Prevalence of cognitive complaints and impairment in patients with chronic subdural hematoma and recovery after treatment: a systematic review

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Reviews

Prevalence of Cognitive Complaints and Impairment in Patients with Chronic Subdural Hematoma and Recovery after Treatment: A Systematic Review

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Abstract

Chronic subdural hematoma (CSDH) is a frequently occurring neurological disease associated with older age and use of anticoagulants. Symptoms vary from headaches to coma, but cognitive deficits can also be present. However, exact prevalence and severity of cognitive deficits in CSDH are still unknown. In this systematic review, we aim to assess cognitive status of patients with CSDH, at presentation and after treatment. PubMed, Embase and PsycInfo were searched for articles concerning cognition in CSDH. We divided cognitive changes into subjective cognitive deficit (cognitive complaints [CC]) and objective cognitive deficit (cognitive impairment [CI]). Two reviewers independently selected studies for inclusion and subsequently extracted data. Quality assessment was done by means of the Newcastle–Ottawa Scale. Reported prevalence of CC and CI was pooled with random effects meta-analysis. Out of 799 identified references, 22 met inclusion criteria. Twenty-one articles reported on prevalence of CC/CI and one study reported solely on CSDH patients with cognitive deficit. Estimated pooled prevalence of both CC and CI in CSDH at presentation was 45% (95% confidence interval [CI]: 36–54%). Four studies concerned a prospective evaluation of the effect of surgical treatment on cognition. These proved to be of fair to good quality after quality assessment. The estimated pre-treatment prevalence of objectified cognitive impairment was 61% (95% CI: 51–70%) decreasing to 18% (95% CI: 8–32%) post-surgery. From this review it can be concluded that CC and CI are very common in CSDH, with a tendency to improve after treatment. Therefore, we underline the importance of increased attention to cognitive status of these patients, with proper testing methods and treatment-testing intervals.

Keywords: chronic subdural hematoma; cognition; cognitive complaints; cognitive impairment; systematic review

Introduction

Chronic subdural hematoma (CSDH) is a frequently occurring neurological disease mostly affecting males, patients ≥60 years of age, and those who use anticoagulants.[1,2] The estimated incidence ranges between 8 and 14 cases per 100.000 per year,[3] but incidence up to 48 per 100,000 per year in elderly patients has been reported.[4] Epidemiological studies have shown that the incidence of CSDH has doubled over the last three decades, and that it is expected to increase even more because of the ongoing aging of the population.[3,5]

The mainstay of CSDH treatment is burr-hole craniostomy (BHC) or twist drill craniostomy (TDC), and less frequently, a craniotomy.[3,6] Non-surgical treatment modalities such as dexamethasone, angiotensin-converting enzyme (ACE) inhibitors, statins, and tranexamic acid are also applied, but mostly in the context of international trials.[3,7,8] Clinicians and patients with their proxies may also opt for a ''wait-and see'' or ''close observation'' policy in

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mild or asymptomatic patients, as spontaneous resolution is not unusual, especially after cessation of oral anticoagulant therapy.[9]

The clinical presentation of CSDH is diverse, varying from mild symptoms, such as headaches and dizziness, up to severe symptoms, including hemiplegia and coma. CSDH can even result in death. Symptoms may differ with age. Young patients most often present with signs of increased intracranial pressure, such as progressive headache, nausea, and vomiting.[10,11] In older patients, ≥65 years of age, cognitive and mental changes are more prevalent.[12,13]

In past decades, most studies on CSDH focused on surgical techniques, risk factors for the development of CSDH, perioperative use of anticoagulants, or optimal treatment modalities. Remarkably, cognitive complaints or cognitive impairment receive relatively little attention in literature, in contrast to studies in other types of traumatic brain injury, in which cognitive deficit is frequently observed and has been shown to have a large effect on the quality of life.[14–16]

In this systematic review, the prevalence of cognitive symptoms at presentation was assessed, together with the effect of treatment on cognitive performance during follow-up in patients with CSDH.

Methods

Study selection

A literature search was performed in PubMed, Embase and PsycInfo for articles on CSDH and cognition. CSDH was defined as a subdural or extra-axial hematoma, bleeding, or hemorrhage. For this review we have taken into account all cognitive problems, both subjective and objective in their broadest sense. We included: learning, memory, attention neurocognitive disorder, dementia, and cognitive impairment. For exact search terms see Table 1.

The search was last updated on April 15, 2020 and went as far back as data were available. This systematic review was conducted in accordance to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.[17]

Inclusion for full text reviewing was performed if articles (1) assessed patients with a CSDH; (2) dealt with patients ≥18 years of age; (3) were written in English, French, German, or Dutch; (4) reported on cognitive status on admission, at discharge and/or at follow-up; or (5) examined the effect of treatment or the natural course of CSDH. Further, studies with all treatment modalities, such as surgical or drug therapies, as well as non-interventional treatments featuring bed rest or a ''wait and see policy'' were included.

Excluded articles were (1) those that only reported on cognition as a possible symptom of CSDH without providing prevalence numbers; (2) dealt with acute subdural hematoma; and (3) case reports, review articles, letters to the editors, and trial designs. Further, articles in which the prevalence of cognitive symptoms could not be calculated from the available data and those that did not focus on cognition in CSDH as a separate entity (such as the prevalence of CSDH in patients with dementia) were excluded. Finally, all articles that did not use computed tomography (CT) or magnetic resonance imaging (MRI) scans for diagnosis of CSDH (e.g., technetium scans, angiography, skull radiographs) were excluded.

Cognition

In the literature, we could not establish a unifying definition for cognitive changes in patients with CSDH. Mostly, memory impairment was mentioned, without distinguishing between subjective complaints and (objective) results of neuropsychological testing. In our review, cognitive changes are described as cognitive complaints/cognitive impairment (CC/CI) to facilitate understanding and reading. The term cognitive complaints (CC) was used for subjective cognitive limitations, for example when reported by patients or their peers. The term cognitive impairment (CI) was reserved only for cases in which CCs were objectively established (e.g., by neurological/psychological testing).

Cognitive tests

The most used cognitive tests in the included manuscripts were:

- The Mini Mental State Examination (MMSE), scored from 0 to 30. A score ≤23 is considered to be abnormal. Specific cutoff scores vary with age and have been discussed in the literature.[18]
- The Hasewaga Dementia Scale Revised (HDS-R) is comparable with the MMSE but consists of fewer items, with a cutoff point for an abnormal score at 24/25 with a maximum of 30 points.

