VILNIUS UNIVERSITY
MEDICAL FACULTY

The Final thesis

PROGNOSTIC FACTORS IN CHRONIC SUBDURAL HAEMATOMA: SELECTION OF CRANIOTOMY

Ann-Kathrin Zernack, group 4

Clinic of Neurology and Neurosurgery

Supervisor: Gunaras Terbetas _____
(signature)

The Head of Department: Prof. Dr. Dalius Jatuzis _____
(signature)

Registration day at Department/Clinic_____
(filled in by technical assistant of Department/Clinic)

Registration n._____
(filled in by technical assistant of Department/Clinic)

Email of the student: ann.zernack@mf.stud.vu.lt

19.05.2022

SUMMARY

Chronic subdural hematoma is one of the most frequently observed pathologies in neurosurgery. Increased use of blood thinners and improved radiologic imaging techniques have led to a sharp increase in the incidence of chronic subdural hematomas in recent years. Although there are different approaches and theories about the origin of CSDH, most literary sources indicate that it is a chain of events that follow an initial event, usually a fall with trauma to the head.

The subdural space is one that is not present in healthy individuals but is created by the complex pathophysiological mechanisms of chronic subdural hematoma.

The formation of new blood vessels, in combination with reduced blood coagulation, leads to progressively enlarging bleedings. The resulting inflammatory and fibrinolytic processes lead to the characteristic patterns of chronic subdural hematoma.

What leads to the more difficult diagnosis are, among other things, the rather unspecific symptoms, especially in the case of minor bleeding. Especially symptoms such as urinary incontinence and memory loss are symptoms that are often overlooked, especially in the older generation, and are blamed on increasing age.

The most important component of the final diagnosis is the evidence provided by radiological images, CT and MRI. Again, a trained eye is needed to avoid misdiagnosing a chronic hemorrhage for an acute one. Specific here is the decreased density of the hemorrhage.

When it comes to therapy, it is often a preference of different surgeons, which method is finally chosen, whereby it must be said that the most invasive technique, the craniotomy is chosen rather rarely. The most popular techniques are burr-hole and twist-drill craniostomy. The choice of evacuation followed by drainage depends, among other things, on the location and size of the hemorrhage, and is an individual decision each time.

Chronic subdural hematoma is a disease that should not be underestimated and where the outcome depends on many factors. Early diagnosis and appropriate treatment methods are essential.

ABBREVATIONS

Ang	Angiopoietin
ASDH	Acute subdural hematoma
BH	Burr-hole craniostomy
CSDH	Chronic subdural hematoma
CSF	Cerebrospinal Fluid

FDP	Fibrin/fibrinogen degradation products
GCS	Glasgow Coma Scale
MMP	Matrix metalloproteinases
NO	Nitric Oxide
TD	Twist drill craniostomy
TDC	Twist drill craniostomy
tPA	Tissue plasminogen activator
VEGF	Vascular endothelial growth factor

1. INTRODUCTION

Chronic subdural hematoma is an accumulation of blood, in a cavity that forms between two newly formed membranes. Subdural refers to the section between the arachnoid and dura mater, as you can see in Fig.1 (addapted from Edlmann E et al. J Neuroinflammation 2017).

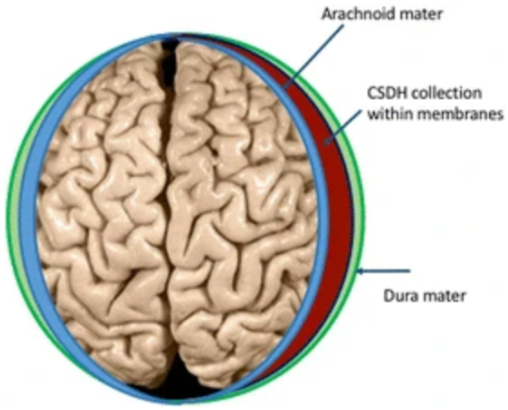

Fig.1 Schematic representation of a CSDH (1)

To date, chronic subdural hematomas are considered a disease of the elderly population. The stereotype is origin after fall on the head. Often, non-specific symptoms lead to a misinterpretation of the actual cause, which not infrequently leads to disastrous outcomes. However, even if a diagnosis of chronic subdural hematoma is made, there is still a risk of postoperative complications leading to the failure of surgery.

The postoperative outcomes are not always sufficient, several patients experience neurological deficits, stuporous in combination with or without focal sign, fall into a coma and the worst case scenario is that the patient dies postoperatively (2). The most common postoperative complications which are surgery-related are manifested in the form of focal or generalized seizures, subdural empyema and intracerebral hemorrhages. Another

complication is the reaccumulation of the hematoma or that the hematoma has not been completely evacuated.

Medical complications are relatively rare, the most common of which is pneumonia, which is usually easily treated with antibiotics. Only a small proportion of patients do not survive this complication. The following list includes the medical complications in order of frequency - the most frequent first - of their occurrence in connection with the postoperative period after chronic subdural hematoma evacuation: cardiac arrhythmias, thromboembolic and septic complications, pneumothorax, myocardial infarction, decompensating heart insufficiency, gastric ulceration and renal failure. Some of these complications had a fatal outcome (2). Especially if reaccumulation of the hematoma occurs or the hematoma has not been completely evacuated, the operation has failed, and further procedures must be considered. In some cases, the operation is repeated, and the application of a drainage system may be considered. Consideration may also be given to moving to the slightly less invasive twist-drill craniostomy in place of a burr-hole craniostomy. All in all, the outcome depends on many factors.

2. LITERATURE SEARCH STRATEGY

This thesis is based on a literature search in PubMed, but it was often redirected from there to other data bases, such as the National Center for Biotechnology Information (NCBI), Oxford academic, Springer Verlag, or Elsevier. It focused on everything related to chronic subdural hematoma.

By using the following keywords, chronic subdural hematoma, burr hole craniotomy chronic subdural hematoma, craniotomy chronic subdural hematoma, twist drill craniostomy chronic subdural hematoma, epidemiology chronic subdural hematoma, pathogenesis chronic subdural hematoma, clinical findings chronic subdural hematoma and drainage chronic subdural hematoma, a total number of 7879 possible articles was yielded. 3971 of these appeared when entering chronic subdural hematoma, 548 when entering burr hole craniotomy chronic subdural hematoma, 886 when entering craniotomy chronic subdural hematoma, 77 when entering twist drill craniostomy chronic subdural hematoma, 427 for epidemiology chronic subdural hematoma, 358 for pathogenesis chronic subdural hematoma, 700 for clinical findings chronic subdural hematoma and 912 for drainage chronic subdural hematoma. The search was narrowed by including primarily articles from the last 20 years, but since many authors cited articles from earlier years, the primary sources also consist of older publications.

