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Published in:
Acta neurologica Scandinavica

DOI:
[10.1111/ane.13518](https://doi.org/10.1111/ane.13518)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Blaauw, J., Meelis, G. A., Jacobs, B., van der Gaag, N. A., Jellema, K., Kho, K. H., Groen, R. J. M., van der Naalt, J., Lingsma, H. F., & den Hertog, H. M. (2022). Presenting symptoms and functional outcome of chronic subdural hematoma patients. *Acta neurologica Scandinavica*, 145(1), 38-46. <https://doi.org/10.1111/ane.13518>

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Presenting symptoms and functional outcome of chronic subdural hematoma patients

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Funding Information

The Netherlands Organisation for Health Research and Development (ZonMw project number 843002824) provided financial support in the form of funding. The sponsor had no role in the design or conduct of this research.

Abstract

Background: Patients with chronic subdural hematoma (CSDH) can present with a variety of signs and symptoms. The relationship of these signs and symptoms with functional outcome is unknown. Knowledge of these associations might aid clinicians in the choice to initiate treatment and may allow them to better inform patients on expected outcomes.

Objective: To investigate if presenting signs and symptoms influence functional outcome in patients with CSDH.

Methods: We conducted a retrospective analysis of consecutive CSDH patients in three hospitals. Glasgow Outcome Scale Extended (GOS-E) scores were obtained from the first follow-up visit after treatment. An ordinal multivariable regression analysis was performed, to assess the relationship between the different signs and symptoms on the one hand and functional outcome on the other adjusted for potential confounders.

Results: We included 1,307 patients, of whom 958 (73%) were male and mean age was 74 (SD ± 11) years. Cognitive complaints were associated with lower GOS-E scores at follow-up (aOR 0.7, 95% CI: 0.5 – 0.8) Headache and higher Glasgow Coma Scale (GCS) scores were associated with higher GOS-E scores. (aOR 1.9, 95% CI: 1.5–2.3 and aOR 1.3, 95% CI: 1.2–1.4).

Conclusion: Cognitive complaints are independently associated with worse functional outcome, whereas headache and higher GCS scores are associated with better outcome. The increased probability of unfavorable outcome in patients with CSDH who present with cognitive complaints favors a more prominent place of assessing cognitive status at diagnosis.

KEYWORDS

chronic subdural hematoma, cognition, functional outcome, presenting symptoms

1 | INTRODUCTION

Chronic subdural hematoma (CSDH) is one of the most common neurological and neurosurgical diseases.¹ CSDH is often regarded as a benign disease; however, it is associated with high recurrence and mortality rates.²⁻⁴ The mainstay of treatment for CSDH is surgical drainage, predominantly by burr hole craniostomy (BHC).¹ Medicinal treatment modalities, such as dexamethasone and atorvastatin, are also being studied as treatment options and the results of a large randomized controlled trial studying the role of dexamethasone have recently been published.^{5,6} CSDH is often preceded by (minor) head trauma and symptom onset may take several days or even weeks. As a consequence, patients sometimes do not even recall the head trauma.^{1,7} Presenting signs and symptoms of CSDH can vary in severity, and headache, gait disturbance, hemiparesis, and cognitive problems are the most common ones.^{1,8}

The relationship between presenting symptoms and functional outcome has been clearly established in acute traumatic brain injury and stroke, but such data are scarce for CSDH patients.⁹⁻¹² Studies that have assessed the association between signs on admission and outcome in CSDH focused on seizures and decreased consciousness as presenting signs.^{4,13-16} These studies revealed that patients with CSDH and seizures or low Glasgow coma Scale (GCS) scores have a worse outcome. Although seizures and lower GCS are prominent signs of CSDH, they reflect the more extreme clinical manifestations of CSDH and are not the most common symptoms at presentation.¹ Increased knowledge on the relationship between the whole spectrum of presenting signs and symptoms and outcome could be of additional value and might aid clinicians in the process of deciding on initiating treatment or type of treatment. Furthermore, it may help clinicians when informing individual patients on prognosis. Hence, it might improve outcome of CSDH patients in general.

