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Practice variation in the conservative and surgical treatment of chronic subdural hematoma

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ABSTRACT

Objective: Chronic subdural hematoma (CSDH) is a condition that is frequently seen in the neurological and neurosurgical practice. Surgical treatment is overall preferred; however, conservative treatment is also an option. Both surgical and conservative treatment of CSDH vary across neurosurgeons. The aim of the present study was to evaluate different treatment strategies for CSDH among neurosurgeons in different countries.
Material and Methods: We designed a survey that was sent to neurosurgeons affiliated with the Congress of Neurological Surgeons.The questions were related to the conservative and surgical treatment methods of CSDH. Furthermore, we also included questions related to post-operative care.
Results: 443 neurosurgeons completed the survey. 46.2 % of the respondents sometimes use dexamethasone as monotherapy. Overall, 26.2 % estimated dexamethasone to have a high efficacy on CSDH.

A Glasgow Coma Score lower than 12 was considered to be the most important indication for surgery by 57.8 %. Double burr hole is the preferred surgical technique by 48.1 % of the respondents. One day after surgery, 69.3 % routinely orders a CT-scan.
Conclusions: The majority of the neurosurgeons worldwide remains reluctant in the use of conservative treatment methods in the management of CSDH. Further research is needed to assess the effectivity and side-effects of these conservative methods.

1. Introduction

Chronic subdural hematoma (CSDH) is a condition that is frequently seen in the neurological and neurosurgical practice. CSDH is most commonly seen in the elderly population [2,6]. With the ageing population there is an expected increase of CSDH worldwide, with an incidence of 58 per 10,000 among people older than 65 [2]. The incidence of CSDH in the general population is 5 per 10,000 [2,4].

Surgery by burr hole drainage is overall preferred in patients with neurological symptoms [1,16]. It is noted that a minor part of the neurosurgeons prescribe medical therapy, instead of or in addition to surgery, for the treatment of CSDH [1]. Conservative treatment may consist of prescription of ACE-inhibitors, corticosteroids, atorvastatin or tranexamic acid. The effectiveness of these medications is expected due to their anti-angiogenic, anti-inflammatory, or antifibrinolytic characteristics, respectively [7,10–13,22].

With regard to the treatment protocols, practice variation is shown by neurosurgeons, especially in the case of CSDH with mild neurological deficits. Treatment of CSDH, both surgical and conservative, varies across neurosurgeons [1,16,22]. Previous studies have shown that conservative treatment is usually not part of their routine [1,6,16]. More specifically, due to the lack of high-class evidence and guidelines, treatment with corticosteroids, ACE-inhibitors, tranexamic acid or atorvastatin is not adapted among neurosurgeons. The aim of the present study was to evaluate the use of different treatment strategies for CSDH among neurosurgeons employed in countries worldwide.

2. Material and methods

2.1. Study design

A survey has been created with SurveyMonkey. Questions were based on the literature and expert opinion [1,3,16,18].

The questionnaire contains twenty-one questions that can be

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divided into four sections:

1 Demographics of respondents
2 Frequency of surgical and conservative treatment methods used (classified as usually, sometimes or never).
3 Expected effectiveness and complications of conservative treatment (classified as highest, high, neutral, low or lowest).
4 Indication for surgery and surgical management (classified as most, more, neutral, less or least).
5 Postsurgical management e.g. indications postoperative CT-scan and timing of resumption of anticoagulants.

The member directory of the Congress of Neurological Surgeons (CNS), an international organization for neurosurgeons worldwide, was used to approach members. Retrievable email addresses of CNS members were used to send the survey in September 2019, with reminders after respectively two, four and six weeks to improve the response rate.

2.2. Statistical methods

Respondents' data were collected and processed with Microsoft Excel. For the quantitative and qualitative data analysis, software program STATA was used for the quantitative and qualitative data analysis. According to the type of data, a logistic regression was performed to estimate causal effects of the variables. Statistical significance was set at a 5% level.

3. Results

3.1. Demographics of respondents

The survey was completed by 443 neurosurgeons (response rate 7.3 %). Of all respondents, the majority was from North America (75.6 %) whereas Australia (0.7 %) and Africa (1.4 %) had the least respondents (Table 1, Fig. 1). The mean age of respondents was 50.5 years (± 13.4), with an average time of neurosurgical practice of 24.3 years (± 16.0). The substantial scope of practice of respondents was spinal surgery (69.3 %), neuro-oncology (58.0 %) and neurotrauma (63.7 %). More than 80 % of the respondents treated more than five patients with CSDH per year.