In total, 102 papers were included in the thesis. Without exception, articles were selected that could be read free of charge or where access rights were obtained with the help of the Vilnius University VPN.

2. EPIDEMIOLOGY

In recent decades, a rapid increase in the incidence of CSDH can be observed (3), which is not only due to the increase in the use of blood thinners (4), but also to the ever-evolving imaging (5). Today, CSDH can be diagnosed that would have gone undetected 40 years ago.
Especially in developing countries, an increasing incidence of CSDH can be observed, which is about 0.0074% in the group over 70 years of age, which is mainly due to the increasing life expectancy (6).
What is striking when you look at the studies on CSDH is that about 50% more men are affected by the disease than women (3). The incidence is also significantly higher in the age group of 70-79 than in the rest of the population (5)(7)(3).
The mean interval between the development of CSDH due to trauma and subsequent surgery is 9 weeks.
In one study (8) (April 2020), 414 patients were observed, all with different age, mean age 79,2 years, and gender. 274 subjects were male, 140 were female. A total of 528 surgeries were performed in this group, due to bilateral occurrence.
Nevertheless, in asymptomatic patients, bleeding is treated conservatively with observation, medical management, and regular monitoring, especially by keeping an eye on intracranial pressure (9).
In addition, the study looked at the most common pre-existing conditions. Arterial hypertension is number one, followed by diabetes mellitus. In addition, other diseases such as cerebrovascular diseases, dementia, arrythmia and ischemic heart disease were listed (8).
Approximately 10.7% of patients with CSDH have a history of alcohol consumption and alcohol (10).

3. PATHOPHYSIOLOGY

3.1 Classical pathophysiology

While an acute subdural hematoma usually occurs as a result of a major traumatic event, with accompanied brain contusion and a hemorrhage which is temporally and causally related to the event(11), one approach to the development of CSDH is the occurrence of a traumatic event, which seems to be minor at first glance (12).

The trauma is thought to damage the veins that connect the cerebral cortex to the dural venous sinus. Especially in older people, the subdural space is enlarged due to atrophy of the brain (13)(14)(15), which makes the veins more stretched and fragile, making them more likely to rupture in the event of trauma and subsequent force (5).
Although many sources cite trauma as the cause, others express doubt that trauma is solely responsible for the progressive course of chronic hemorrhage.

3.2 More probable and modern understanding of pathophysiology

In the meantime, the theory that the hemorrhage is caused by damage to bridging veins connecting the cerebral cortex and the dura has been rejected.
And for good reason. The above-mentioned venous hemorrhage would lead to symptoms much faster than the definition of chronic subdural hematoma allows.
An alternative hypothesis has been put forward, considering an minor trauma followed by inflammatory process as the origin of the hemorrhage (1).
In Fig.2 (adapted from Edlmann et al. Journal of Neuroinflammation 2017), the mechanism is demonstrated.
The origin of a CSDH is seen in the dural border cells. The cells in this border have the task to either phagocytose or to develop into connective tissue, which in turn would lead to new formation of membranes (16).
When damage to the dural border cells occurs, an inflammatory response is initiated, due to which an attempt is started to repair this damage.
But instead of repair occurring, the proliferation of the cells happens and a new membrane is formed (1), called the outer membrane of the hematoma.
Within the first four days, the outer hematoma membrane is formed, which consists of a thin layer of fibrin and fibroblasts. Within the next two weeks, formation of the inner hematoma membrane occurs on the opposite side (17). Between these two membranes a new space is formed, the subdural cavity, which is considered a space for the accumulation of blood and fluids (1).

3.2.1 Angiogenesis

Angiogenesis describes the process of new blood vessel formation and forms the origin of bleeding source in the development of CSDH (1).

The two membranes differ mainly in their vascularization. While the inner one is hardly permeated by blood vessels, the outer one is highly vascularized(18) and is considered as source for further bleeding events and supports the growth of the hematoma (5)(19).
The difference is due to a varying concentration of angiopoietin (Ang) between the inner and outer membrane.
It has long been known that angiopoietins play an important role in the permeability of the blood-brain barrier. The concentrations of Ang-1 and Ang-2 are particularly striking, as the effects of the two are very different (20). Ang-1 is known to provide a stable microvascular network and lower permeability than Ang-2, so it is not surprising that the outer membrane of the CSDH has a high concentration of Ang-2 (21)(22). Ang-2 leads to the instability of blood vessels and an increased bleeding tendency.
Also to be named as a pro-angiogenic factor is vascular endothelial growth factor (VEGF). Like angiopoietins, VEGF has an influence on the permeability of vessels (23). It has been shown that VEGF is present in increased concentrations in CSDH fluid compared to blood from peripheral parts of the body (22)(24–29).
A product which is critical in the process of angiogenesis is nitric oxide (NO). NO is produced by phosphatidylinositol 3-kinase-serine/threonine kinase (PI3-Akt) pathway, where VEGF is part of (30). In addition, the pathway influences and regulates cell proliferation, leading to the conclusion that the concentration of VEGF has a direct influence on angiogenesis and leads to excessive vascular permeability in the outer membrane (25).
Finally, matrix metalloproteinases (MMPs) should be addressed in the context of the angiogenesis process (31). MMPs also alter membrane permeability, and meanwhile additionally participate in many other inflammatory processes by modulating other mediators such as cytokines and chemokines (32). A high concentration of MMPs leads to disruption and instability of membranes and ultimately this leads to increased bleeding propensity (32).
This pathological formation of blood vessels in combination with a reduced blood coagulation leads to an unstoppable enlargement of the hematoma (19).

3.2.2 Inflammation

The external membrane also contains a number of inflammatory cells such as neutrophils, lymphocytes, macrophages and eosinophils which in combination with layers of fibroblasts and collagen fibers are the main factor in the growth of the hematoma (24–26,33–35). These cells, which are responsible for inflammatory processes, are highly regulated by cytokines. There are both pro- and anti-inflammatory cytokines, but the concentration gradient is

strongly in the direction of the pro-inflammatory cytokines when the fluid in the CSDH is examined (36)(37).
The external membrane also shows an evolutionary change, which is accompanied by inflammatory processes, followed by scarring. Within this process, again, there are cuttings on the membrane, which recurrently start to bleed into the cavity (1)(33).

In summary, the clinical development of CSDH goes through three phases (38). The first phase consists of the minor traumatic event (39), followed by a symptom-free phase that lasts from weeks to years (39–42). During this time, the hematoma has time to increase in volume, which eventually leads to the third phase, the appearance of symptoms (13).