In this study, we aimed to assess the prevalence of the whole range of presenting signs and symptoms of CSDH, together with their association with functional outcome.

2 | METHODS

2.1 | Study population

All CSDH patients who presented at the outpatient clinics or emergency departments of three neurosurgical facilities in the Netherlands were included. Inclusion periods varied between the participating centers, due to data availability as a result from transferring to electronic patient dossier in center 1 inclusion was from January 2004 to January 2019, center 2 included between January 2006 and May 2019, and center 3 between January 2011 and May 2019. The three neurosurgical centers, one academic and two large teaching hospitals, serve as referral hospitals for all patients requiring neurosurgical treatment in their region.

The three centers provide the neurosurgical care for about 2,5–3 million inhabitants.

Inclusion criteria were age 18 years or older, and a CSDH defined as a minimum of two third of the hematoma being hypodense on CT. Patients with a history of arteriovenous malformation or intracerebral tumors were excluded, as the required surgical intervention in these cases could lead to the development of a CSDH. The local medical ethical committees of all three hospitals approved this study.

2.2 | Measures and definitions

Patient demographics included age and sex, comorbidity expressed by the Charlson Comorbidity Index (CCI) an ordinal scale measuring comorbidity based on medical history and age,¹⁷ clinical severity assessed with Markwalder Grading Scale (MGS) a scale ranging from 0 to 4, with higher numbers indicating more severe signs and symptoms¹⁸ and the GCS score. Treatment modality, side of hematoma, and millimeters midline shift were also retrieved.

Signs and symptoms at presentation were collected from the patients' medical files and divided into seven subgroups: Focal neurological deficit, headache, gait disorder, consciousness, seizures, cognitive complaints, and other (for definitions see Table 1). In this study, we use the term signs for objective evidence of CSDH and symptoms when referring to subjective (or patient reported) abnormalities.

2.3 | Treatment modalities

The used treatment modalities in the three neurosurgical centers were overall similar. Surgery was performed through burr hole craniostomy, twist drill craniostomy, or craniotomy on the discretion of the treating physician. Postoperative drainage was routinely performed with a subdural drain, unless this was technically impossible. Choosing the duration and dosage of dexamethasone therapy and when to initiate treatment, operating under general or local anesthesia, and postoperative admission to intensive care was performed following the local protocol of the hospital.

2.4 | Outcome measures

The primary outcome was the Glasgow Outcome Scale Extended (GOS-E)^{19,20} score at the *first* follow-up visit after initiating treatment. If a "wait and see" policy was chosen, treatment date was considered as the date the patient was seen by the neurologist or neurosurgeon who decided on the policy. GOS-E was deduced from notes of the outpatient follow-up. In case of more than one follow-up visit, the date closest to three months after start of treatment was used. Secondary outcomes were recurrence rates and mortality at 3 months.

TABLE 1 Classification of presenting signs and symptoms of CSDH into seven groups

Group	Focal neurological deficit	Headache	Gait disorder	Consciousness	Seizure	Cognitive complaints	Other
Symptoms	Loss of motor function, hemiparesis, sensory deficit, language and speech disorders, transient neurological deficit	Headache	Frequent falling, unstable walking, balance problems	As defined by Glasgow Coma Scale (GCS) score, and analyzed as a continuous variable	Focal or generalized seizures (only if present before initiating treatment)	Memory deficits, confusion, bradyphrenia altered behavior, apraxia	Vomiting, nausea, vertigo, malaise, collapse

Note: If diagnosed as such by the treating physician and only if they occurred at presentation.

2.5 | Data collection

In all three centers, patient and study data were collected from the electronic patients' files by a local investigator. A comprehensive list of how to collect and interpret data together with a hand-out of a structured interview for GOS-E was provided to these investigators to promote uniformity in data gathering. Also, the corresponding author checked samples of the collected data for validity. The local investigators were blinded for the research question of this study at the time of data collection, to prevent any influencing of outcomes.