Table 1
Demographics of respondents.

Variable	N (%)	**Variable**	N (%)
Age, mean (SD)	50.5 (± 13.4)	**Patients with CSDH seen yearly**	N (%)
		0	5 (1.13%)
Gender, N(%)		1 to 5	36 (8.1%)
Male	395 (89.2%)	6 to 10	82 (18.5%)
Female	48 (10.8%)	11 to 20	137 (30.9%)
		More than 20	178 (40.2%)
Scope of practice	N(%)	Other	5 (1.13%)
Spine	307 (69.3%)		
Neuro-oncology	257 (58.0%)	**Operative procedures on CSDH yearly**	**N (%)**
Pediatric	87 (19.6%)	0	6 (1.4%)
Neuro-vascular	154 (34.8%)	1 to 5	73 (16.5%)
Neurotrauma	282 (63.7%)	6 to 10	138 (31.2%)
Functional	52 (11.7%)	11 to 20	105 (23.7%)
Epilepsy	42 (9.5%)	More than 20	118 (26.6%)
Peripheral	86 (19.4%)	Other	3 (0.7%)
Skull Base	152 (34.3%)		
		Continent, N (%)	
Time of practice, mean (± SD)	24.3 (± 16.0)	North America	335 (75.6%)
		South America	26 (5.9%)
		Europe	33 (7.5%)
		Asia	40 (9.0%)
		Australia	3 (0.7%)
		Africa	6 (1.4%)

3.2. Expected effectiveness and complications of conservative management

For conservative treatment of CSDH, dexamethasone was most frequently used: 25 (7.4 %) respondents reported to prescribe it "usually" and 157 (46.2 %) "sometimes" (Fig. 2). Other non-surgical options were rarely applied; ACE-inhibitors, atorvastatin and tranexamic acid were never prescribed by 92.0 %, 89.8 % and 78.7 % of the respondents, respectively. Other nonsurgical treatment options applied by single respondents were vitamin B or C, blood platelets or the Japanese herbal medicine Goreisan.

The expected clinical features of atorvastatin, ACE-inhibitors, dexamethasone and tranexamic acid are shown in Fig. 3. Nineteen (5.6 %) and 70 (20.6 %) respondents valued the expected effectiveness of dexamethasone to be the high or highest, respectively. As for the other treatment options, most respondents remained neutral towards the expected effectiveness: 41.5 % of the respondents have mentioned to be neutral about atorvastatin, 41.2 % about ACE-inhibitors and 51.6 % about tranexamic acid respectively.

Expected complication risk was the lowest for atorvastatin: 84 (27.2 %) and 52 (16.8 %) respondents expect it to be low or lowest, respectively (Fig. 3). Seventy-four (22.2 %) of the respondents expect the complication risk of dexamethasone to be high. The majority of respondents were neutral with regard to the expected recurrence risk of atorvastatin (N = 187, 60.1 %), ACE-inhibitor (N = 190, 61.3 %), dexamethasone (N = 173, 52.1 %) or tranexamic acid (N = 190, 60.9 %).

3.3. Indication for surgery and surgical management

Respondents were asked what clinical aspects of CSDH were expected to be the most important to indicate surgery (Fig. 4). The most important clinical indication for surgery is a Glasgow Coma Score (GCS) lower than 12 (57.8 %), followed by a motor response of 5 or lower on the GCS. The extent of the hematoma on the CT-scan is considered as another important indication; 42.6 % as more important and 49.0 % as most important indication, respectively.

Single burr hole and double burr holes were the techniques that were applied mostly (30.4 % and 48.1 %, respectively) (Fig. 2). Of all respondents, 95 (30.4 %) usually uses single burr hole and 150 (47.9 %) of the respondents sometimes uses this technique. Double burr holes are usually chosen for by 153 (48.1 %) respondents and sometimes used by 131 (41.2 %) respondents, followed by twist drill trephination, (usually used by n = 36, 11.6 % and sometimes by n = 87 28.2 %). Hemicraniotomy is never used by 134 (43.2 %) of the respondents. Furthermore, other treatment options applied were middle meningeal artery embolization (by 8 respondents) and minicraniotomy (by 18 respondents).