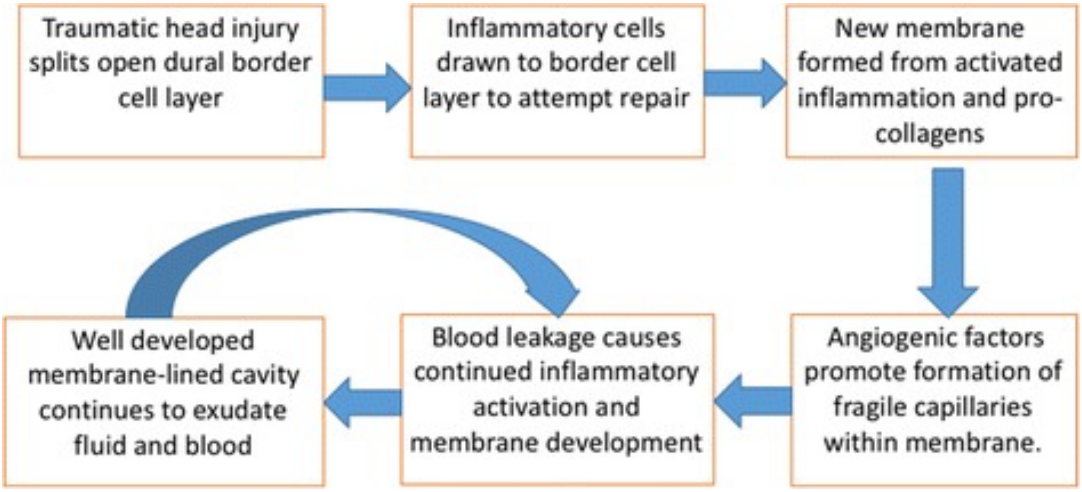

Fig.2 The CSDH cycle. Summary of the pathophysiological processes involved in the formation of a CSDH (1).

3.2.3 Fibrinolysis

The lowered blood clotting, which is observed in CSDH, is favored, among other things, by an increased concentration of tissue plasminogen activator in the outer hematoma membrane, which lowers the natural blood clots and the coagulation in the hematoma.
tPA, which is also considered to be an inflammatory drive and mediator of angiogenesis, among other things (43)(44), is responsible for the conversion of plasminogen into plasmin, which in turn helps in the conversion of fibrinogen and fibrin (5)(43) into fibrin/fibrinogen degradation products, which acts as a breakdown of clots (45).
It has been shown that there is an increased concentration of FDPs and D-dimers in the external hematoma membrane, which is why blood in CSDH remains fluid and does not

coagulate (12)(46), due to elevated fibrinolysis and continuously hemorrhagic process (47–49).

In different types of CSDH, different concentrations of fibrin and FDPs were observed. Among others, in the mixed density and layered CSDH types, an increased concentration was found, from which it can be concluded that fibrin and FDPs have an influence on the amount of bleeding, and thus affect the growth and the different patterns of the hemorrhage (49).

Fig 3 (adapted from Edlmann et al. Journal of Neuroinflammation 2017) illustrates both angiogenesis, the inflammatory mechanism, and the fibrinolytic one.

3.3 Other etiological events

In addition to developing CSDH directly because of minor trauma, CSDH can also develop as a secondary consequence of ASDH (11). However, this rarely occurs, as it can only happen if the pre-morbid condition is suitable (39). If it occurs, its mainly when treatment of the primary hemorrhage is not possible because the patient is in such a poor condition that he cannot be expected to undergo a craniotomy under general anesthesia.

When changing to a CSDH, liquefaction occurs, which can become an advantage in unstable patients, as the hematoma can then be treated by minimally invasive techniques(11).

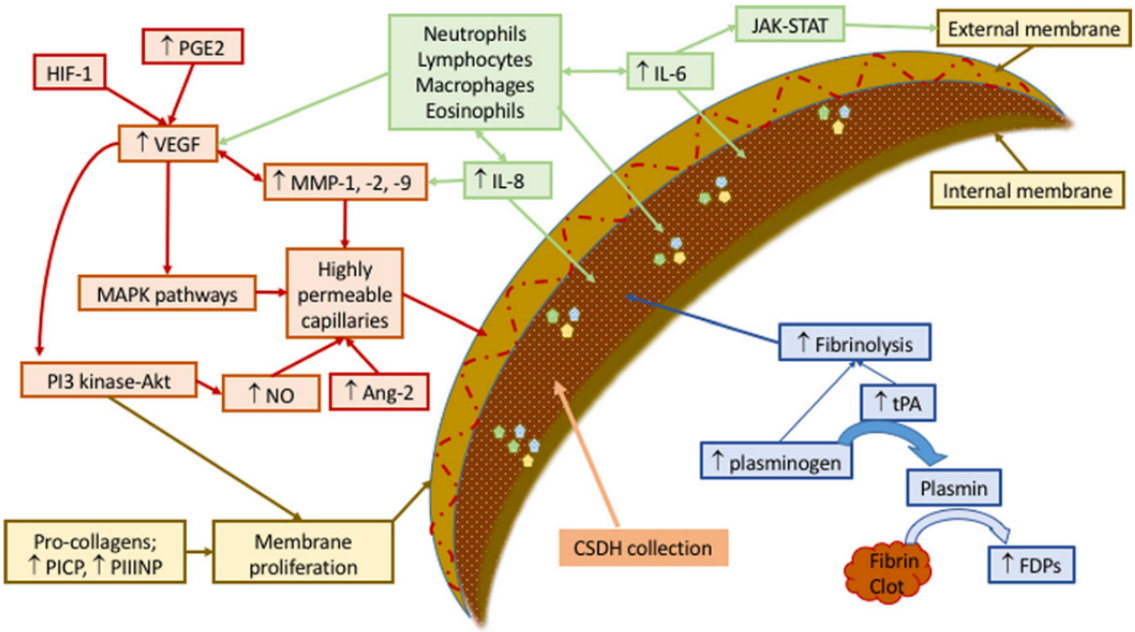

Fig. 3 "Summary of molecules associated with CSDH formation including recruitment of inflammatory cells (green), angiogenesis of highly permeable and leaky capillaries (red), processes supporting membrane formation (brown) and fibrinolysis promoting further hemorrhage (blue). Abbreviations: Ang angiopoietin, FDPs fibrin/fibrinogen degradation

products, HIF hypoxia-inducible factor, IL interleukin, JAK-STAT Janus kinase-signal transducer and activator of transcription, MAPK mitogen-activated protein kinase, MMP matrix metalloproteinase, NO nitric oxide, PGE prostaglandin E, PI3-Akt phosphatidylinositol 3-kinase-serine/threonine kinase, PICP procollagen type 1, PIIINP procollagen type 3, tPA tissue plasminogen activator, VEGF vascular endothelial growth factor" (1)

4. CLINICAL PICTURE OF CSDH

Common presentations

When a patient presents with CSDH, it is not always a clear presentation of symptoms, but there may be variations, up to complete symptom lessness. One of the most common symptoms is the occurrence of hemiparesis in 58% of cases (50) with accompanying change of character (5). A deficit such as drowsiness, is usually accompanied by limb weakness, which usually occur contralaterally (50). There may also be experiences of seizures, decreased memory and speech, difficulty swallowing or walking (12).