2.6 | Statistical analysis

The relationship between the different signs and symptoms and functional outcome was expressed as an odds ratios (OR) with a corresponding 95% confidence interval (CI). Adjustments were made for age, sex, CCI, millimeters midline shift, laterality of hematoma (left, right, bilateral), postoperative complications, 3-month recurrence, time to follow-up, and treatment modality (surgical, dexamethasone, surgery and dexamethasone or expectative/wait and see) by means of multivariable ordinal logistic regression.

Additionally, outcomes were adjusted for MGS score on admission. When adjusting for MGS, scores 3 and 4 were grouped together due to limited numbers in the individual groups. Missing values for the different presenting signs and symptoms, confounders, and GOS-E score at follow-up were imputed using single imputation in SPSS to prevent bias. All statistical analyses were performed with IBM SPSS 23. Figures were created with R studio using the ggplot2 package.

3 | RESULTS

3.1 | Demographics and clinical data

We included 1,307 patients with CSDH (Table 2). Of these patients, 958 (73%) were male and mean age was 74 (SD \pm 11) years. The most frequent MGS scores were 1 (37%) and 2 (55%). The most common CCI scores were 3 (N = 268, 21%) 4 (N = 317, 24%) and 6 or more (N = 261, 20%).

Diagnosis of CSDH was established with CT or MRI in all patients, 511 (39%) of the hematomas were left sided, 444 (34%) right sided, and 352 (27%) of patients had bilateral CSDH. Mean midline shift was 6.9 millimeters (SD \pm 5.3). Surgical treatment was performed in 830 patients (64%), surgery with adjuvant dexamethasone in 191 (15%). Eighty patients (6%) were treated with exclusively dexamethasone and a wait and see policy was applied in 197 (15%). The vast majority of the surgical patients (N = 996, 97%) were treated with BHC.

3.2 | Signs and symptoms

In the 1,307 patients, a total of 2006 signs and symptoms were recorded (Table 2). Focal neurological deficit (46%), headache (41%),

gait disorders (31%), and cognitive complaints (31%) were the most prevalent (Table 2). Seizures occurred in 30 (2%) of patients and mean GCS was 14.2 (SD \pm 1.5). The signs and symptoms vomiting,

nausea, vertigo, malaise, and syncope were present in 27 cases (2%), with vomiting and nausea being the most frequent in 20 (20/27, 74%) patients.

TABLE 2 Clinical characteristics of 1307 CSDH patients

Variable	N (%) Total = 1307
Age (mean \pm SD)	74 (\pm 11)
Male sex	958 (73)
Markwalder Grading Scale (MGS) at presentation	
MGS 0	41 (3)
MGS 1	480 (37)
MGS 2	718 (55)
MGS 3	38 (3)
MGS 4	6 (0.5)
Unknown	24 (2)
Charlson Comorbidity Index (CCI)	
CCI 0	34 (3)
CCI 1	62 (5)
CCI 2	150 (12)
CCI 3	268 (21)
CCI 4	317 (24)
CCI 5	207 (16)
CCI 6 or more	261 (20)
Unknown	8 (0.5)
Midlineshift in mm. (mean \pm SD)	6.9 (\pm 5.3)
Treatment modality	
Surgery	838 (64)
Surgery and dexamethasone	191 (15)
Dexamethasone	80 (6)
Wait and see	197 (15)
Unknown	1 (0.1)
Burr hole craniostomy when surgery was applied	996 (97)
Hematoma side	
Left	511 (39)
Right	444 (34)
Bilateral	352 (27)
Presenting symptoms	
Focal neurological deficit	592 (46)
Headache	531 (41)
Gait disorder	400 (31)
Cognitive complaints	400 (31)
Seizures	30 (2)
Other	53 (4)
Mean GCS at diagnosis	14.2 (SD \pm 1.5)
Unknown	6 (0.5)

Abbreviations: CCI, Charlson Comorbidity Index; GCS, Glasgow Coma Scale; MGS, Markwalder Grading Scale.