As for the surgical procedures, double burr hole is seen as most effective by most respondents (37.5 %) followed by hemicraniectomy (29.8 %) and single burr hole (13.9 %) (Fig. 5). Twist drill trephination was expected to have the lowest effectiveness. Hemicraniotomy and double burr hole surgery were expected to have the lowest recurrence risk (26.7 % and 13.5 % respectively). Of all respondents, 68.2 % routinely left a drain; 57.6 % subdural while 10.6 % subperiosteal. This in contrast to 7.5 %, that never leaves a drain. A logistic regression analysis showed no causal relation between tenure and gender of the surgeon, continent of employment or case load of CSDH treated and the preferred surgical or conservative treatment strategy.

3.4. Postsurgical management

3.4.1. Post-operative CT scan

Of the respondents, 69.3 % usually orders a CT-scan one day after surgical procedure (Fig. 6). With regard to resuming medication, 69.4 % and 59.6 % of the respondents orders a CT-scan before resuming oral anticoagulants or antiplatelet therapy, respectively.

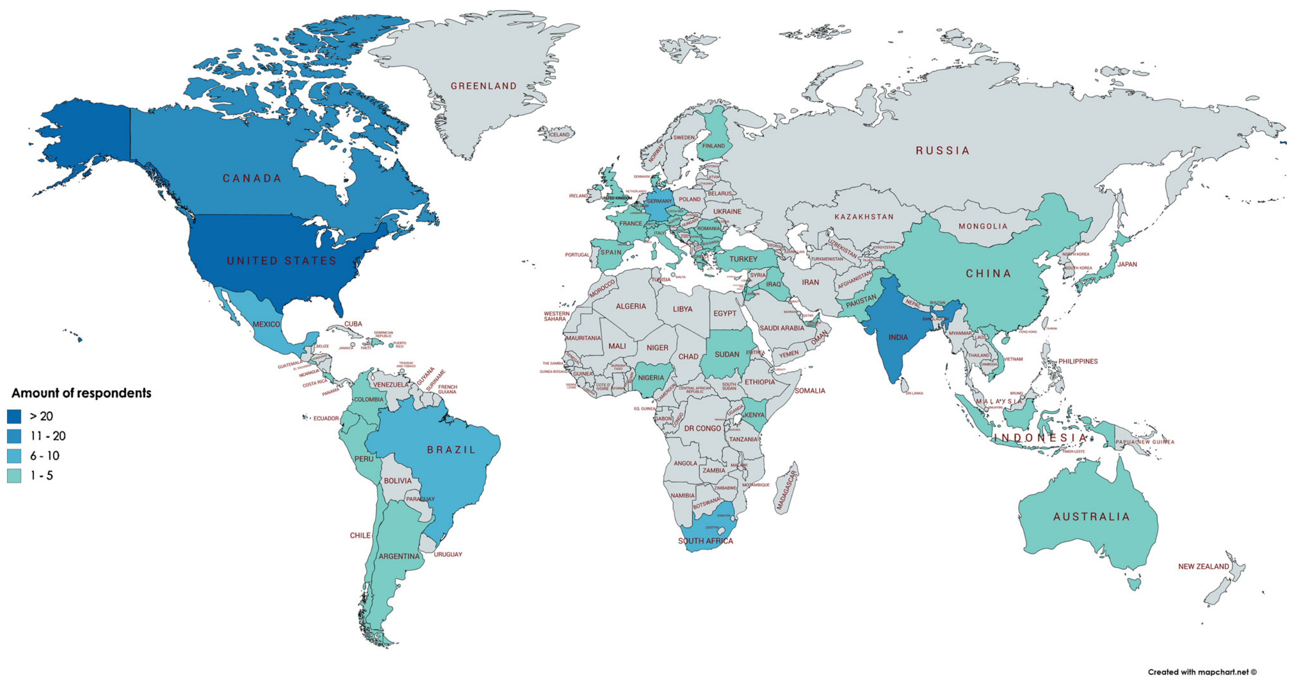

Fig. 1. Graphical overview of the respondents working locations.