Symptoms such as limb weakness, memory loss, and urinary incontinence were more common in older patients, and younger patients with CSDH were more likely to present with seizures and headache (10).

In addition, a pronounced altered mental state can be observed in older people between 50-70% (51)(52)(53). This altered mental state is often defined as confusion, accompanied with drowsiness and in worse cases coma. In extreme cases, psychotic symptoms can also be seen, and depressive episodes and paranoia can occur because of CSDH. Especially such symptoms are difficult to recognize with preexisting psychical problems and are often attributed to them (54).

While some sources point out that headaches are common, but usually occur in conjunction with focal neurological deficits, and rarely alone (5), others name headaches as the most common symptom(10). Generally you can say, that headaches appear more frequently in younger patients with underlying CSDH then in elderly's (55). Since CSDH is characterized by a whole cluster of non-specific neurological symptoms, the diagnosis tends to be confused with, for example, transient ischemic attack (also called TIA) (5)(56).

When it comes to examining the Glasgow Coma Scale, a high average of 13-15 is common (10).

It is rare that once neurological deficits have occurred that they fluctuate but rather that they occur slowly and increase continuously (50)(57).

Uncommon presentations

Rare manifestations in patients with CSDH include isolated neurological deficits. This category includes vertigo and nystagmus. It is assumed that these are caused by the increasing intracranial pressure, since it comes to stretching of the cranial nerves and thus the symptoms are triggered (58–60).

Another group of syndromes that have been observed in association with CSDH are extrapyramidal syndrome. Both parkinsonian phenomenon (61) and akinetic rigid syndrome have been observed. Complete resolution of akinetic rigid syndrome occurred after CSDH was treated surgically (62). These symptoms are thought to be caused by compression of the midbrain (51).

Also, a syndrome that is shown to be reversible after surgery is Gerstmann's syndrome. This is a syndrome with symptoms such as disorientation between left and right, finger agnosia and acalculia. In connection with this, quadriparesis has also been observed (63)(64). Again, the patients showed a good outcome postoperatively (51).

Grading System

With the Markwalder grading system (Fig.4 adapted from Markwalder M.D. Journal of Neurosurgery 1981), patients can be divided into five different grades based on the severity of their symptoms, ranging from grade 0 to grade 4, last-mentioned being the most severe (65).

Grade 0	No neurologic deficits
Grade 1	Mild symptoms (ie, headache, absent or mild neurologic deficits like reflex asymmetry)
Grade 2	Drowsiness or disoriented with variable neurologic deficit (ie, hemiparesis)
Grade 3	Stupor, severe focal neurologic deficit (ie, hemiplegia)
Grade 4	Coma, posturing, or absence of motor response to noxious stimulation

Fig. 4 Markwalder scale for grading clinical condition in chronic subdural hematoma (65)

5. RADIOLOGICAL PICTURE OF CSDH

Chronic subdural hematomas can present in a wide variety of patterns.

In addition to a detailed medical history interview, a complete physical examination as well as a blood test is an integral part of the diagnosis of CSDH. This is followed by the radiological examination. CSDH can be detected by MRI or CT.

In radiological classification, a distinction is made between MRI and CT scans. CT (Fig. 5 adapted from Fujisawa H et al. Neurologia medico-chirurgica 2006) can reveal five different forms of appearance: low, high, and mixed density, isodensity and layered. Based on the density, you can further distinguish (Fig. 6 adapted from Shen et al. Risk Management and Healthcare Policy 2019). MRI (Fig. 7 adapted from Fujisawa H et al. Neurologia medico-chirurgica 2006), on the other hand, distinguishes between low, high, mixed intensity, isointensity and layered. Additionally to that you can subdivide the high intensity type into moderately and very high (66).

The differentiation of the different densities helps, among other things, to make a prognosis of recurrent bleeding. Among others, hyperdense, laminar and separated types are considered bleedings with increased risk of recurrence (67).

In contrast, the homogenous and trabecular CSDH types are considered to have a low recurrence rate (68).

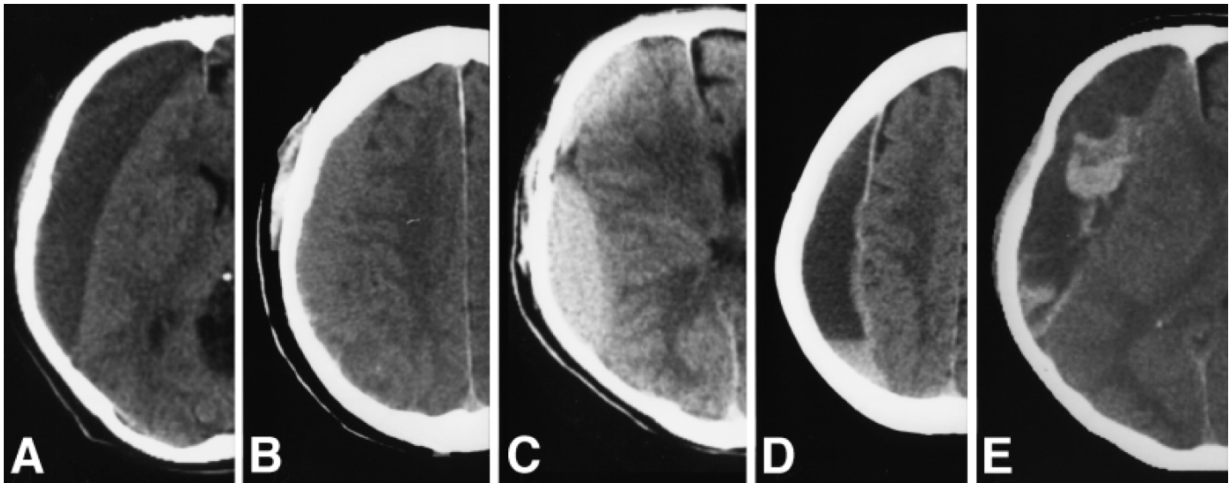

Fig.5

"Computed tomography appearance of chronic subdural hematoma. A: low density, B: isodensity, C: high density, D: layered, E: mixed density" (66)