3.3 | Outcomes

Most prevalent GOS-E scores were 7 (355 patients, 27%) and 8 (374 patients, 29%) (Table 3). Median interval between treatment and follow-up was 53 days (range 1–271). Three-month mortality and recurrence rates were 5% and 12%, respectively. Headache was independently associated with higher GOS-E scores (aOR 1.9, 95% CI: 1.5–2.3) as was the subgroup Others (aOR 2.7, 95% CI: 1.5–4.9). Higher GCS score at presentation (measured as a continuous variable) was associated with better outcome: (aOR 1.3 05% CI 1.1–1.5) (Table 4 and Figure 1) Cognitive complaints at presentation was associated with lower GOS-E scores (aOR 0.7, 95%CI: 0.5–0.9). Focal neurological deficit, gait disorder, and seizures were not statistically significant related to functional outcome. The distribution of the GOS-E scores, in percentages, between the presence and absence of headache, cognitive complaints and other are visualized in Figure 2. As consciousness was measured by GCS on a continuous scale, the distribution of GOS-E scores is not presented in Figure 2.

TABLE 3 Functional outcome, postoperative complications, 3 months recurrence, and mortality rates of 1307 CSDH patients

Glasgow Outcome Scale –Extended (GOS-E) at follow-up:	N = 1307
GOS-E 1: Death	69 (5)
GOS-E 2: Vegetative State	0 (0)
GOS-E 3: Lower severe disability	35 (3)
GOS-E 4: Upper severe disability	32 (2)
GOS-E 5: Lower moderate disability	78 (6)
GOS-E 6: Upper moderate disability	160 (12)
GOS-E 7: Lower good recovery	355 (27)
GOS-E 8: Upper good recovery	374 (29)
Unknown	204 (16)
3-month recurrence	152 (12)
3-month mortality	69 (5)
Postoperative complications	111 (11)*
Type of postoperative complication, N = 117* (%)	
Delirious state	34 (29)
Pneumencephalus	22 (18)
Empyema/wound infection	15 (13)
Seizures	14 (14)
Bleeding of operation wound	11 (9)
Systemic infection	8 (7)
Thrombosis/embolism	4 (3)
Other (CSF leakage, aphasia, traumatic subarachnoidal hemorrhage resulting from surgery)	9 (8)

*Total number of 117 postoperative complications in 111 patients.

TABLE 4 Relationship of signs and symptoms at diagnosis and GOS-E at follow-up. Adjusted for age at diagnosis, sex, Charlson Comorbidity Index, midlineshift, laterality of hematoma, time to follow-up, recurrence, postoperative complications, and treatment modality

Symptom	aOR	95% CI
Focal neurological deficit	1.0	0.8–1.1
Headache	1.9	1.5–2.3
Gait disorder	1.1	0.9–1.4
Cognitive complaints	0.6	0.5–0.8
Consciousness	1.3	1.2–1.4
Seizures	0.8	0.4–1.6
Other	3.4	1.1–10.1

Note: Consciousness is presented by the GCS score on a continuous scale.

To determine the predictive value of the MGS score, we performed an additional analysis, including adjustment for MGS at presentation. This analysis did not statistically differ from the aforementioned outcomes.

4 | DISCUSSION

We aimed to assess the prevalence of the various presenting signs and symptoms of patients with CSDH and to study their association with functional outcome. In this study, we found that focal neurological deficit (46%), headache (41%), gait disorders (31%), and cognitive complaints (31%) were the most prevalent symptoms in patients with CSDH. Cognitive complaints and decreased consciousness were related to unfavorable short-term functional outcome, and headache was associated with good functional outcome.

The effect of cognition on functional outcome has been well established in patients with other forms of acute neurologic disruption such as traumatic brain injury and stroke, but not for CSDH.^{21–23} Our study showed that cognitive problems were very common in CSDH patients with 31% of patients experiencing cognitive complaints. Furthermore, we found that the aforementioned association between cognitive symptoms and outcome is also present in CSDH patients.

