100B blood samples drawn between March 1st of 2022 and March 1st of 2023. Patients had to be > 18 years n = 964 Excluded, n = 646 Intensive care unit, n = 626 Other departments, n = 20 All S100B blood samples drawn in the Emergency Department n = 318 Excluded, n = 82 Incomplete journals, n = 59
Patients who left against medical advice, n = 19
No head trauma, n = 4 Types of head trauma n = 236Minimal head trauma Moderate head trauma Mild head trauma Mild head trauma, high-risk Mild head trauma n = 173medium-risk

Figure 2: Flowchart of inclusion and exclusion process.

#### Results

#### Patient characteristics

This study included 236 patient cases, of which 55.1% were men. The majority (n = 173/236, 73.3%) was in the low-risk, mild head trauma category. No patients had GCS 3-8; therefore, no patients were included in the "severe" head trauma category.

A total of 102 head CTs were performed for all head trauma categories, and 11 (n = 11/102, 10.8%) had positive findings, including intracerebral hemorrhages, contusions, and skull fractures. No patients needed neurosurgical intervention or had a fatal outcome. Other baseline and clinical characteristics are summarized in Table 1.

#### Guideline adherence

Guideline adherence was achieved for 152 (n = 152/236, 64.4%) out of 236 patient cases across all head trauma cat-

egories. Adherence to the SNC guideline was only possible for the low-risk, mild head trauma category, as S100B blood sampling was only indicated for these patients according to the SNC guideline. The adherent group was defined as patients with S100B drawn < 6 hours after head trauma and treated according to the SNC guideline with regard to the S100B concentration (n = 147/236, 62.3%). A few patients (n = 5/236, 2.1%) with S100B above the threshold were admitted for observation instead of a head CT. These patients were also in the adherent group. Non-adherence accounted for an overall of 84 (n = 84/236, 35.6%) patient cases, referring to 21 (n = 21/173, 12.1%) in the low-risk, mild head trauma category. The non-adherence group consisted of the following four subgroups (Fig. 3).

**Table 1.** Baseline and clinical characteristics of patient cases.

	Minimal head trauma (n = 50)	Mild head trauma, low risk, (n=173)	Mild head trauma, medium risk, (n=3)	Mild head trauma, high risk, (n=9)	Moderate head trauma, (n=1)	All head trauma categories, (n=236)
Age (y), n (%)						
- <b>18-39</b>	28 (56.0)	75 (43.4)	-	3 (33.3)	1 (100.0)	107 (45.3)
- <b>40-64</b>	13 (26.0)	66 (38.2)	-	2 (22.2)	-	81 (34.3)
- ≥65	9 (18.0)	32 (18.5)	3 (100.0)	4 (44.4)	-	48 (20.3)
Age (y), median (IQR)	33.6 (26.0-61.0)	44.6 (25.1-61.2)	77.2 (73.0-83.8)	47.3 (26.3-82.5)	27.2 (27.2-27.2)	43.1 (25.5-61.8)
Gender, n (%)						
- Male	24 (48.0)	99 (57.2)	2 (66.7)	5 (55.6)	-	130 (55.1)
- Female	26 (52.0)	74 (42.8)	1 (33.3)	4 (44.4)	1 (100.0)	106 (44.9)
GCS, n (%)						
- 15	50 (100.0)	148 (85.6)	3 (100.0)	8 (88.9)	-	209 (88.6)
- 14	-	25 (14.4)	-	1 (11.1)	-	26 (11.0)
- 13	-	-	-	-	1 (100.0)	1 (0.4)
Cause of injury, n (%)						
<ul> <li>Incidental fall</li> </ul>	25 (50.0)	104 (60.1)	3 (100.0)	7 (77.8)	1 (100.0)	140 (59.3)
<ul> <li>Traffic accident</li> </ul>	15 (30.0)	46 (26.6)	-	-	-	61 (25.6)
<ul> <li>Violent assault</li> </ul>	6 (12.0)	5 (2.9)	-	1 (11.1)	-	12 (5.1)
- Other	4 (8.0)	18 (10.4)	-	1 (11.1)	-	23 (9.8)
Blood thinners, n (%)						
- None	50 (100.0)	163 (94.2)	-	6 (66.7)	1 (100.0)	220 (93.2)
- Anticoagulants	-	-	-	3 (33.3)	-	3 (1.3)
- Antiplatelets	-	10 (5.8)	3 (100.0)	-	-	13 (5.5)
Head CT, n (%)						
- Yes	14 (28)	78 (45.1)	3 (100.0)	6 (66.7)	1 (100.0)	102 (43.2)
- No	36 (72)	95 (54.9)	-	3 (33.3)	-	134 (56.8)