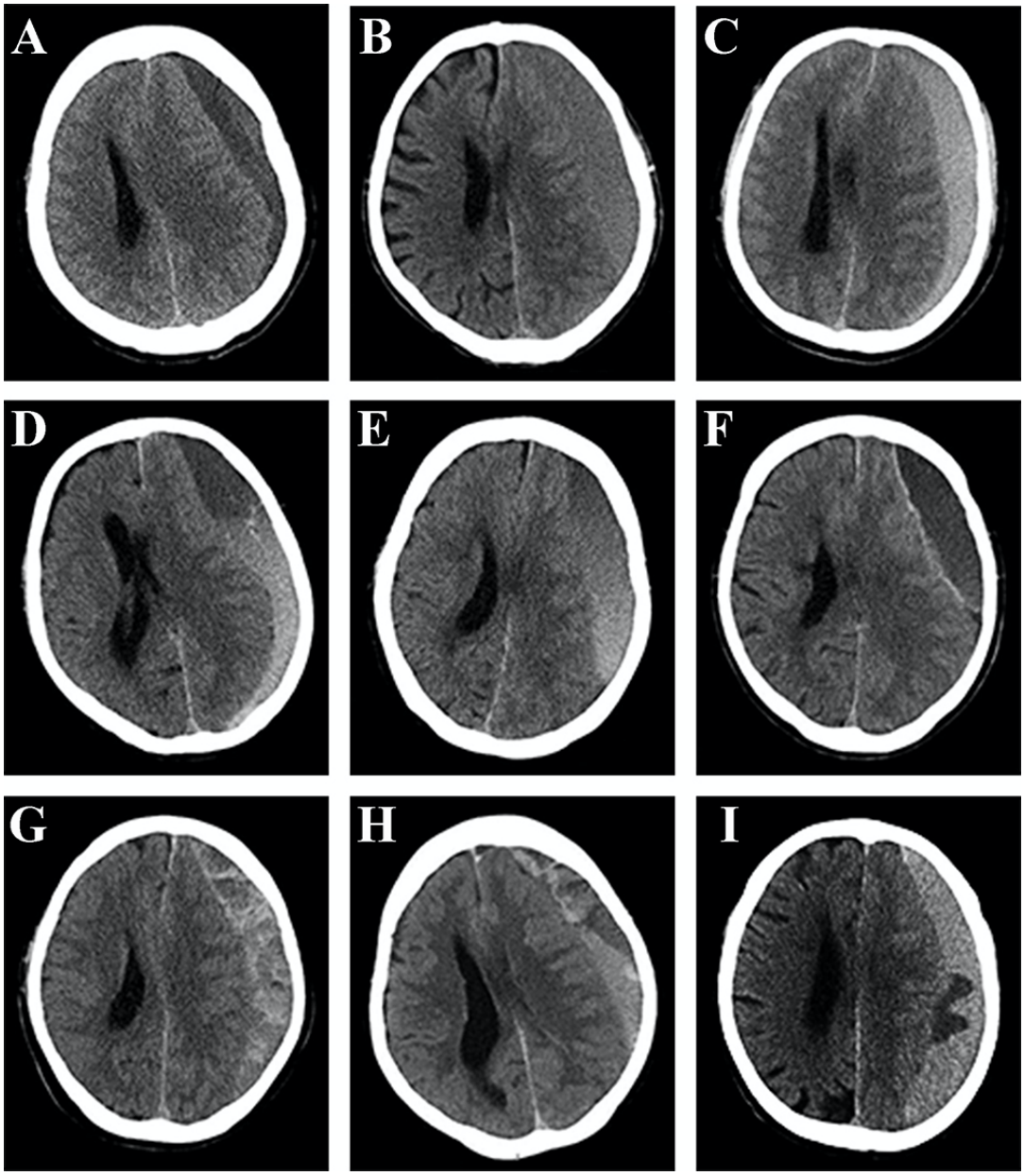

Fig. 6

"CT performance: (A) Homogenous hypodense. (B) Homogenous isodense. (C) Homogenous hyperdense. (D) Separated type, the two components of the hematoma are clearly separated. (E) Gradation type, the density of the hematoma gradually changes from hyperdense to hypodense. (F) Laminar type, a linear hyperdense located in the inner membrane of the hematoma. (G) Trabecular type, the hematoma was separated by several high-density septa. (H and I) Mixed density, two or more types of CT density appear on one layer or on the different layer in one patient"(67)(69)

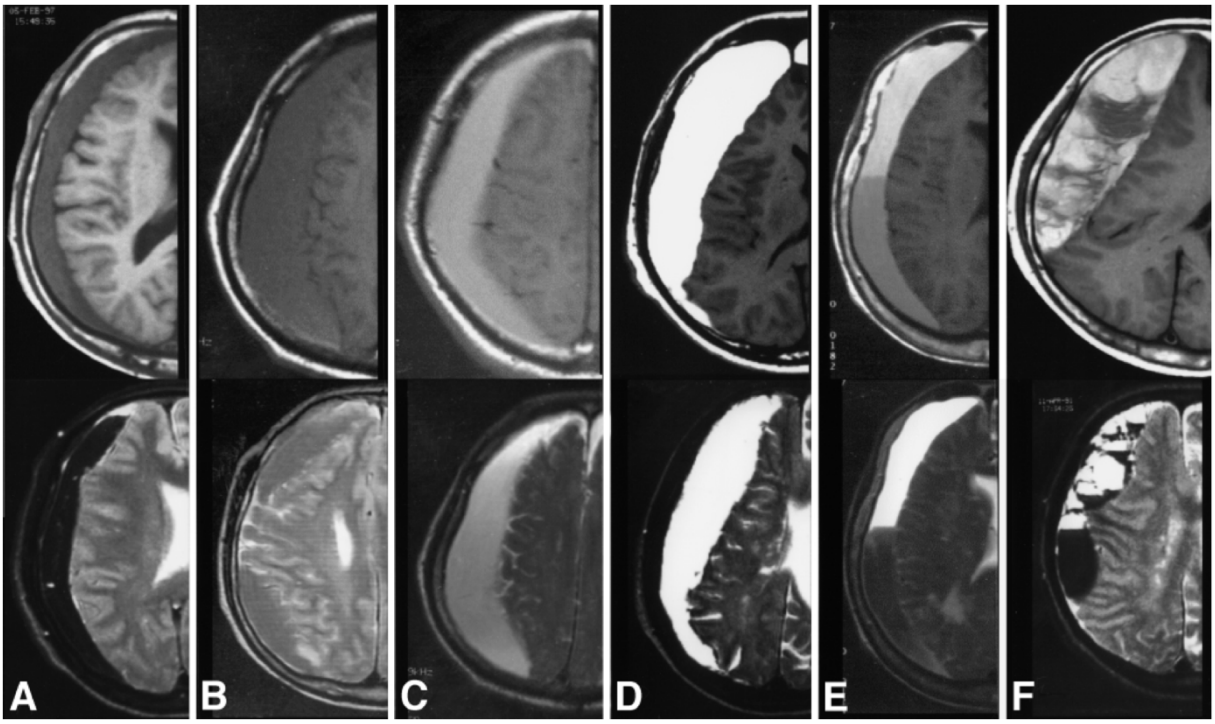

Fig.7

"Magnetic resonance imaging appearance of chronic subdural hematoma. The hematomas were classified into five types: low intensity (A), isointensity (B), high intensity (C, D), layered (E), and mixed intensity (F) on both T1- (upper row) and T2-weighted (lower row) images. The high intensity type could be subdivided into the moderately high (C) and very high intensity (D) types. (66)