CSDH is reported to be a cause of dementia,^{24,25} and several studies report that cognitive status can improve or even be reversed after treatment of the CSDH.^{26–29} However, the exact role of cognitive status in facilitating treatment decisions is unknown. The prevalence, effect on functional outcome, and their reversibility when treated, suggests a need for increased awareness for cognitive complaints at presentation and might even imply that they deserve a place when choosing treatment modality. A prior, large study on CSDH patients over 80 years, already reported that cognitive status of patients has an impact on surgical decision-making.³⁰ Even though they classified cognitive status as good, marginal, or poor and could only report on the cognitive status in a minority of

patients, it is concluded that patients who underwent surgery more often showed a preoperative good cognitive status. This finding is troublesome, because the poor cognitive status could simply be caused by the hematoma itself. It is unclear where this blind spot for cognitive status in CSDH patients arises from, but a possible explanation may be the MGS. The MGS heavily focuses on GCS scores and focal deficit and leaves relatively little room for interpretation of the cognitive status. Our finding that adjusting for MGS did not change results of the ordinal regression, further underscores the limitations of the MGS classification. However, it should be addressed that, in our retrospective cohort, cognitive status was only based on subjective or self-reported symptoms. None of the patients underwent cognitive or memory tests to objectively determine cognitive status. Nevertheless, we suggest a more prominent place of cognitive status when examining CSDH patients, which could be facilitated by incorporating cognition in the clinical classification of CSDH. Whether this increased awareness of the importance of cognitive status also leads to better outcome in these patients, should be the subject of further research.

In contrast to previous studies, we did not find an association between seizures and poor outcome in our study.^{4,16} This might be due to the definition of seizures in earlier research. One study included all seizures that had a “close temporal relationship” to the CSDH.¹⁶ A close temporal relationship was defined as occurring within one week of diagnosis or recurrence, including postoperative seizures. Whereas we only included seizures if they were present before initiating treatment. Furthermore, previous studies had less precise measures of outcome: one study only defined outcome as good recovery, no change, worse or dead, without clear descriptions of the groups, and the other only concluded that unfavorable outcome (mRS 3–6 vs. 0–2) is more often present in patients with seizures.^{4,16} Also, and possibly of most importance is that they also included patients with postoperative seizures, which have a different pathophysiology and therefore possibly other implications for outcome.¹⁶ This might also explain the higher prevalence of seizures in their study compared to ours (15% vs. 2%).

In line with our results that show an association between higher GCS scores and better functional outcome, a decreased consciousness has been linked to poor outcome in several previous studies.^{13–15} However, these studies either had limited numbers of patients (ranging from 116 to 256) or drew conclusions based on stratifying their patient into GCS groups (GCS <8, GCS 8–12, GCS >13), hampering clinical usability.

The association between decreased consciousness and poor outcome can be explained by the size of the hematoma (resulting in more mass effect) which is believed to be larger in patients with more severe signs such as a decreased consciousness, leading to worse outcomes.¹⁴ Another explanation is the higher presence of abnormal CT findings such as hydrocephalus and higher hematoma densities, suggesting more acute components, in patients with a decreased consciousness.³¹ When combining these two hypotheses they both might represent the presence of increased intracranial pressure (ICP).³² Only severely increased ICP leads to a decreased