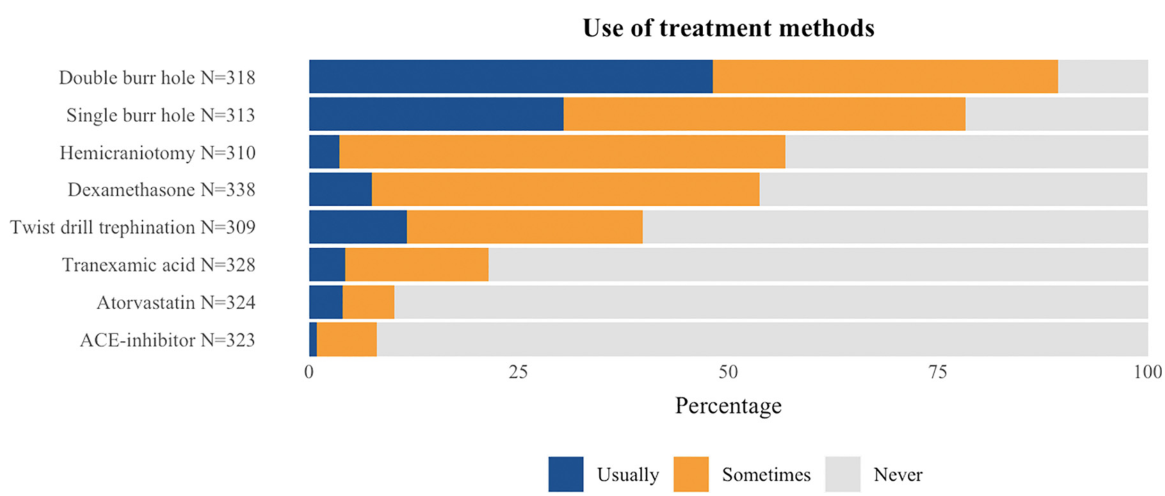

Fig. 2. Graphical overview of the surgical and nonsurgical treatment methods applied.

3.4.2. Resumption of antiplatelet and anticoagulant therapy

The resumption of antiplatelet or anticoagulant therapy one or two weeks after surgery is advised by respectively 107 (32.5 %) and 94 (28.8 %) of the respondents (Fig. 7). Twenty-two (5.0 %) of the respondents will allow resumption of anticoagulants and 6.7 % resumption of oral antiplatelet therapy within 1 week after surgery. Based on a postoperative CT scan 25.2 % of the respondents advises resumption of antiplatelet therapy and 32.1 % of oral anticoagulants.

4. Discussion

The aim of this international survey was to explore currently applied treatment strategies of CSDH. Among 443 neurosurgeons of which the majority treated more than five patients with CSDH yearly, conservative treatment methods such as atorvastatin, ACE-inhibitors and tranexamic acid were almost never used in practice. Sometimes dexamethasone was used by almost half of the respondents. Single and double burr hole surgery were the preferred surgical treatment options among neurosurgeons. Twist drill trephination and hemicraniotomy were infrequently used treatment options.

4.1. Comparison with other studies

The use of steroids in the treatment of CSDH has recently gained popularity as a treatment alternative [13]. Our survey shows that 46.6 % of the neurosurgeons sometimes used dexamethasone as a monotherapy. Miah et al. conducted a study to compare the clinical outcomes of patients with CSDH treated with dexamethasone as monotherapy versus primary surgical management [13]. They found similar clinical outcomes regarding to the modified Rankin Scale and Markwalder Grading Scale in patients treated with dexamethasone versus surgical management. At three months, 70 % of the patients in the group who received primary burr hole surgery had a favorable score on the modified Rankin Scale (0–3) versus 76 % of the patients who received dexamethasone initially. Furthermore, 96 % of both groups had a favorable score on the Markwalder Grading Scale (0–1). However, only 17 % of the patients treated with dexamethasone eventually did not had to undergo surgery. This “conservative first” treatment strategy,