The density of the hematoma depends on the time between the hemorrhage and the resulting image. If there are only a few hours between the event and the CT, the hemorrhage will be hyperdense against normal brain tissue. In this period, the bleeding is still considered acute. If there is some time between the onset of bleeding and imaging, in the subacute period, degradation of the clot occurs and the density is reduced. Subacute bleedings can be slightly hyperdense but also up to isodense in comparison to the brain parenchyma. Thus, the density of the hemorrhage is an important factor in the diagnosis of CSDH because the density decreases the further the onset of the bleeding event.
When considering homogenous isodense hematoma, it is sometimes difficult to judge where the hematoma ends and normal brain tissue begins. Therefore a lot of patients with revealed CSDH by CT undergo MRI to distinguish further (69). If you have fresh bleeding within a CSDH, the fresh blood is seen hyperdense against the hypodense CSDH on CT (arrow Fig. 8 adapted from Masdeu J. et al. Bradley and Daroff's Neurology in Clinical Practice 2022).

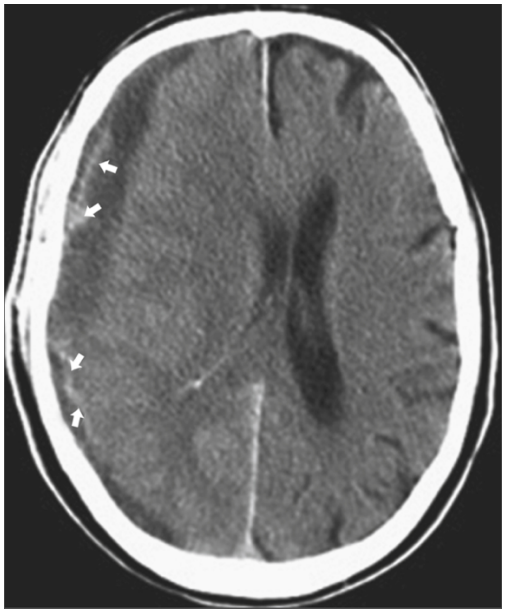

Fig. 8

"Chronic Subdural Hematoma on Computed Tomography (CT).
Axial non-contrast CT scan shows a hypodense subdural collection over the right frontal and parietal lobes. Right hemisphere is compressed, and midline shift is present. Note hyperdense areas within the subdural collection, suggestive of another more recent bleeding episode (arrows)" (70)

On magnetic resonance imaging CSDH appears with decreased intensity compared to the normal brain tissue but due to the higher protein content, the bleeding appears with increased intensity against the cerebrospinal fluid on T1/T2-weighted images. Within the hemorrhages, hemosiderin depositions occur (arrow in Fig. 9 adapted from Masdeu J. et al. Bradley and Daroff's Neurology in Clinical Practice 2022), which are hypointense (70).

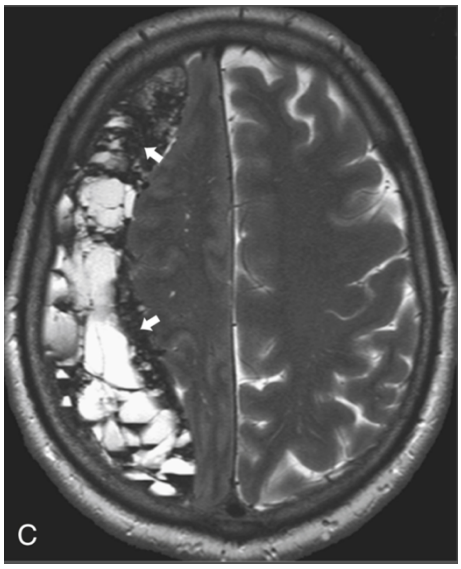

Fig.9

"Axial T2-weighted image of a different case. Within the hyperintense subdural collection, multiple hypointense zones are seen; these are due to hemosiderin deposition (arrows)
There is prominent mass effect on the hemisphere." (70)

If the hemorrhage is stable, the hemorrhage is isointense to the cerebrospinal fluid in the T1 image, hyperintensity of the hemorrhage compared to the CSF occurs when there is a rebleed or infection.
In contrast, stable hemorrhage in the T2 image of the MRI shows isointense against the CSF and when rebleeding occurs, it appears hypointense (71).

In 2001, Nakaguchi classified the various architecture of the CSDH.
When the hematoma has a homogeneous density, it is called homogenous type.
If it is possible to radiologically visualize a layer with high density along the inner membrane, it is the subtype of the homogenous type, the laminar type.
If one visualizes a hemorrhage that consists of two different density components, again separated by a clearly apparent boundary, it is the separated type.
The trabecular type is defined as an inhomogeneous hematoma and has a high-density septum. This runs between the inner and outer membrane on a background of low to isodense density (72)(68)(73).

When the CSDH is considered in context to the surrounding tissue, the chronic hemorrhage stands out as hypodense to the adjacent cortex and is isodense when compared to the cerebrospinal fluid. There is no mistaking the similarity with the subdural hygroma.
Sometimes calcified CSDH is seen, which occurs when the periphery of the hematoma calcifies (71).
You cannot distinguish a CSDH from a subdural hygroma just by taking a CT scan, especially since it can also coexist with a subdural hematoma (71).

6. TREATMENT

Asymptomatic patients with no evidence of midline shift or no brain compression should be spared invasive surgery and treated conservatively.
In some cases, minor hematomas may resolve on their own and not require surgical treatment (74). If this is not the case, you can choose between three different surgical methods.
Craniotomy, twist drill (TD) and burr hole (BH) craniostomy (Fig. 10 adapted from Lee K. M.D. Journal of Korean Neurosurgical Society 2019).
Nevertheless, it is generally accepted that a patient presenting with chronic subdural hemorrhage with neurologic symptoms should be treated surgically.
Especially if there are changes in the neurological status, surgical operation is indicated.

The decision becomes more complicated when the brain is compromised but the patient presents asymptomatic. In widespread use, a hematoma with a thickness of more than 1 cm is considered an indication for surgery (73).