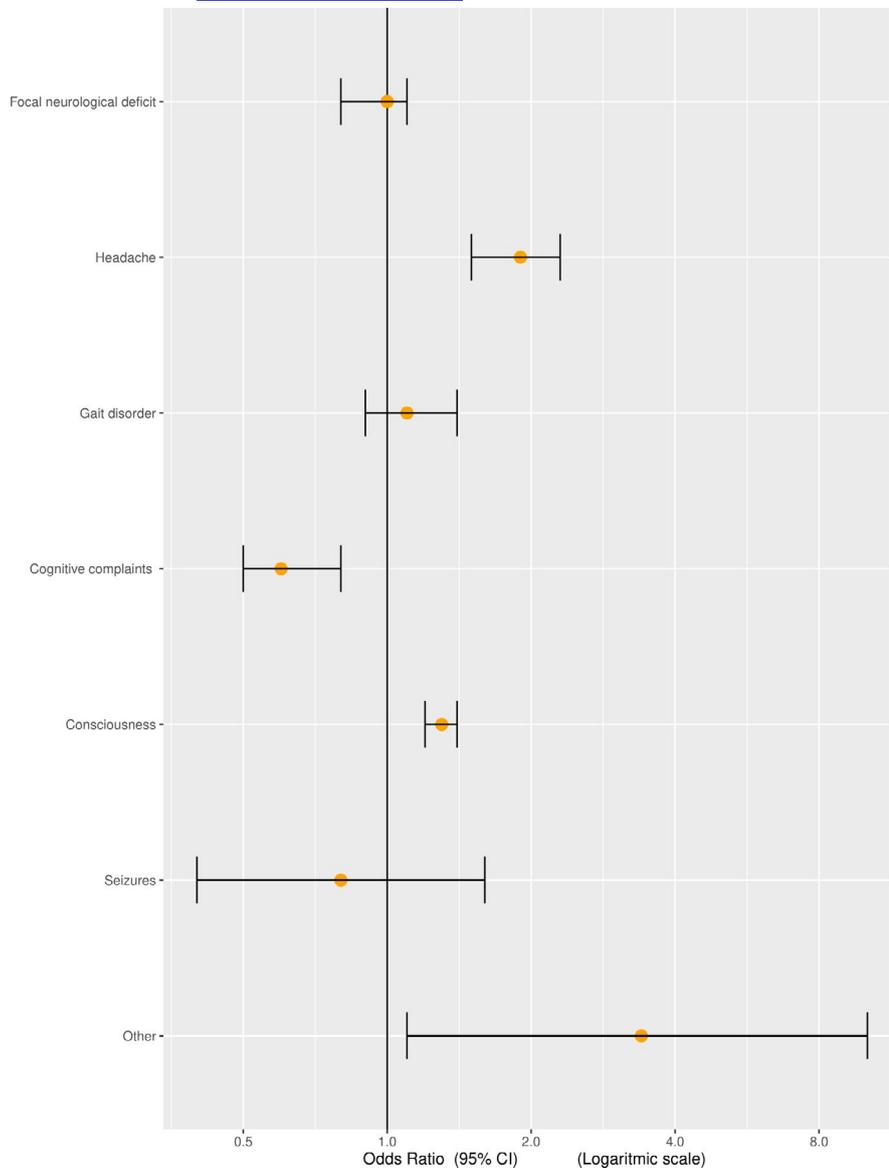


FIGURE 1 Forest plot of odds ratios and 95% CI for relationship of presenting signs and symptoms with functional outcome. The subgroup “other” consists of the symptoms of vomiting, nausea, vertigo, malaise and collapse