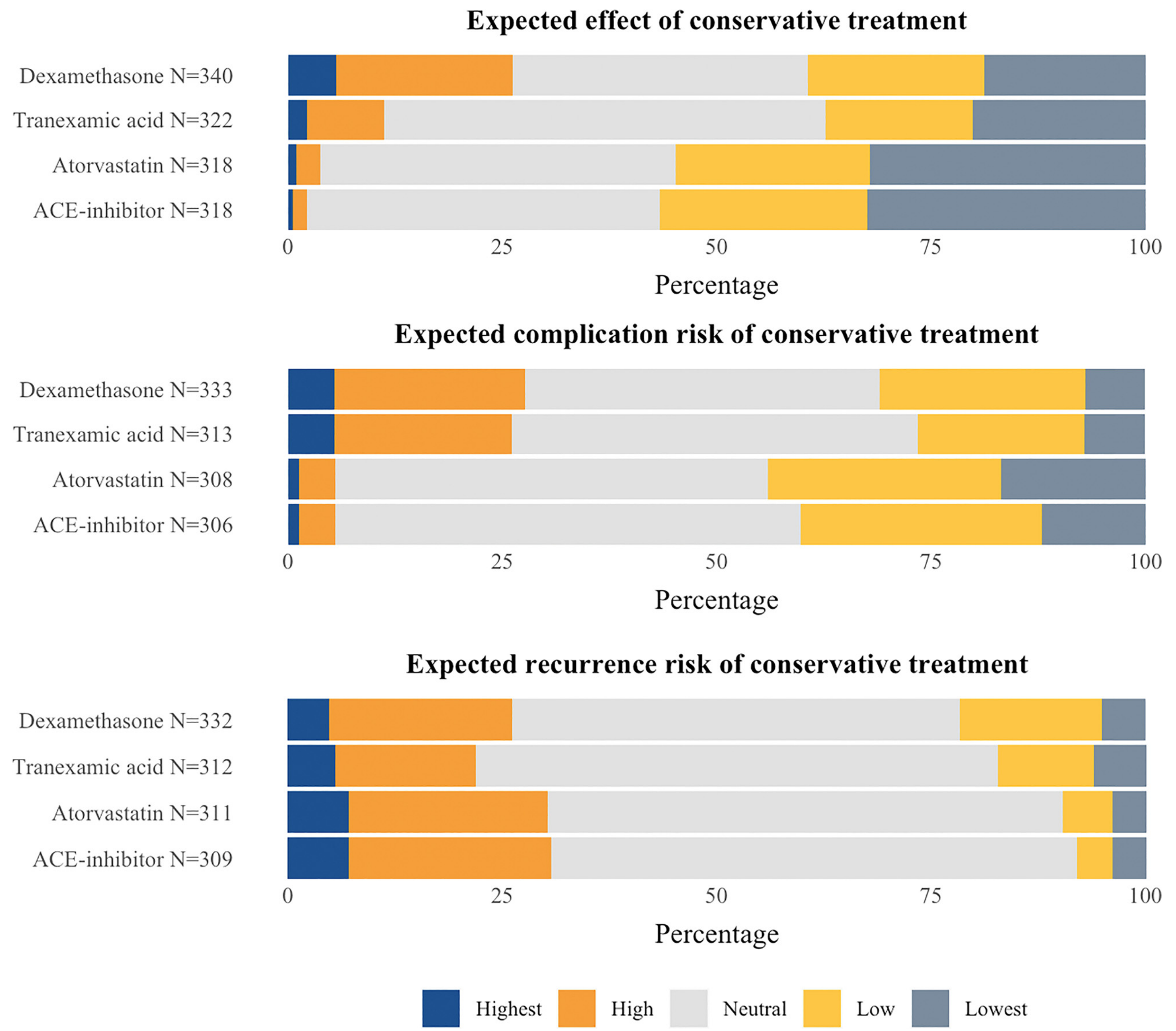

Fig. 3. Graphical overview of the clinical expectations of nonsurgical treatment methods.

however, resulted into longer hospitalization and a higher complication rate than primary burr hole surgery. Another retrospective study concluded that the use of dexamethasone after burr hole trephination reduces disease recurrence and complication risk [15,20]. The use of dexamethasone in the treatment of CSDH is currently subject of large randomized controlled trials of which the results are highly anticipated

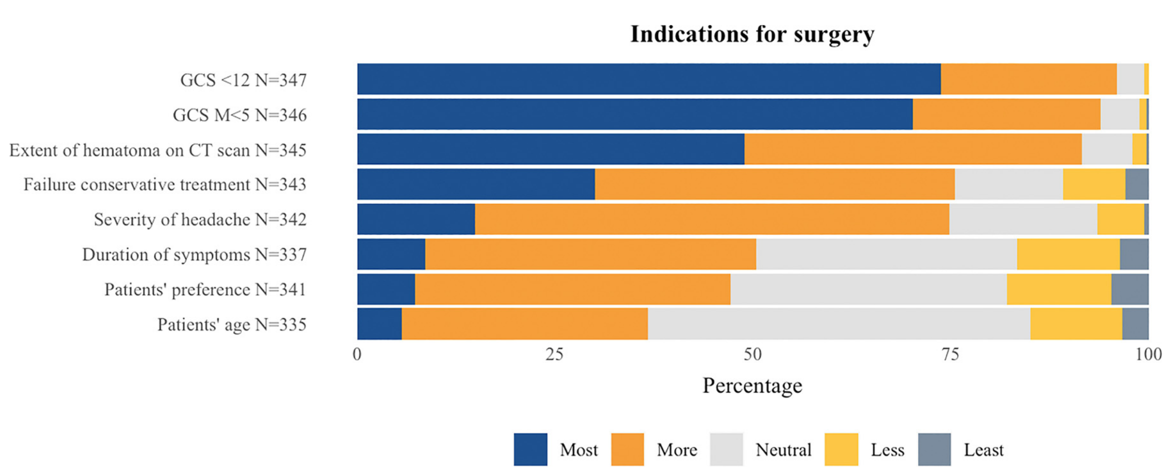

Fig. 4. Graphical overview of the indications for surgery.