The value zero is visualized by -.

n= number

y= years

IQR= interquartile range

- 1) All patient cases in other head trauma categories than the low-risk, mild head trauma category as S100B were not indicated for these patients (n = 63/84, 75%)
- 2) Late blood sampling consisting of patient cases with S100B drawn  $\geq$  6 hours after the time of head trauma (n = 12/84, 14.3%)
- 3) Patient cases where S100B was below the threshold and a head CT was still carried out leading to excessive CTs (n = 3/84, 3.6%)
- 4) Patient cases where S100B was above the threshold and the patient was discharged without a head CT and without being admitted for observation (n = 6/84, 7.1%), resulting in missing CTs.

S100B blood sampling, when not indicated, was the biggest cause of non-adherence in this study and, therefore,

most prevalent in the minimal head trauma category. Twenty S100B blood samples were above the threshold in the minimal head trauma category, but only 14 led to a head CT.

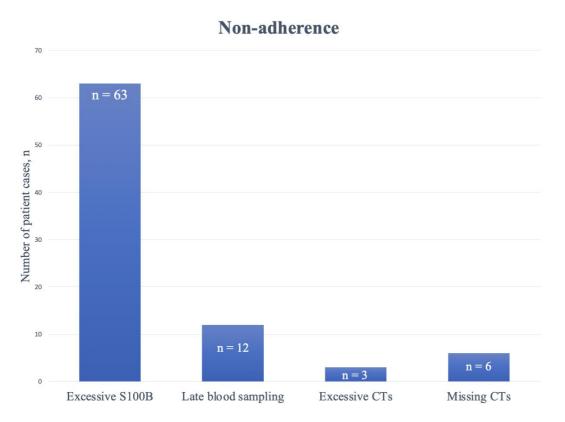
Non-adherence due to missing head CTs and excessive CTs was calculated for the low-risk, mild head trauma category, as S100B was only indicated for this group.

Discussion

# Summary of findings

This study explored the usage of S100B and adherence to the SNC guideline. A total of 236 patient cases were included in the study, mainly consisting of patients with minimal and low-risk, mild head trauma. Adherence was seen in the majority of the patient cases. Non-adherence was mainly due to excessive S100B testing seen in all other head trauma categories than the low-risk, mild head trauma category. Excessive head CTs, missing CTs,

**Figure 3.** Bar chart of S100B non-adherence



and late S100B blood sampling were also causes of non-adherence.

# Guideline adherence

Several studies have investigated adherence to the SNC guideline (7,12). Faisal et al. found low adherence to the SNC guideline, especially concerning the minimal and low-risk, mild head trauma categories (7), as reported in this study as well. Guideline non-adherence was 12.1% for the low-risk, mild head trauma category. One could argue that a non-adherence at 12.1% is within an acceptable range. However, overall non-adherence at 35.6% still demonstrates that guideline adherence is challenged. Furthermore, Faisal et al. also found low adherence led to longer admission and excessive use of head CTs. The latter was also true

for our study but to a limited extent, as excessive head CTs were a minor part of the non-adherence findings.

The excessive S100B testing could be due to physicians seeing blood sampling as an easy and inexpensive way to further help the diagnostic process regardless of the head trauma category. As there are very few adverse effects from blood sampling contrary to a head CT, it could be considered a safe and precautionary choice. However, our study found that six out of 20 patients with unnecessary S100B blood samples above the threshold did not receive a corresponding head CT. This is also seen in the study by Ananthaharan et al. and calls into question the usefulness of S100B blood sampling as a precaution when the result of

S100B is not interpreted correctly by the physician accord-

ing to the SNC guideline (13). The excessive testing could

also, in part, be explained by requisition bias as patients

with minimal head trauma are often triaged at a low level

and, therefore, often seen by nurses before being seen by a

physician. The current practice in the Danish ED is based

on nurses performing a quick examination of the patient,

measuring vital signs, and ordering blood tests. If the nurses

are not familiar with the SNC guideline, it could lead to ex-

cessive S100B blood testing.

A study by Heskestad et al. explored guideline adherence to

an older version of the SNC guideline published in 2000

(8). They came to the same conclusions: lower adherence in

the minimal and mild head trauma categories led to exces-

sive head CTs and longer admissions. The prior version of

the SNC guideline did not subdivide mild head trauma into

categories based on risk factors, but their findings still indi-

cate a problem with guideline adherence in patients with

non-severe head trauma (14).