Table 1. Search Terms in PubMed, Embase, and Psycinfo

PubMed	*Embase*	*Psycinfo*
(''Hematoma, Subdural, Chronic''[Mesh] OR chronic subdural hematoma* [tiab] OR csdh [tiab] OR chronic subdural haematoma* [tiab] OR chronic extra axial hematoma* [tiab] OR chronic extra axial haematoma* [tiab] OR subdural bleed* [tiab] OR subdural hemorrhage* [tiab] OR subdural haemorrhag* [tiab]) AND (''Cognition''[Mesh] OR cognit* [tiab] OR ''Learning''[Mesh] OR memor* [tiab] OR attention [tiab] OR ''Neurocognitive Disorders''[Mesh] OR ''Confusion''[Mesh] OR confus* [tiab] OR Neurocognitive Disorder* [tiab] OR ''dement* [tiab] OR neuropsych* [tiab])	('chronic subdural hematoma*':ab,ti OR csdh:ab,ti OR 'chronic subdural haematoma*':ab,ti OR 'chronic extra axial hematoma*':ab,ti OR 'chronic extra axial haematoma*':ab,ti OR 'subdural bleed*':ab,ti OR 'subdural hemorrhag*':ab,ti OR 'subdural haemorrhag*':ab,ti) AND ('cognition'/exp OR 'disorders of higher cerebral function'/exp OR cognit*:ab,ti OR attention:ab,ti OR memor*:ab,ti OR confus*:ab,ti OR 'neurocognitive disorder*':ab,ti OR dement*:ab,ti OR neuropsych*:ab,ti)	(''chronic subdural hematoma*''OR csdh OR ''chronic subdural haematoma*'' OR ''chronic extra axial hematoma*'' OR ''chronic extra axial haematoma*'' OR ''subdural bleed*'' OR ''subdural hemorrhage*'' OR ''subdural haemorrhag*'') AND (DE ''Cognition'' OR DE ''Animal Cognition'' OR DE ''Mental Lexicon'' OR DE ''Mind Wandering'' OR DE ''Cognitive Impairment'' OR DE ''Learning'' OR DE ''Neurocognitive Disorders'' OR DE ''Mental Confusion'' OR TI (cognit* OR memor* OR attention OR confus* OR neurocognitive disorder* OR dement* OR neuropsych*) OR AB (cognit* OR memor* OR attention OR confus* OR neurocognitive disorder* OR dement* OR neuropsych*))

- The Rivermead Behavorial Memory Test (RBMT) is a test that specifically predicts everyday memory problems. It comprises 12 different components such as remembering names, picture recognition, immediate and delayed recall, and orientation. The score is given in two summarized scores: (1) the screening score: a pass–fail ranging from 0 to 12 points, and (2) the standardized profile score ranging from 0 to 24.[19]

Data extraction and synthesis

Two authors (J.B. and A.G.B.) independently screened titles and abstracts blinded to the authors and journal titles identified through database searches, and excluded articles that did not fulfill inclusion criteria. Articles without abstracts were automatically passed into the full text-screening phase. We obtained the full text of the remaining articles and independently selected studies meeting the inclusion criteria for this review. Disagreements were resolved by discussion and by consultation with a third author (H.M.d.H.), if necessary. The following data were retrieved: year of publication, number of patients included, number of patients with CC or CI at presentation and at follow up, age, definition of CC/CI and further specification of CC/CI if given, and cognitive testing modality.

Additionally, from articles reporting on changes in CC/CI after treatment, we recorded the type of intervention and the time between treatment and cognitive testing. No restriction in follow-up length was applied. The references of all included manuscripts were scrutinized for possible additional articles.

Statistical analysis

Using Rstudio, a meta-analysis was performed for the prevalence of CC/CI after dividing the studies into three groups: (1) CC, (2) CI, and (3) not specified. Finally, we analyzed the pre- and post-treatment prevalence in studies that reported on CI. For interpretation, the random effects model was used, which better accounts for the heterogeneity among studies. Heterogeneity of studies was assessed through I^2, and 95% confidence intervals were calculated, together with prediction intervals for the overall estimated prevalence if I^2 was >75%.

Quality assessment

Studies were independently scored by two reviewers (J.B. and A.G.B.), using the Newcastle–Ottawa Quality Assessment Form for Cohort Studies or in short the Newcastle–Ottawa Scale (NOS).[20] This scoring model is validated and designed for the use in systematic reviews, and is placed in the best 5% of quality assessments for non-randomized studies.[21,22] The NOS form consists of eight items categorized into three groups, and describes the quality of selection, comparability, and outcome. For visual understanding, articles are given ''stars'' in all subsections of categories, and two in the comparability section, leading to a possible total of nine stars.

Results

Search result

The online search of databases identified 1028 articles, of which 796 remained after removing double references (Fig. 1). An additional 3 articles were identified by screening references of other included articles, leading to a total of 799. After screening of the titles and abstracts, 687 articles were excluded. We assessed the full text of the remaining 112 articles for eligibility, after which we excluded another 82. For eight articles, no full text was available for reviewing, even after a request through our university medical library's international, interlibrary loan system.

Of the remaining 22 articles, 16 reported only on the prevalence of CC/CI in CSDH patients,[4,6,23–36] and 6 reported on the pre-treatment prevalence and the improvement of CC/CI after treatment.[12,37–41] Five of these six articles also reported on prevalence of CC/CI, making a total of 21 articles that reported on prevalence of CC/CI. Of these 21 articles, 16 retrospectively studied their patients, and 5 had a prospective design.

Assessment of cognition

Cognitive status was measured with only the MMSE in two studies,[12,41] with only the RBMT in one,[39] and with the MMSE and HDS-R in another one.[40] In most other studies types of CI or CCs varied and lacked clear definitions. The most reported CC/CI were confusion, mental changes, and dementia. Some reported subjective complaints such as failing memory, confusion, or cognitive decline, which could be classified as CC, whereas others just mentioned ''demential syndrome'' without further specification.

Prevalence of cognitive problems

A total of 21 studies reported on the prevalence of CC/CI in their study population (Table 2 and Fig. 2). The estimated prevalence was 45% for CC (95% confidence interval: 36–54%), 50% for CI (95% confidence interval: 38–63%), and 23% for not specified (95% confidence interval: 0–68%).

The overall estimated prevalence was 45% (95% confidence interval: 39–52%), with a heterogeneity of 94%. A 95% prediction interval was calculated: 18–74%.