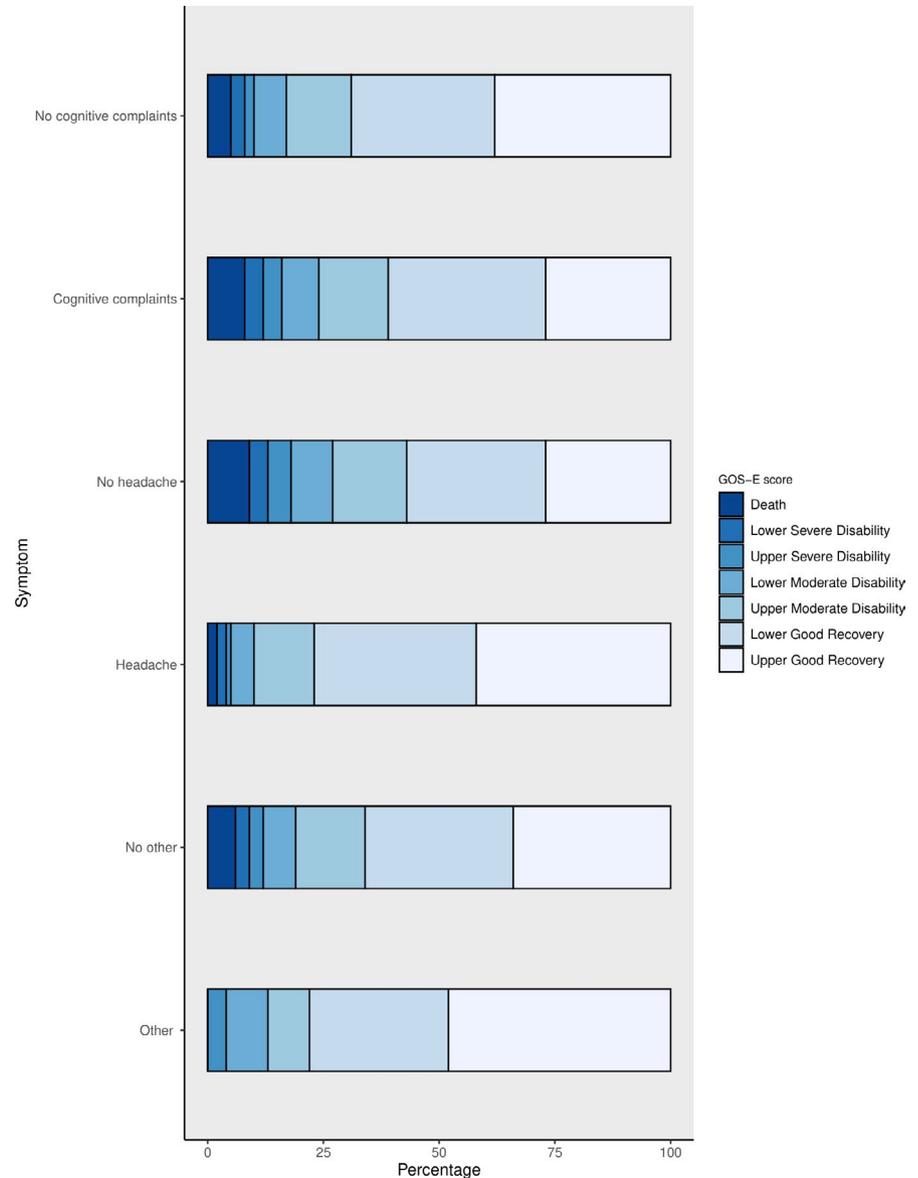
consciousness, which might reflect a more advanced stage of CSDH.³² Therefore, we hypothesize that the poor outcome in these patients is related to them being diagnosed and treated later in their disease process.

Following this reasoning, our finding that the symptom headache is related to better functional outcome, might be the result of the exact opposite. Headache is a very common symptom in the general population and is one of the most frequent causes for patients to visit their doctor.³³ The better outcome in patients presenting with headache could be related to the fact that these patients seek medical attention sooner than patients with cognitive signs and symptoms, leading to treatment early in the disease process. Furthermore, in a recent study focusing on headache in CSDH patients, the authors conclude that headache does not result from high ICP, but rather from stretching or twisting of the pain-sensitive meningeal arteries or veins.³⁴ This supports the idea that headache is an early symptom in the development of CSDH which proceeds other clinical symptoms, such as a decreased consciousness, that does result from increased ICP.^{32,35,36} Furthermore, CSDH patients with headache

are reported to be significantly younger than those without, which might explain the better functional outcome.³⁴ The association of headache with favorable functional outcome could also suggest that imminent treatment of CSDH patients with headache is not always indicated. However, our findings of a favorable association are based on a predominantly surgically treated group of patients. Whether postponing (surgical) treatment of CSDH patients is safe and beneficial, deserves further study. Another explanation might be the association between headache and larger midlineshift.³⁷ The presence of large midlineshift is reported to be a clear indication for treatment.³⁸ Therefore, patients with substantial midlineshift, and subsequent headache, might sooner or more often receive treatment, improving their functional outcome.