Barriers and ways to improve guideline adher-

ence

A qualitative study by Vestlund et al. identified several

themes regarding ways to improve adherence to the SNC

guideline (12). According to their study, the leading cause

for non-adherence was poor accessibility to the SNC guide-

line, including a lack of physical printouts in the work en-

vironment and poor design of the hospital's intranet. Other

factors contributing to non-adherence were high patient

flow and stressful work situations, both common in the

ED. Finding the proper guideline can be time-consuming,

leading to less experienced doctors seeking advice from

senior colleagues instead of using guidelines (12). The SNC

guideline is highly available at the Danish ED in question.

There are numerous large printouts of the modified SNC

flowchart in the ED, and the printouts are also available at

the Department of Radiology, as this department collabo-

rates with the ED on the request for head CTs. Additionally,

new employees are introduced to guidelines in advance by

email before their first day in the ED. They also receive spe-

cific instructions on using guidelines from more experi-

enced colleagues. It is reasonable to assume that all physi-

cians working in the ED are familiar with the SNC guide-

line. Therefore, the possible reasons for non-adherence dis-

cussed by Vestlund et al. are presumably absent in the ED.

According to Heskestad et al., knowledge and correctly us-

ing existing guidelines are essential for guideline adherence

(8). However, the study found that despite an extensive im-

plementation process consisting of annual mandatory

courses and repeated lectures on the use of the SNC guide-

line by neurosurgeons, guideline adherence was still low at

51% for minimal and mild head trauma (8).

Hvad tilføjer denne artikel til vores viden?

• En større indsats for korrekt brug af SNCs guideline kan reducere antallet af unødvendige undersøgelser.

Accepteret til publikation: 21.11.2024

Another reason for non-adherence could be clinical judg-

ment overruling guidelines. The article presenting the SNC

guideline 2013 specified that experienced doctors should be

able to defer from guidelines and trust their clinical judg-

ment (4). Every patient is different, and guidelines might

not apply to all patients. This was also stated as a reason for

non-adherence in a study by Volovici et al., which focused

on guideline adherence for severe head trauma (15).

Further studies are needed to determine and identify barri-

ers and ways to improve guideline adherence. Prospective

studies with registration of reasons for non-adherence in

each patient case could shed light on possible problems

physicians encounter in the ED when assessing patients,

though with a risk of bias. Qualitative studies could,

through interviews and field research, aid in the clarifica-

tion of work processes and collaboration between groups of

health professionals regarding guideline adherence.

Strengths and limitations

A strength of this study was the inclusion of consecutive

S100B blood samples from an entire year with no missing

data. Since the primary investigators collected all the data,

an agreed-upon systematic approach was established, and

therefore, a high internal validity was achieved, thus mak-

ing it high-quality data. However, the present study had

limitations. By being a retrospective study, all data was

based on existing patient records; therefore, all variables

depended on the available information in the records. An-

other limitation is the small sample size and being a single-

center study. Therefore, the results might not reflect other

hospitals.

Due to the nature of the data, there was the potential for

selection bias. Registering patients with head trauma with-

out an S100B blood sample was not possible, which per-

haps created groups of unreported patients and potentially

affected our results for adherence and non-adherence. Ex-

amples of unreported patient cases were cases solely based

on head CTs or patient cases with neither head CTs nor a

blood sample. An unreported group of mild, low-risk head

trauma patients with head CTs without S100B blood sam-

ples could have skewed our results concerning non-adher-

ence by obscuring the actual number of excessive head CTs.

This group could have consisted of patients with minimal

head trauma treated according to the SNC guideline. These

patients would have been discharged without S100B blood

sampling, and the SNC guideline would have been followed

correctly.

Conclusion

The SNC guideline and biomarker S100B is used in the di-

agnostic process regarding head trauma, and S100B is in-

tended for patients with low-risk, mild head trauma. Over-

all, guideline adherence, based on S100B blood sampling,

was challenged, especially for the minimal head trauma cat-

egory. Guideline non-adherence in the low-risk, mild head

trauma category was within an acceptable range. Non-ad-

herence was primarily due to excessive S100B blood sam-

pling and, to a lesser extent, due to missing head CTs, ex-

cessive head CTs, and late blood sampling. We conclude

Accepteret til publikation: 21.11.2024

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that new research is needed to explore ways to improve guideline adherence and reasons for non-adherence to the SNC guideline.

# Conflicts of interest

Louise Cecilie Jensen: None declared.

Neusha Gharai-Moghadam: None declared.

Jesper Revsholm: None declared.

Stefan Posth: None declared.

Willy Altinok Krone: None declared.

Ole Graumann: Speaker honoraria, Advisory Board

member, and research grant: Boston Scientific.

Theresa Junker: Research grant: Boston Scientific

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