Improvement of cognition after treatment

Of the six included studies that assessed cognition after treatment, two were retrospective cohort studies,[37,38] and four had a prospective design (Table 3).[12,39–41] All studies reported on surgically treated patients of whom the vast majority was treated with BHC. Hence there were no patients who received drug therapy or non-interventional treatment. Three of the prospective studies reported on the time between surgery and cognitive testing.[39–41]

Prospective studies

The number of included patients varied from 16 to 79, with a total of 151.[19,12,39,40] Reported age differed among the studies, with mean ages between 69 and 73. Pre-operative MMSE score differed from 16 to 23, which improved to 20–27 after surgery.[40,41] Post-operative tests were performed between 24 h and 2 weeks after surgery. Pre-operative MMSE scores <24 were reported in 54–69% of patients.[12,40,41] Improvement of MMSE >24 points or improvement of CI was seen in 50–85% of the cases.

Based on the three studies that prospectively assessed cognitive status with the MMSE,[12,40,41] the estimated pre-treatment prevalence of CI was 61% (95% confidence interval: 51–70%), which decreased to 18% (95% confidence interval: 8–32%) post-treatment (Figs. 3 and 4).

Patients who did not improve were significantly older, and had significantly lower pre-treatment MMSE scores.[12,40] One study also found a higher pre-operative Katz Index of Independence in Activities of Daily Living (KATZ-ADL) (a measure of independent living where lower scores indicate more independence) to be related to worse improvement after treatment.[40] There were no significant differences between improved and unimproved patients regarding hematoma volume, midline shift, or sex.[12,40]

Retrospective studies

One study reported that 192 patients (56%) had CC prior to treatment. After treatment, this improved to 51 patients (15%).[38]

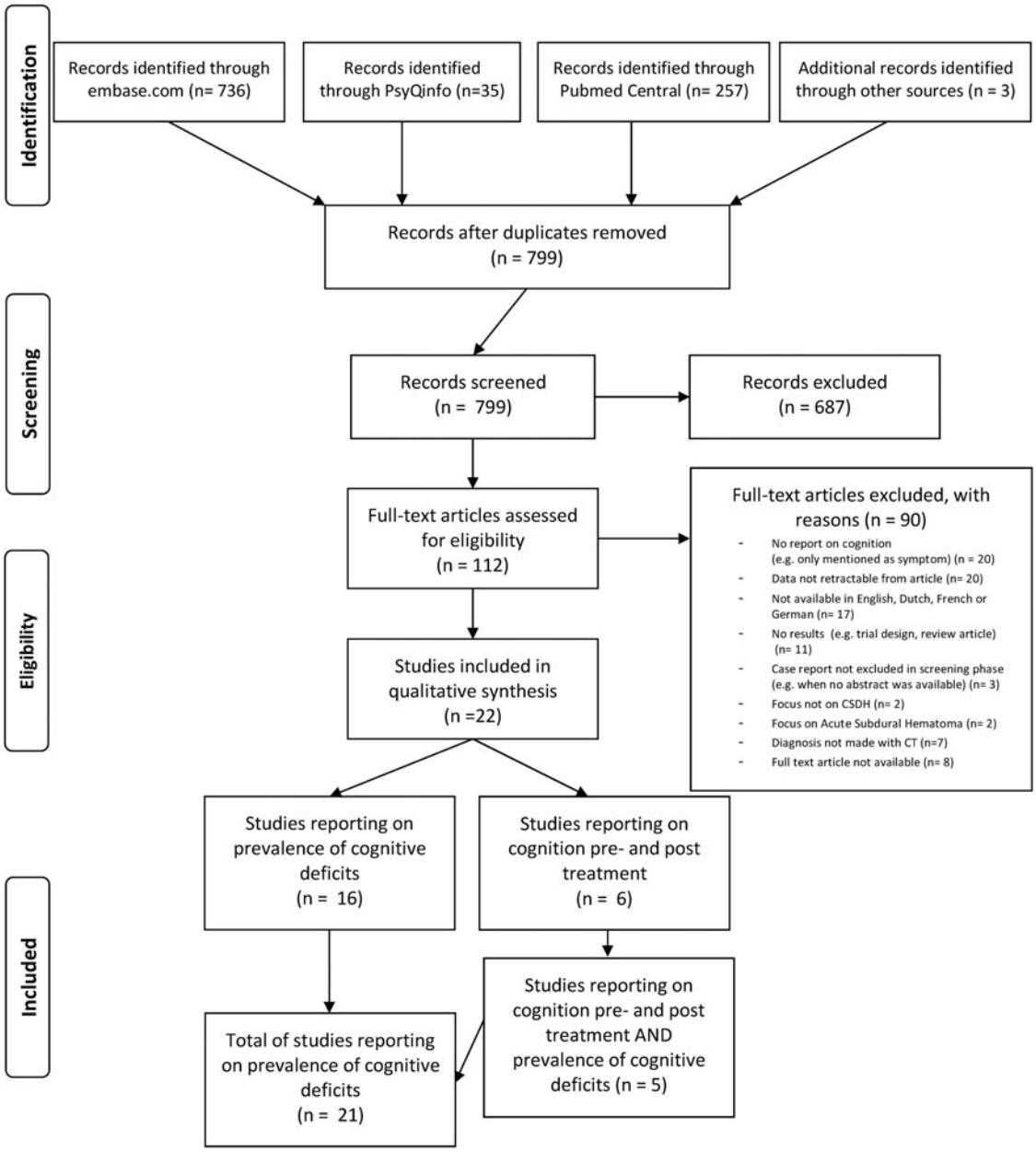

FIG. 1. Flow chart diagram of the literature search and selection.

Another study did not distinguish between CI or CC, but showed an improvement from 315 (45%) to 86 (12%).[37]

Quality assessment

Four prospective studies that reported on pre- and post-treatment CI were assessed. Two studies were scored to be of good quality based on the NOS;[40,12] the other two had a fair quality (Table 4).[39,41]

Discussion

This review showed that CC and CI are often present in patients with CSDH, with an estimated pooled prevalence of 45%. Further, we have shown that CI can improve after surgical treatment. To our knowledge, this is the only systematic review that has reported on this subject. It is known that in patients with stroke and neurotrauma, cognitive impairment can seriously affect quality of life, independent living, and survival.[42–44] It can be expected that this applies to CSDH patients as well. Therefore, we suggest increased