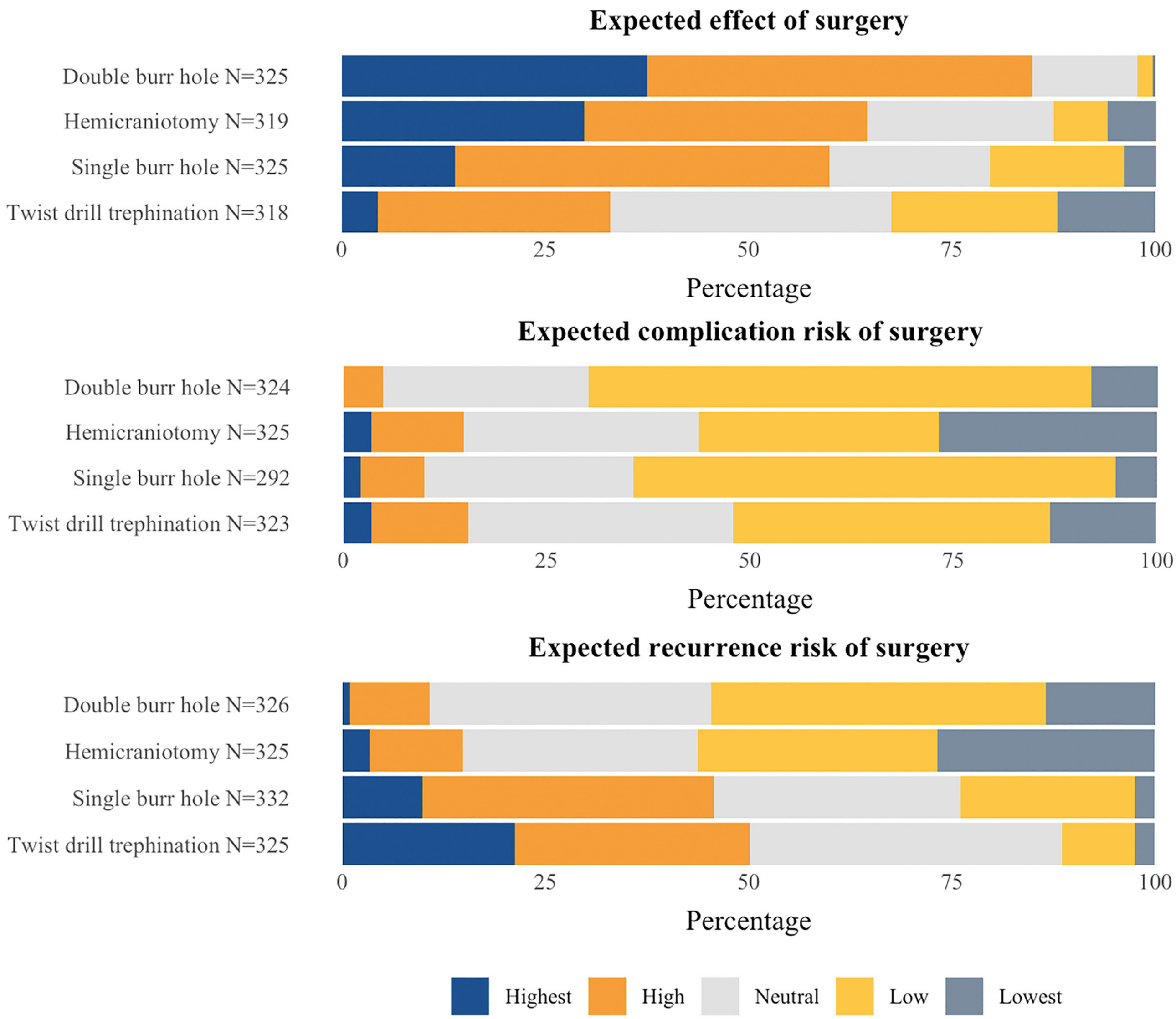

Fig. 5. Graphical overview of the clinical expectations of surgical treatment methods.