Item	Craniotomy	Burr hole	Twist drill
Anesthesia	General	General or local	Local or general
Place	Operating room	Operating room or bedside	Bedside or operating room
Operation time	Around 3 hours	Around 1 hour	Less than 1 hour
Complications	High	Low	Low
Recurrence	Low	Slightly high	High (?)

Fig.10
Characteristics of three operative methods (75)

Craniotomy

Craniotomy is the most invasive surgical procedure and describes a skull opening of more than 30mm in diameter.
During this operation, the largest part of the brain is exposed, but this also opens up the largest surgical field for the surgeon.
Compared with the other two surgical techniques, the morbidity is significantly higher in craniotomy (76).
Among other reasons, this is also due to the fact that both the operation time is the longest, the blood loss is the highest and due to the high invasiveness there are the most postoperative complications (73).

Burr-hole craniostomy

In most often cases, surgeons decide to evacuate a CSDH by proceeding with Burr-hole craniostomy (2,77), since it remains the gold standard choice for treatment (78). Moreover, with this treatment option, there is a good balance between an envious recurrence rate and morbidity and mortality (73). In BH craniostomy you have a skull opening of up to 30mm in

diameter (76). BH can be either performed under general or local anesthesia (79). You can perform this surgery by using a single hole, others use two. Nevertheless, there is some evidence that when performing with a single hole, the patient's recovery period is significantly facilitated by a shorter stay in the hospital, a lower likelihood of recurrence of hemorrhage and a lower surface for attack by infectious diseases (80). However, even with this example, there are contrary studies that believe it makes no difference whether you choose single hole or double hole procedure (81)(82).
Also controversial is whether irrigation after concluding burr hole is beneficial or not. There is also the option of continuous inflow and outflow irrigation, which some sources cite as a reason for lower recurrence (83). Clearly, irrigation has no influence on mortality or morbidity (73)(83)(84).

Twist-drill craniostomy

TD craniostomy is an opening of the skull of 5mm, and thus the most minimally invasive surgical method (76).
One of the great advantages of TD craniostomy is that it can be performed both bedside and under local anesthesia. This makes it especially attractive for patients who have various pre-existing conditions that make surgery with general anesthesia impossible (79).
As a common procedure, a closed drainage system is placed after surgery to promote brain expansion and counteract postoperative complications (79).

Non-Surgical treatment

A popular non-surgical treatment option for CSDH is the steroid dexamethasone, which is known for its anti-inflammatory and anti-angiogenic effects.
The drug is thought to significantly lower mortality (85), which may be partly due to the fact that dexamethasone inhibits the remodeling of blood vessels, thus preventing the development of additional sources of bleeding (86). Additionally to that, dexamethasone has proven to reduce the recurrence rate (87,88).
Both the drug dexamethasone and atorvastatin are said to prevent the need for BH treatment (89)(90). Atorvastatin also leads to a better neurological function, plus if it is given additionally to surgery, it decreases the recurrence rate of CSDH (91,92).

7. SURGICAL APPROACH

When it comes to the treatment of CSDH, one can resort to both surgical and non-surgical methods. Surgical intervention should be considered when conservative treatment has not been successful or cannot be seen as a treatment option (78).

The approach to surgical treatment of CSDH has changed significantly in recent decades. Diagnostic capabilities have also improved, allowing the detection of CSDH that would have remained undetected a few years ago (75).

The decision on which surgical procedure to choose is affected by many different factors, among other things, of the appearance of the bleeding by imaging or the general status of the patient (79).

Craniotomy

When a patient presents with a solid hematoma, usually craniotomy is the procedure of choice. Also when you have reaccumulation of blood and symptoms reoccur, or the chance of reoccurrence is high, you would choose this treatment option (51). If the CSDH presents with very thick membranes and is already calcified, despite the increased risk for intra and post-operative complications, you would consider craniotomy as first choice operation (93). Another indication for craniotomy is when the brain fails to expand and obliterate the subdural space, or numerous thick membranes are present (73).

Twist drill craniostomy

TD craniostomy or trephination was considered a safe surgical method, with a low mortality rate, few cases of reoccurrence, and compared with burr-hole craniostomy, the hospitalization time was much shorter (94). Although it must be said that the risk of contamination is increased when the procedure is performed bedside.

Twist-drill craniostomy is an attractive treatment option when the blood is almost completely liquefied and membranes are not present (73).

Burr Hole craniostomy

When a patient presents with an uncomplicated hematoma, which nevertheless requires a surgical evacuation, BH is the operation technique of choice (95).

BC has the ideal balance between mortality rate, recurrence and limited complications when viewed in relation to the other two Surgical approaches (95).

Non-surgical treatment

If a patient presents with mild symptoms and the hematoma on imaging proves to be small and rather isodense, and there is also no obvious ventricular dilatation, the patient has the best chance of spontaneous resolution (74).

In such patients one can apply medications to support the resolution process. For patients who would not withstand surgical intervention, this is also the first-choice treatment option (73).

8. NEED OF DRAINAGE

The placement of a drain is very common especially when evacuating the bleeding through the burr hole procedure. Efficacy is characterized by reduced recurrence and improved outcome within the next 6 months (96). In addition, mortality is reduced (73).

However, the introduction of a drain also carries some risks. Especially if misplacement occurs in the wrong place. Among other things, symptoms such as unwanted bleeding, swelling of the brain and prolonged hospitalization can be the result (96).

In some situations, it is believed that the benefits of drainage do not outweigh the risks. Unintended risks such as infection, hemorrhage from neomembranes, and brain damage that can occur during drainage make it a very risky procedure (97)(94).

In order to reduce the risk of complications, the placement of drains in the subperiosteal space was presented as an alternative to the subdural space. It is assumed that there are fewer complications when the drain is placed in the subperiosteal space, but the recurrence is lower when the drain is placed in the subdural space (98). Generally, drainage into the subperiosteal room is recommended in patients over 80 years or in those where a higher rate of complications is suspected (98).

In combination with irrigation, closed-system drainage can be used, which in contrast to irrigation without closed-system drainage has a minimal positive effect on the rate of recurrence (97)(99).