Table 2. Prevalence of Cognitive Impairment and/or Complaints in CSDH

Study	*Study specifics*	*Type of study*	*Patients with cognitive deficit (%)*	*Definition of cognitive deficit*	*Specification*
Adhiyaman et al.[4] 2017	66 patients >65 years of age	Retrospective	30 (45)	Increasing confusion	Not otherwise specified
Battaglia et al.[23] 2012	161 patients, surgically treated	Retrospective	65 (40)	Cognitive deficits	Not otherwise specified
Black[24] 1984	79 patients focus on occurrence of CC/ CI	Retrospective	46 (58)	Mental changes	Delirium, dementia, coma, organic effective, mixed type.
Bourgeois et al.[25] 1999	80 patients >80 years of age	Retrospective	53(66)	Confusion and impaired mentality	Not otherwise specified
Brennan et al.[6] 2017	823 patients, 787 surgically treated	Prospective	480 (58)	Cognitive impairment	Not otherwise specified
Gill et al.[41] 2018	30 patients, surgically treated	Prospective	20 (67)	Cognitive impairment	Tested with MMSE
Hammer et al.[26] 2017	73 patients, surgically treated	Retrospective	11 (15)	Confusion	Not otherwise specified
Ishikawa et al.[40] 2002	26 patients, surgically treated	Prospective	18 (69)	Dementia	Tested with MMSE
Kidangan et al.[27] 2020	80 patients, surgically treated	Retrospective	42 (53)	Altered sensorium or decreased memory	Not otherwise specified
Kwon et al.[28] 2018	154 patients, surgically treated	Retrospective	70 (46)	Disorientation	Not otherwise specified
Májovský et al.[29] 2016	34 patients, surgically treated	Prospective	2 (5.9)	Cognitive disturbances	Not otherwise specified
Mori and Maeda[30] 2001	500 patients, surgically treated	Retrospective	123(25)	Dementia	Not otherwise specified
Neal et al.[31] 2013	159 patients, surgically treated	Retrospective	58 (36)	Altered mental status	Not otherwise specified
Ramachandran et al.[32] 2007	647 patients, 607 surgically treated	Retrospective	370 (57)[a] 428 (66)	Cognitive disturbance Altered behavior	Not otherwise specified
Ramnarayan et al.[33] 2008	42 patients >65 years age	Retrospective	21 (50)	Cognitive decline	Not otherwise specified
Santarius et al.[34] 2009	205 patients, surgically treated	Prospective	71 (35)[a] 67 (33)	Mental deterioration Acute confusion	Not otherwise specified
Schebesch et al.[38] 2008	356 patients surgically treated	Retrospective	192 (56)	Mnestic deficits	Cognitive decline Confusion
Schoedel et al.[37] 2016	697 patients, surgically treated	Retrospective	315 (45)	Mnestic deficits	Not otherwise specified
Thavara et al.[35] 2019	109 patients, surgically treated	Retrospective	53 (48)	Altered sensorium/ memory loss	Not otherwise specified
Windhager et al.[36] 1988	14 patients >60 years of age	Retrospective	5 (36)	Confused	Not otherwise specified
Ye et al.[12] 2008	79 patients, surgically treated	Prospective	43 (55)	Cognitive impairment	Tested with MMSE
Total number of patients: 4414		Total of CC/ CI (%): 2088 (47)			

[a]Number used for calculation.
CC, cognitive complaints; CI, cognitive impairment; MMSE, Mini Mental State Examination.

attention to the cognitive status of patients with CSDH. starting with more awareness not only of CC/CI as presenting symptoms of CSDH, but also of the presence of CC/CI after treatment.

In total, we found 22 studies that specifically reported on CC and/or CI in CSDH, of which only a small number reported on the effect of treatment on CSDH. Overall, these studies were very heterogenic. This is partially explained by the inclusion criteria of the included reports: some have focused specifically on cognitive problems in patients with CSDH,[24,40] whereas other studies only concerned surgical techniques.[29] Further, and probably of greatest importance explaining the wide prevalence range, might be the heterogeneous definition of cognitive changes, ranging from memory deficits, dementia, and disorientation to mental changes. In order to determine the actual prevalence after CSDH, a conclusive definition is needed. We propose to use the terms ''cognitive complaints'' for subjective symptoms, and ''cognitive impairment'' for objectively determined abnormalities in cognitive functioning.

Ideally, screening tests are used to determine which cognitive domains need further attention, and assessment with more extensive testing modalities.[45] However, in most included articles, only the MMSE was used to screen for CI. In general, MMSE scores are influenced by the level of literacy and cultural or ethical norms, and are not reliable in patients with <5 years of education.[46] Additionally, the MMSE primarily targets orientation and the language cognitive domains, and focuses less on memory.[47] Also, even though the MMSE is a quick and easy method, it remains a

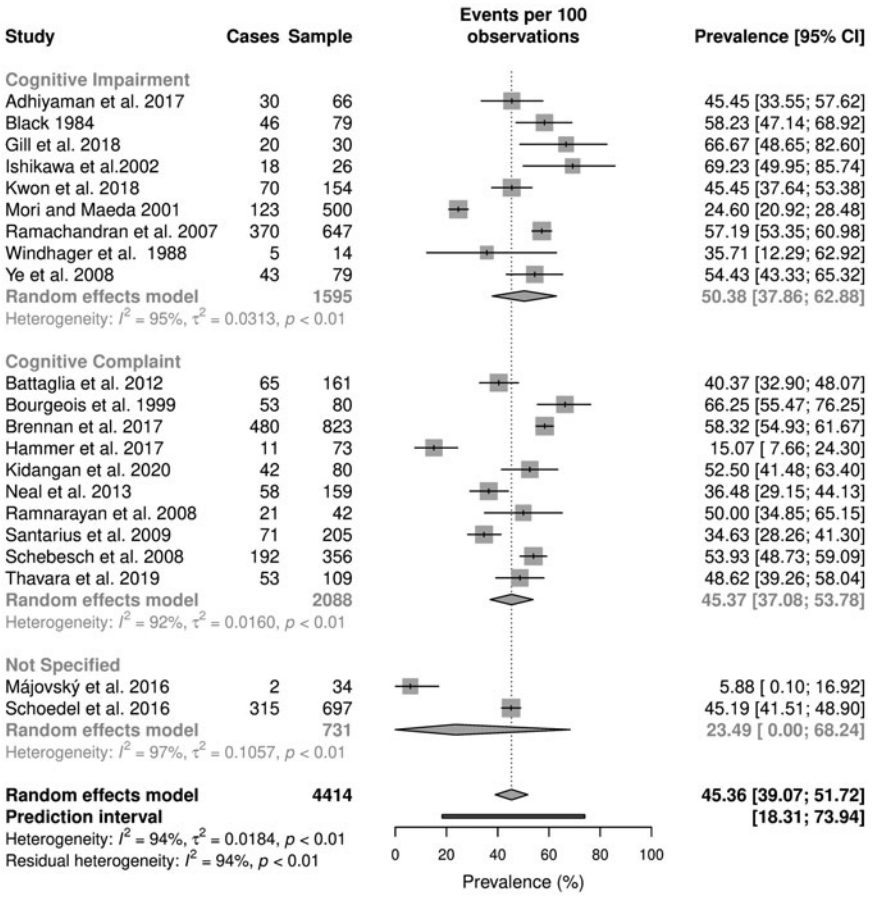

FIG. 2. Meta-analysis of prevalence of cognitive complaints and cognitive impairment in 21 studies.