[4,14]

Atorvastatin is a conservative treatment method that is also expected to suppress inflammation at the site of the hematoma. Studies have also shown that atorvastatin elevates angiogenin levels and increases the expression of vascular endothelial growth factor [22]. The inflammation subsequent to the subdural hemorrhage has been suspected to disrupt the endothelial barrier cells, resulting in blood vessels that 'leak'. Through this mechanism, atorvastatin could be of merit in the management of patients with CSDH, reducing the hematoma, recovering neurological function and decreasing the need for surgery [10]. In our survey, most surgeons are reluctant to use atorvastatin as monotherapy as 89.9 % never uses it. A recent randomized controlled trial in which patients with CSDH were randomized between atorvastatin and placebo, showed that patients who received atorvastatin had a significantly more reduced hematoma as measured on CT-imaging and had improved more neurologically as compared to patients who

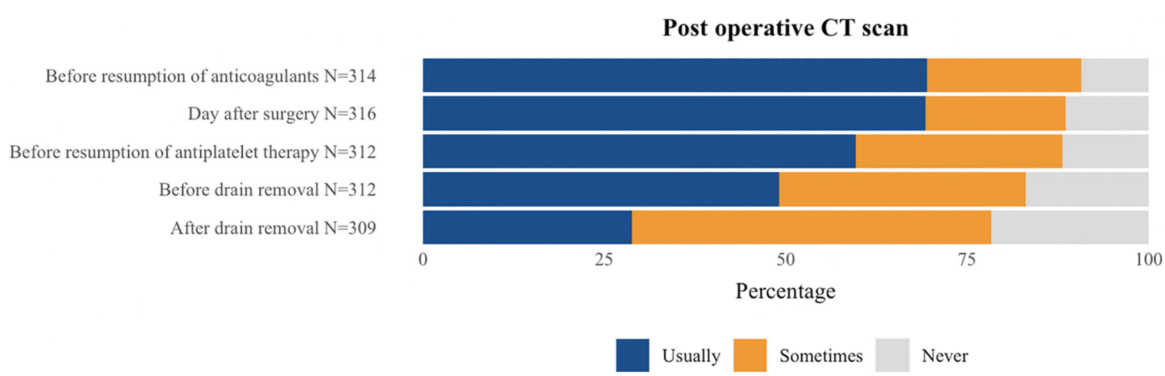

Fig. 6. Graphical overview with indications for a postoperative CT-scan.

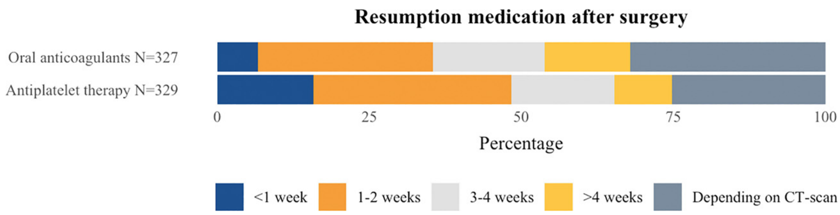

Fig. 7. Graphical overview when resumption of antiplatelet of anticoagulant medication is advised.

received placebo [10]. Also, in a pooled meta-analysis of 6 studies, the use of atorvastatin resulted in a decrease of recurrent CSDH requiring surgery [7]. Therefore, the use of atorvastatin could be an effective addition to the treatment of CSDH with and without surgery.

Tranexamic acid is a drug that has an antifibrinolytic and anti-inflammatory effect. It inactivates plasminogen. Therefore, it was hypothesized by Kageyama et al. that it inhibits hyperfybrinolytic activity that occurs at the site of a CSDH [11]. It is also thought to increase the permeability of cerebral vessels, thus increasing absorption of the hematoma [21]. In the retrospective study of Kageyama et al., 21 patients received tranexamic acid in the treatment of CSDH. Three of these patients received tranexamic acid concomitant to burr hole surgery. The other 18 patients received tranexamic acid as monotreatment. No adverse events occurred, including thromboembolic events. All patients in this study improved clinically while being treated with tranexamic acid. All patients were seen as cured and had no recurrence of their hematoma, underlining the clinical potency of tranexamic acid as a treatment option. In our study, tranexamic acid rarely had a place in the treatment of CSDH as 78.7 % of the surgeons never prescribe it.

A frequent adverse event after drainage of CSDH is recurrence of the hematoma. In the literature, recurrence rates of up to 30 % can be found [23]. Placing a subdural drain after hematoma evacuation has been shown to reduce the risk of recurrence by two to three times as compared to not placing a drain. Even on the long-term, placing a subdural drain after evacuation of CSDH is associated with improved survival. In our study, placement of drains was adopted by 68.2 % of the respondents. 7.5 % of the respondents stated to not leave a drain usually despite shown advantages.