Whether presentation of patients early in the disease process is also the explanation for the better outcomes in the group “other” is debatable. This group contains patients with nausea and vomiting, vertigo, malaise, and syncope. The majority of this group (74%) consists of nausea and vomiting which are signs/symptoms for which we expect patients to quickly consult their physician. Also, a previous

FIGURE 2 Stacked bar graph representing distribution of GOS-E scores between the presenting symptoms with statistically significant relationship to GOS-E. The group other consists of the symptoms: vomiting, nausea, vertigo, malaise, and syncope



study describes vertigo and vomiting to be one of the early signs/symptoms of CSDH, even though they do result from increased ICP.³⁹ Furthermore, vomiting is described to be more frequently present in young CSDH patients,⁸ possibly resulting in better outcomes. However, in our regression analyses, we adjusted for age, so that this seems unlikely to be the explanation. The aforementioned arguments suggest a better outcome in patients with early signs of CSDH (headache, vomiting, and nausea) because they seek medical attention more promptly. However, given the uncertainties resulting from the aforementioned and the limited sample size for these symptoms and a wide 95%CI, no definite conclusion can be drawn.

4.1 | Strengths and limitations

Strengths of this study are that it comprises a large cohort with extensive data collection, allowing us to adjust for potential confounders. Another strength, when comparing our study with previous

studies on signs and symptoms and outcome in CSDH, is that we provided results with a clear outcome measure, namely the GOS-E. Including patients from different neurosurgical facilities and treatment modalities are both a strength and a limitation. The strength being that it improves generalizability of the outcomes, as it reflects daily clinical practice in CSDH management. The weakness, however, could be that of confounding by indication as the followed procedures and indications for treatment and management could vary per center. Some other limitations have to be discussed. First, our study has a retrospective design, and as a result, we might have introduced a reporting bias. It is possible that patients did not report, for instance, headache or cognitive complaints and that the treating physician did not ask them for these symptoms. Also, it can be that the treating physician had more attention for a specific symptom, if it was regarded as a more prudent complaint, again leading to a reporting bias of other less prudent symptoms. Second, the documentation on precise outcome was brief or missing in some cases. Nevertheless, we believe that the brief documentation (for instance

"All is well, no headaches or focal deficits.") will more possibly result in an overestimation of functional outcome (better outcome) than an underestimation. Therefore, the number of unfavorable outcomes and effect of cognitive signs and symptoms is possibly even higher than we have reported. Third, better and worse outcomes for the different signs and symptoms could be the result of differences in intervals between treatment and follow-up. As a result, patients with a longer follow-up time have had more time to recover and therefore may have a better outcome. However, adjusting our analysis with follow-up time as a confounder still did not attenuate the association between the studied variables and functional outcome. Fourth, there was a relative short time of follow-up. This may be too short for patients to recover, especially when they experience cognitive problems.⁴⁰ Another limitation in our study is that due to the retrospective nature of our study we were not able to formally test cognitive status at baseline with an objective cognitive (screening) test such as the Montreal Cognitive Assessment.⁴¹ This added information would have provided valuable information on the degree and amount of cognitive deficits, rather than the heterogeneous definition of cognition that is present in our current study. Finally, given the large incidence of cognitive deficits or even dementia in the predominantly older population of which CSDH consists of the possibility of pre-CSDH cognitive impairment should be taken into account. As, again, the retrospective nature of this study did not allow ascertainment of pre-CSDH cognitive status, the possibility of cognitive impairment not being caused by CSDH should be considered. Therefore, these results should be interpreted with caution, as causality could not be determined.

In conclusion, we showed that signs and symptoms of CSDH at the moment of diagnosis are related to functional outcome in patients with CSDH. Patients with cognitive complaints and decreased consciousness at presentation more frequently have worse short-term functional outcome compared to patients with headache. Currently, cognitive status is not incorporated in the MGS, which seems to be an important shortcoming of this clinical classification scale for CSDH.

Our study advocates that cognitive deficits may be taken into account in the establishing of the clinical picture of the patient with a CSDH. Our present findings suggest that cognitive dysfunction needs to be weighed in the tailoring of treatment of the CSDH. However, further research on this topic is warranted to definitely establish the effect of cognitive dysfunction on functional outcome in CSDH patients.

CONFLICTS OF INTEREST

The authors declare no financial or other conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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How to cite this article: Blaauw J, Meelis GA, Jacobs B, et al. Presenting symptoms and functional outcome of chronic subdural hematoma patients. *Acta Neurol Scand*. 2021;00:1-9. <https://doi.org/10.1111/ane.13518>