TABLE 3. IMPROVEMENT OF COGNITION AFTER CSDH TREATMENT

Study	*Study specifics*	*Type of CD*	*Intervention type*	*Cognitive test*	*Outcome*		*Time until post- treatment test*
					Pre-treatment	*Post-treatment*	
Gill et al.[41] 2018	30 patients Prospective	Cognitive impairment	BHC	MMSE	23[a]	27*	24 h
Ye et al.[12] 2008	79 patients Prospective	Cognitive impairment	BHC	MMSE	Patients with CI: 43 (54, 4%)	Patients with CI: 12 (15.2%)	Not reported
Ishikawa et al.[40] 2002	26 patients Prospective	Dementia	BHC	MMSE, HDS-R	MMSE 16[a] (SD 10) HDS-R 14[a] (SD 9)	22[a] (SD 10) 20[a] (SD 10)	2 weeks
Kawasaki et al.[39] 2012	16 left-sided CSDH patients with only CD	Memory impairment and cognitive dysfunction		RBMT	4[a] (SD: 2)	7.4[a] (SD: 1.4)	48 h
Schebesch et al.[38] 2008	356 patients Retrospective patients chart study	Mnestic deficits	96.4 % BHC	None	Patients with CC 192 (56%)	Patients with CC 51 (15%)	Not reported
Schoedel et al.[37] 2016	697 patients Retrospective patients chart study	Mnestic deficits	96.5 % BHC	none	Patients with CI/CC 315 (45%)	CI/CC 86 (12%)	Before discharge

[a]Indicates mean score.

BHC, burr hole craniostomy; CC, Cognitive complaints; CD, cognitive dysfunction; CI, cognitive impairment; CSDH, chronic subdural hematoma; HDS-R: Hasewaga Dementia Scale Revised; MMSE, Mini Mental State Examination; RBMT, Rivermead Behavioral Memory Test; SD, standard deviation.

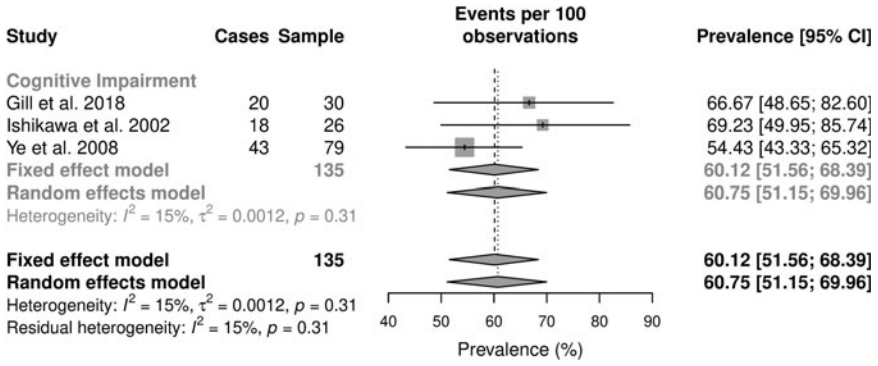

FIG. 3. Meta-analysis of reported cognitive impairment before treatment.

screening test and should be interpreted as such. For testing full cognitive status, tests should cover six key cognitive domains: attention/working memory, new verbal learning and recall, expressive language, visual construction, executive function, and abstract reasoning.[45] We recognize that a full neuropsychological examination is time consuming, and might not be feasible in clinical practice; therefore, reasonable alternatives have been suggested by others. For example, the Modified Mini Mental State Examination (3MS) and the Cognitive Ability Screening Instrument (CASI) are reported to be validated tests, covering all six key domains, with an administering time of <20 min.[45] Further, the Mini-Cog and Addenbrooke's Cognitive Examination-revised (ACE-R) tests have been described as the best performing screening tests for detecting dementia, and the Montreal Cognitive Assessment (MoCA) has been described as the best test for mild cognitive impairment. All of these three screening tests take <20 min to administer.[48]

Cognitive status may be related to certain characteristics of CSDH, and, therefore, an observed limitation in the included articles is the lack of information about hematoma characteristics and their natural course. Although studies provide patient characteristics involving worse recovery (low pre-treatment MMSE, increase in age) hardly any information is presented on the resolution of the hematoma.[12,40,41] It is possible that in patients who do not show improvement of CC/CI, no sufficient release of brain tissue was achieved. This assumption is also suggested by other authors.[39]

Choices in treatment, such as of anesthesia modality or administering corticosteroids can also influence the cognitive status of patients.[49,50] However, in standard daily care of CSDH, at this moment, we do not anticipate the effects of choices of treatment on cognitive status. This is further illustrated by how the indication for treatment of CSDH is set: it is based on physical neurological symptoms or hematoma size.[51] Presence of CC/CI are not as routinely taken into account, examined, or recognized as potential hazards for long term outcome.

In addition to the definition of CC/CI and the testing modality used for determination of cognitive impairment, we also would like to underline that the timing of testing after treatment and follow-up is important. This timing varied in the included studies from 24 h to 14 days after, in this case, surgery. We believe that the 24 h between surgery and post-operative testing is too short for the recovery of cognitive status, and also doubt the validity of testing at 2 weeks, because of learning effects reported by studies in dementia patients on a variety of cognitive tests. These findings have resulted in proposing an interval of at least 3 months to minimize practice effects.[52] This 3 month time interval is also suggested in studies concerning the evaluation of post-operative cognitive dysfunction. They state that at 3 months, the acute effects of hospitalization, anesthesia, and surgery have been reduced, therefore allowing the proper testing of cognitive functioning.[53,54] This proposed time interval would also permit reliable identification of cognitive problems after therapeutic intervention in patients with CSDH.

The overall results of this review suggest that even though the prevalence of CC/CI in CSDH patients is high, the importance/clinical relevance of this issue seems to be underestimated. Current clinical practice is predominantly focused on symptoms such as headache and hemiparesis,[51] whereas the effect of cognitive problems on quality of life and functional outcome is underexposed. The identification of factors contributing to poor recovery of the cognitive status in CSDH patients should therefore regarded as an important aspect of further research.