The location of leaving the drain has been controversial [18]. In our study sample there was a clear favoritism for placing the drain subdural versus subperiosteal (57.6 % versus 10.6 %). Recently, results of a multicenter randomized controlled trial comparing subperiosteal versus subdural drain after evacuation of CSDH were published [19]. In that study, 220 patients were randomized to one of both drain strategies with the primary endpoint set on recurrence of CSDH requiring reoperation. Even though the predefined non-inferiority criteria were not met, placement of a subperiosteal drain led to lower recurrence rates and significantly lower surgical infections and drain misplacements. Together with nine other studies, of which two randomized studies, the results of this trial were pooled in a recently published meta-analysis [5]. The meta-analysis enforces the conclusion that subperiosteal drainage is associated with less recurrence of CSDH and lower rates of parenchymal injury of neurological deficit. The pooled results however, showed that rates of mortality, seizures, postoperative hemorrhage and infections were similar. Since two out of three randomized studies have only been published in recent years, we hypothesize that the implementation of subperiosteal drainage is expected in the coming period.

In this study sample, 69.3 % of the neurosurgeons ordered a routine postoperative CT-scan, one day after surgery. The value of these routine CT-scans has been the focus of discussion throughout the years. A recent study compared two neurosurgical centers with different policies; one frequently ordered routine postoperative CT-scans while the other only ordered CT-scans postoperatively if there was any neurological decline [8]. Postoperatively, patients of the first center underwent a median of 4 scans while patients at the latter underwent a median of 0 scans. Despite this difference in postoperative scans, there were no significant differences between both centers in number of reinterventions, while all re-interventions were preceded by neurological decline. In a single-center randomized controlled trial, Schucht et al. found no benefit in a routine CT-scan at 2 and 30 days postoperatively as compared to a CT-scan only by indication in regards to 6 month survival without severe disability (0–3 on modified Rankin scale) [17]. The latter group also underwent fewer repeat surgeries.

Other studies have reported comparable outcomes as this study. A survey held among Iranian neurosurgeons showed a strong preference for treating CSDH with a single burr hole with drain placement [9]. This procedure was applied in 64 % of the cases. Baschera et al. reported a slightly different conservative treatment pattern. Results from a survey among neurosurgeons in Austria, Germany and Switzerland showed that 45 % of the respondents at least once prescribed tranexamic acid [3]. In our study, tranexamic acid was used infrequently as 78.7 % of our respondents answered to never prescribe tranexamic acid. The strong favoritism for placing a drain subdural (which is the preference of 90 % of the respondents) in Baschera et al. is in line with the results from our study. In the same study, only 13 % of the respondents would not postoperatively order a routine CT-scan.

As only a proportion of 7.3 % completed the survey, the question raises if the results are representative. However, the absolute number of responses, 443 responses, is still higher than in other surveys conducted in this field so far. We assumed that the choice of completing a survey does not interact with management strategies of CSDH. Another limitation is that the strategy of watchful waiting has not been included in this study as a treatment option. Furthermore, embolization of the middle meningeal artery was not included in this survey as a treatment option as this procedure is often done by intervention radiologists in some countries, while this survey was more focused on neurosurgeons. However, neurosurgeons had the opportunity to give additional answers as an open-end response. As this study sample only included neurosurgeons, the treatment variation might differ in practice. CSDH is not only treated by neurosurgeons, but also neurologists. We assume that compared to neurologists, neurosurgeons tempt to be more biased concerning the conservative treatment methods. Therefore, these results might not reflect the treatment variation fully in practice.

5. Conclusion

Neurosurgeons remain reluctant in the use of conservative therapy in the treatment of CSDH. This might be due to the lack of evidence-based information and guidelines. However, studies have shown that several treatment options could play an important role in the management of patients with CSDH due to their anti-inflammatory and anti-fibrinolytic characteristics. These treatments could be administered in combination with surgery or as monotherapy. Further research is necessary to assess the effectivity and side-effects of these particular medicines. Furthermore, evidence-based guidelines need to be composed for the conservative management of CSDH. In order to do so, the pathophysiology of CSDH needs to be further studied.

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Declaration of Competing Interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

This article does not contain any studies with human participants performed by any of the authors.

CRediT authorship contribution statement

Eric R.A. Laldjising: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing - original draft. **Fleur M.G. Cornelissen:** Conceptualization, Formal analysis, Methodology, Supervision, Validation, Visualization, Writing - review & editing. **Pravesh S. Gadjradj:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Supervision, Visualization, Writing - review & editing.

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