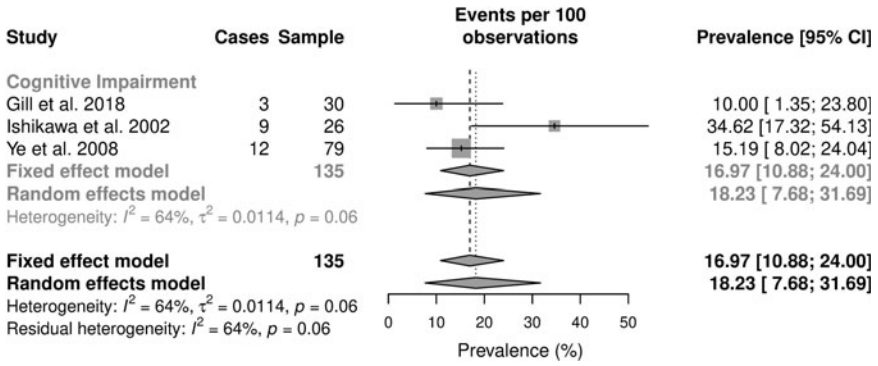

FIG. 4. Meta-analysis of reported cognitive impairment after treatment.

Table 4. Quality Assessment Using the Newcastle–Ottawa Scale

	Selection				*Comparability*	*Outcome*			
Study	*Representativeness of exposed cohort*	*Selection of the unexposed cohort*	*Ascertainment of exposure*	*Certain that outcome of interest was not present at start of study*	*Comparability of cohorts*	*Assessment of outcome*	*Follow-up long enough for outcome to occur*	*Adequacy of follow-up*	*Quality Score*[a]
Gill et al.[41] 2018	30 patients in a tertiary center, 23 male 7 females, very wide age spread (7-85 years) ★	Only 20 of 30 patients experienced cognitive complaints.	Sure records ★	No, pre-morbid cognitive status unknown.	Controlled for age ★	Sure records ★	24 h after surgery	Complete follow-up, all subjects accounted for ★	Fair quality
Ishikawa et al.[40] 2002	26 patients with CSDH, 21 male, mean age 73 ★	18 patients scored <24 on the MMSE ★	Sure records ★	No, pre-morbid cognitive status unknown	Controlled for age, hematoma characteristics, preoperative MMSE, ADL, HDS-R ★★	Sure records ★	2 weeks after surgery ★	Complete follow-up, all subjects accounted for ★	Good quality
Kawasaki et al.[39] 2012	Only left-sided CSDH with only cognitive complaints, no other deficits.	Comparison with healthy controls ★	Sure records ★	No, pre-morbid cognitive status unknown	Controlled for location and characteristics of hematoma ★	Sure records ★	48 h after surgery	Complete follow-up, all subjects accounted for ★	Fair quality
Ye et al.[12] 2008	79 patients of whom 43 had proven cognitive impairment ★	Only patients with cognitive complaints, proven by MMSE ★	Sure records ★	No, pre-morbid cognitive status unknown	Controlled for age, hematoma characteristics, pre-operative MMSE ★★	Sure records ★	Unknown timing of post-operative test	Complete follow-up, all subjects accounted for ★	Good quality

[a]Good quality: three or four stars in selection domain *and* one or two stars in comparability domain *and* 2 or 3 stars in outcome domain. Fair quality: two stars in selection domain *and* one or two stars in comparability domain *and* two or three stars in outcome domain. Poor quality: no or one star in selection domain *or* 0 stars in comparability domain *or* no or one stars in outcome domain.

ADL, activities of daily living; CSDH, chronic subdural hematoma; HDS-R, Hasewaga Dementia Scale- Revised; MMSE, Mini Mental State Examination.

Limitations

The main limitations of this meta-analysis are related to the methodology of the included articles concerning the testing modality, definition of CC/CI, and the time until testing. In addition to these points, some other issues have to be discussed.

First, there is a lack of variation in treatment modalities, hence we only included articles reporting on surgically treated patients, as studies with alternative therapies did not fulfill the selection criteria. Second, there was no information on pre-morbid cognitive functioning of included patients. It is therefore unknown if CC/CI are present a result of CSDH, or if they were already present in these patients, although when looking at the improvement of CI after surgery, CSDH has to be regarded as the probable cause of the observed cognitive impairment. However, if the CC/CI in these patients result from the CSDH itself, or if cognitive deficits were already present prior to CSDH, remains difficult to determine, given that the population of CSDH patients is primarily older.[55] Finally, with heterogeneity of included studies of >90%, performing a meta-analysis of included studies is debatable, and outcomes should be interpreted with caution.[56] Lastly, we could only include three prospective studies reporting on pre- and post-treatment cognitive status that were analyzed with the same testing modality. This has led to a small number of cases included for this meta-analysis, which might have affected the results. On the other hand, the limited number underlines that cognitive status in CSDH patients, despite the importance, is often overlooked.

Conclusion

In conclusion, we have shown that cognitive impairment and complaints are common in CSDH patients, underscoring the need for increased attention to the cognitive status either at presentation or after (surgical) treatment in this group. Future studies on this subject are needed in which CI and CC should be properly defined, and validated screening tools are needed to determine the extent of cognitive problems. Preferably, the interval between treatment and follow-up testing of the cognitive status of patients with CSDH should be at least 3 months.

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References

1. Sim, Y.W., Min, K.S., Lee, M.S., Kim, Y.G., and Kim, D.H. (2012). Recent Changes in risk factors of chronic subdural hematoma. J. Korean Neurosurg. Soc. 52, 234–239.
2. Adhiyaman, V., Asghar, M., Ganeshram, K.N., and Bhowmick, B.K. (2002). Chronic subdural haematoma in the elderly. Postgrad. Med. J. 78, 71–75.
3. Kolias, A.G., Chari, A., Santarius, T., and Hutchinson, P.J. (2014). Chronic subdural haematoma: Modern management and emerging therapies. Nat. Rev. Neurol. 10, 570–578.
4. Adhiyaman, V., Chattopadhyay, I., Irshad, F., Curran, D., Abraham, S., Clwyd, G., and Hospital, W.M. (2017). Increasing incidence of chronic subdural haematoma in the elderly. QJM 110, 375–378.
5. Rauhala, M., Luoto, T.M., Huhtala, H., Iverson, G.L., Niskakangas, T., Öhman, J., and Helén, P. (2019). The incidence of chronic subdural hematomas from 1990 to 2015 in a defined Finnish population. J. Neurosurg. [Epub ahead of print].
6. Brennan, P.M., Kolias, A.G., Joannides, A.J., Shapey, J., Marcus, H.J., Gregson, B.A., Grover, P.J., Hutchinson, P.J., and Coulter, I.C. (2017). The management and outcome for patients with chronic subdural hematoma: a prospective, multicenter, observational cohort study in the United Kingdom. J. Neurosurg. 127, 732–739.
7. Delgado-López, P.P.D., Martín-Velasco, V., Castilla-Díez, J.M.J., Rodríguez-Salazar, A., Galacho-Harriero, AM Fernández-Arconada, O., Galacho-Harriero, A.M., and Fernández-Arconada, O. (2009). Dexamethasone treatment in chronic subdural haematoma. Neurocirugia 20, 346–359.
8. Jiang, R., Zhao, S., Wang, R., Feng, H., Zhang, J., Li, X., Mao, Y., Yuan, X., Fei, Z., Zhao, Y., Yu, X., Poon, W.S., Zhu, X., Liu, N., Kang, D., Sun, T., Jiao, B., Liu, X., Yu, R., Zhang, J., Gao, G., Hao, J., Su, N., Yin, G., Zhu, X., Lu, Y., Wei, J., Hu, J., Hu, R., Li, J., Wang, D., Wei, H., Tian, Y., Lei, P., Dong, J.F., and Zhang, J. (2018). Safety and efficacy of atorvastatin for chronic subdural hematoma in Chinese patients: a randomized clinicaltrial. JAMA Neurol. 75, 1338–1346.
9. Kim, H.C., Ko, J.H., Yoo, D.S., and Lee, S.K. (2016). Spontaneous resolution of chronic subdural hematoma: Close observation as a treatment strategy. J. Korean Neurosurg. Soc. 59, 628–636.
10. Bartek, J., Sjåvik, K., Dhawan, S., Sagberg, L.M., Kristiansson, H., Ståhl, F., Förander, P., Chen, C.C., and Jakola, A.S. (2019). Clinical course in chronic subdural hematoma patients aged 18–49 compared to patients 50 years and above: a multicenter study and meta-analysis. Front. Neurol. 10, 1–9.
11. Sousa, E.B., Brandão, L.F.S., Tavares, C.B., Borges, I.B.C., and Neto, N.G.F. (2013). Epidemiological characteristics of 778 patients who underwent surgical drainage of chronic subdural hematomas in Brasília, Brazil. BMC Surg. 13, 5.
12. Ye, H.H., Kim, J.H., Kim, Y.S., Cho, C.W., and Kim, D.J. (2008). Cognitive impairment in the elderly with chronic subdural hematoma. J. Korean Neurotraumatol. Soc. 4, 66–69.
13. Fogelholm, R., Heiskanen, O., and Waltimo, O. (1975). Chronic subdural hematoma in adults: Influence of patient's age on symptoms, signs, and thickness of hematoma. J. Neurosurg. 42, 43–46.
14. de Freitas Cardoso, M.G., Faleiro, R.M., de Paula, J.J., Kummer, A., Caramelli, P., Teixeira, A.L., de Souza, L.C., and Miranda, A.S. (2019). Cognitive impairment following acute mild traumatic brain injury. Front. Neurol. 10, 1–9.
15. Dijkers, M.P. (2004). Quality of life after traumatic brain injury: a review of research approaches and findings. Arch. Phys. Med. Rehabil. 85, 21–35.
16. Berger, E., Leven, F., Pirente, N., Bouillon, B., and Neugebauer, E. (1999). Quality of life after traumatic brain injury: a systematic review of the literature. Restor. Neurol. Neurosci. 14, 93–102.
17. Moher, D., Tetzlaff, J., Liberati, A., and Altman, D.G. (2010). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int. J. Surg. 8, 336–341.
18. Crum, R.M., Anthony, J.C., Bassett, S.S., and Folstein, M.F. (1993). Population-based norms for the mini-mental state examination by age and educational level. JAMA 269, 2386–2391.
19. Balen, van, H.G.., Westzaan, P.S.., and Mulder, T. (1996). Stratified norms for the rivermead behavioural memory test. Neuropsychol. Rehabil. 6, 203–217.
20. Wells, G., Shea, B., O'Connel, D., Peterson, J., Welch, V., Losos, M., and Tugwell, P. (2000). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis. Ottowa Hosp. Res. Inst. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (Last accessed August 27, 2019).
21. Sanderson, S., Tatt, I.D., and Higgins, J.P.T. (2007). Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. Int. J. Epidemiol. 36, 666–676.
22. Deeks, J., Dinnes, J., D'Amico, R., Sakarovitch, C., Song, F., Petticrew, M., and Altman, D. (2003). Evaluating non-randomised intervention studies. Health Technol. Assess. (Rockv). 7, iii-x, 1-173
23. Battaglia, F., Lubrano, V., Ribeiro-filho, T., Pradel, V., and Roche, P. (2012). Incidence et impact clinique des crises comitiales périopératoires pour les hématomes sous-duraux chroniques Incidence and clinical impact of seizures after surgery for chronic subdural haematoma. Neurochirurgie 58, 230–234.
24. Black, D.W. (1984). Mental changes resulting from subdural haematoma. Br. J. Psychiatry 145, 200–203.

25. Bourgeois, P., Sleiman, M., Louis, E., Haddad, E., Touzet, F., Fichten, A., and Lejeune, J.. (1999). Chronic subdural hematoma in patients over 80 years of age. Neurochirurgie 45, 124–128.
26. Hammer, A., Tregubow, A., Kerry, G., Schrey, M., Hammer, C., and Steiner, H. (2017). Predictors for recurrence of chronic subdural hematoma. Turk. Neurosurg. 27, 756–762.
27. Kidangan, G.S., Thavara, B.D., and Rajagopalawarrier, B. (2020). Bedside percutaneous twist drill craniostomy of chronic subdural hematoma-a single-center study. J. Neurosci. Rural Pract. 11, 84–88.
28. Kwon, C., Al-awar, O., Richards, O., Izu, A., and Lengvenis, G. (2018). Predicting prognosis of patients with chronic subdural hematoma: a new scoring system. World Neurosurg. 109, e707–e714.
29. Májovský, M., Masopust, V., Netuka, D., and Beneš, V. (2016). Flexible endoscope-assisted evacuation of chronic subdural hematomas. Acta Neurochir. (Wien). 158, 1987–1992.
30. Mori, K., and Maeda, M. (2001). Surgical treatment of chronic subdural hematoma in 500 consecutive cases: clinical characteristics, surgical outcome, complications, and recurrence rate. Neurol. Med. Chir. (Tokyo) 41, 371–378.
31. Neal, M.T., Hsu, W., Urban, J.E., Angelo, N.M., Sweasey, T.A., and Branch, C.L. (2013). The Subdural Evacuation Port System : outcomes from a single institution experience and predictors of success. Clin. Neurol. Neurosurg. 115, 658–664.
32. Ramachandran, R., and Hegde, T. (2007). Chronic subdural hematomas — causes of morbidity and mortality. Surg. Neurol. 67, 367–373.
33. Ramnarayan, R., Arulmurugan, B., Wilson, P.M., and Nayar, R. (2008). Twist drill craniostomy with closed drainage for chronic subdural haematoma in the elderly: an effective method. Clin. Neurol. Neurosurg. 110, 774–778.
34. Santarius, T., Kirkpatrick, P.J., Ganesan, D., Chia, H.L., Jalloh, I., Smielewski, P., Richards, H.K., Marcus, H., Parker, R.A., Price, S.J., Kirollos, R.W., Pickard, J.D., and Hutchinson, P.J. (2009). Use of drains versus no drains after burr-hole evacuation of chronic subdural haematoma : a randomised controlled trial. Lancet 374, 1067–1073.
35. Thavara, B.D., Kidangan, G.S., and Rajagopalawarrier, B. (2019). Comparative study of single burr-hole craniostomy versus twist-drill craniostomy in patients with chronic subdural hematoma abstract. Asian J. Neurosurg. 14, 513–21.
36. Windhager, E., Reisecker, F., Huber, H.., Trenkler, J., Witzmann, A., Pröll, S., and Dejaco, R.M. (1988). Chronisches Subduralhämatom beim Alterspatienten [Chronic subdural hematoma in aged patients. Diagnostic problems]. Dtsch. Med. Wochenschr. 113, 883–888.
37. Schoedel, P., Bruendl, E., Hochreiter, A., Scheitzach, J., Bele, S., Brawanski, A., and Schebesch, K. (2016). Restoration of functional integrity after evacuation of chronic subdural hematoma-an age-adjusted analysis of 697 patients. World Neurosurg. 94, 465–470.
38. Schebesch, K.-M., Woertgen, C., Rothoerl, R.-D., Ullrich, O.-W., and Brawanski, A.T. (2008). Cognitive decline as an important sign for an operable cause of dementia. Zentralbl. Neurochir. 69, 61–64.
39. Kawasaki, Y., Fujiki, M., Ooba, H., Sugita, K., Hikawa, T., Abe, T., Ishii, K., and Kobayashi, H. (2012). Short latency afferent inhibition associated with cortical compression and memory impairment in patients with chronic subdural hematoma. Clin. Neurol. Neurosurg. 114, 976–980.
40. Ishikawa, E., Yanaka, K., Sugimoto, K., Ayuzawa, S., and Nose, T. (2002). Reversible dementia in patients with chronic subdural hematomas. J. Neurosurg. 96, 680–683.
41. Gill, M., Maheshwari, V., Narang, A., and Lingaraju, T.S. (2018). Impact on cognitive improvement following burr hole evacuation of chronic subdural hematoma: a prospective observational study. J. Neurosci. Rural Pract. 9, 457–460.
42. Nakling, A.E., Aarsland, D., Næss, H., Wollschlaeger, D., Fladby, T., Hofstad, H., and Wehling, E. (2017). Cognitive deficits in chronic stroke patients: neuropsychological assessment, depression, and self-reports. Dement. Geriatr. Cogn. Dis. Extra 7, 283–296.
43. Merriman, N.A., Sexton, E., McCabe, G., Walsh, M.E., Rohde, D., Gorman, A., Jeffares, I., Donnelly, N.A., Pender, N., Williams, D.J., Horgan, F., Doyle, F., Wren, M.A., Bennett, K.E., and Hickey, A. (2019). Addressing cognitive impairment following stroke: Systematic review and meta-analysis of non-randomised controlled studies of psychological interventions. BMJ Open 9, 1–10.
44. Gorgoraptis, N., Zaw-Linn, J., Feeney, C., Tenorio-Jimenez, C., Niemi, M., Malik, A., Ham, T., Goldstone, A.P., and Sharp, D.J. (2019). Cognitive impairment and health-related quality of life following traumatic brain injury. NeuroRehabilitation 44, 321–331.
45. Cullen, B., O'Neill, B., Evans, J.J., Coen, R.F., and Lawlor, B.A. (2007). A review of screening tests for cognitive impairment. J. Neurol. Neurosurg. Psychiatry 78, 790–799.
46. Devenney, E., and Hodges, J.R. (2017). The Mini-Mental State Examination: pitfalls and limitations. Pract. Neurol. 17, 79–80.
47. Carnero-Pardo, C. (2014). Should the Mini-Mental State Examination be retired? Neurologia 29, 473–481.
48. Tsoi, K.K.F., Chan, J.Y.C., Hirai, H.W., Wong, S.Y.S., and Kwok, T.C.Y. (2015). Cognitive tests to detect dementia a systematic review and meta-analysis. JAMA Intern. Med. 175, 1450–1458.
49. Belanoff, J.K., Gross, K., Yager, A., and Schatzberg, A.F. (2001). Corticosteroids and cognition. J. Psychiatr. Res. 35, 127–145.
50. Silverstein, J.H. (2014). Cognition, anesthesia, and surgery. Int. Anesthesiol. Clin. 52, 42–57.
51. Soleman, J., Taussky, P., Fandino, J., and Muroi, C. (2014). Evidence-based treatment of chronic subdural hematoma, in: *Traumatic Brain Injury,* F. Sadaka (ed.). IntechOpen Rijeka, pps. 249–281.
52. Helkala, E.L., Kivipelto, M., Hallikainen, M., Alhainen, K., Heinonen, H., Tuomilehto, J., Soininen, H., and Nissinen, A. (2002). Usefulness of repeated presentation of mini-mental state examination as a diagnostic procedure - A population-based study. Acta Neurol. Scand. 106, 341–346.
53. Evered, L.A., and Silbert, B.S. (2018). Postoperative cognitive dysfunction and noncardiac surgery. Anesth. Analg. 127, 496–505.
54. Murkin, J.M., Newman, S.P., Stump, D.A., and Blumenthal, J.A. (1995). Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery. Ann. Thorac. Surg. 59, 1289–1295.
55. Alexander, M., Perera, G., Ford, L., Arrighi, H.M., Foskett, N., Debove, C., Novak, G., and Gordon, M.F. (2015). Age-stratified prevalence of mild cognitive impairment and dementia in european populations: a systematic review. J. Alzheimer's Dis. 48, 355–359.
56n. Barendregt, J.J., Doi, S.A., Lee, Y.Y., Norman, R.E., and Vos, T. (2013). Meta-analysis of prevalence. J. Epidemiol. Community Health 67, 974–978.

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