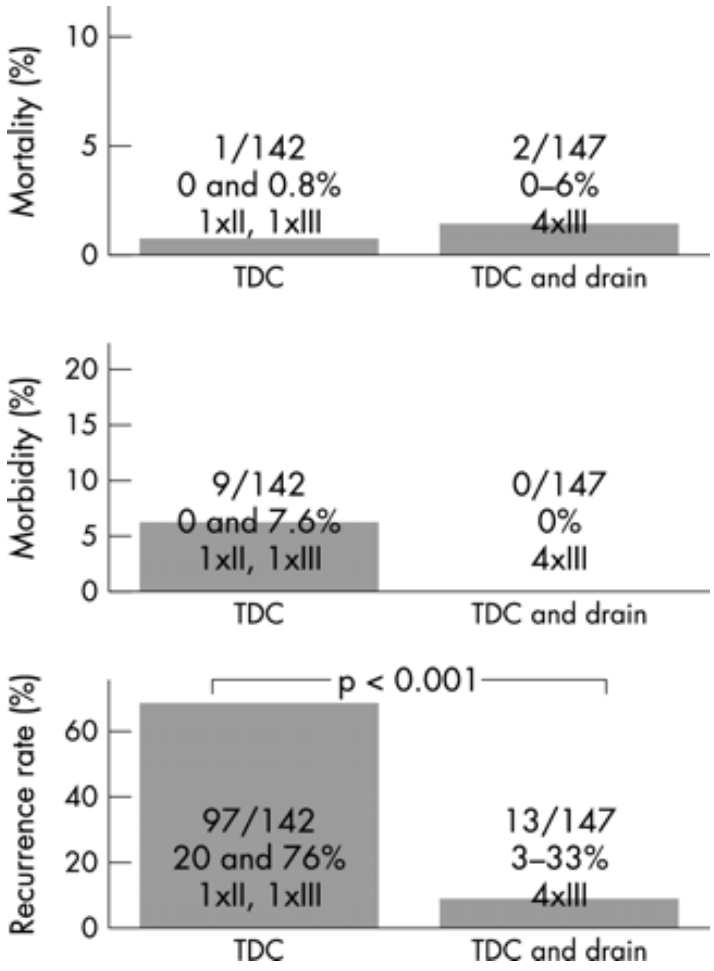

Fig. 11

"The effect of a drain in twist drill craniostomy. Comparison of mortality, morbidity, and recurrence rate for simple twist drill craniostomy (TDC) and TDC with drain. The grey columns show the relative percentage of summarized data on corresponding treatment groups from different publications. The absolute numbers are shown in the legend within the columns. In addition, the range of relative values and the number of studies which provided statistical data are listed with their classes of evidence." (76).

Class I: Evidence provided by one or more well designed randomized controlled clinical studies.

Class II: Evidence provided by one or more well designed clinical studies such as prospective open, case–control studies, etc.

Class III: Evidence provided by expert opinion, non-randomized historical controls, or case reports of one or more patients (76).

Figure 11 (adapted from Weigel et al. Journal of Neurology, Neurosurgery & Psychiatry 2003) shows the advantages of drainage in combination with TDC. There is a clear reduction in morbidity and recurrence rate (99).
At least it can be said that closed-system drainage reduce the rate of symptomatic recurrence (100).
Approximately half of CSDHs appear homogeneous with high intensity on T1 MRI, suggesting plasma or CSF transport as a possible mechanism for CSDH enlargement. Therefore, placement of a drain may prevent recurrence. On the other hand, low or isointensity on T1 MRI imaging may suggest enlargement due to rebleeding from neomembrane microvessels. In these cases, recurrence may occur regardless of surgical methods and placement of drainage, and they should be closely monitored by regular CT or MR scans (100).

9. DISCUSSION

When it comes to CSDH, there are many different approaches in each area. Starting with the pathophysiology. The controversial ones seemed to me to come from the fact that in earlier articles the clinical picture was looked at more generally. With further development of medicine and the knowledge about further mechanisms in the body, the understanding of the clinical picture of CSDH has also developed. The possible pathophysiology I mention above tries to show a simple and logical explanation for the development of CSDH. However, that it is much more complex has become apparent over the years.
When it comes to the clinical diagnosis based on the presenting symptoms, it quickly becomes apparent what pitfalls this involves. CSDH does not present with disease-specific symptoms, but includes symptoms that are typical of many diseases. As differential diagnoses many other diseases could be considered, e.g. stroke, depending on the severity of the symptoms they could even be misinterpreted as simple migraine, or if a patient has dementia, the symptoms could be lost in the clinical picture.
Accordingly, a radiologic review is essential to the clinical diagnosis, but again, a trained eye is required to avoid misdiagnosing a chronic hemorrhage as acute or subacute. Especially when there is acute bleeding accompanying the chronic bleeding, it is radiologically challenging. Sometimes it is also difficult to accurately differentiate the hemorrhage from the healthy brain tissue.
Once you have managed to diagnose a chronic bleed, there is still the difficulty of finding the right treatment modality.

When you look at the patients postoperatively, it came out that there were a couple of factors that were indicative of recurrence. Among other things, if patients had an elevated level of tPA, this was an indication of recurrence of bleeding. Also, high levels of plasminogen, or generally markers of hyperfibrinolysis, are considered as predictive factors (1)(101).
When predicting the outcome of different surgical techniques, no clear favorites can be identified. All three surgical techniques show similar success rates, with no major differences in cure mortality ratio (102).
Studies have demonstrated that TD and BH did not show major differences in post-operative outcomes. In terms of the rate of healing, recurrence, and morbidity, they were at the same level. Only the more invasive procedure, craniotomy, showed a slightly increased morbidity (75)(102).
After surgical evacuation, the further postoperative course should be closely followed. Minimally invasive surgery is used to keep the rate of complications as low as possible. It is hoped that there will be no further bleeding and that the patient will develop in a stable manner. If conservative treatment is chosen, the independent regression of the bleeding would be a success and would be considered a positive result. If the diagnosis of CSDH is due to neurological status changes, these should be kept in mind, and a decrease in these can also be considered as success.
It is not possible to generalize which surgical method is the best, because for each patient a different one is suitable. Each patient brings with them different basic requirements. Some patients are very fragile, for whom conservative therapy is more likely to be considered, while other patients are physically fitter, where surgical intervention would be easier to tolerate. The exact location of the hemorrhage is different in each patient, the mass is treated differently, and each patient's body compensates in a different way.
Radiological improvement is indicated by a reduction in the size of the mass and the absence of fresh hemorrhage. It should be avoided that there are further injuries during the operation or the postoperative drainage, as this could result in an increase in intracranial pressure, which could have fatal consequences.

10. CONCLUSION

Whether the outcome for a chronic subdural hematoma is good or bad depends on a number of factors. In recent years, the diagnostic possibilities have developed in a good direction, so that the diagnosis has become much easier. However, it still often happens that symptoms are misinterpreted, and a different clinical picture is diagnosed.

It has taken many years to define the pathogenesis and to look behind the complex mechanisms in the development of chronic subdural hematoma.

Once a successful diagnosis has been made, the surgeons have various options for surgical techniques, and it is often at their discretion and experience which method is finally chosen. In general, it is recommended to choose a minimally invasive method as far as possible to keep the rate of complications as low as possible.

In addition, there is the possibility of considering the placement of a drain postoperatively. The scientific community is currently in disagreement about the beneficial effect of drainage after postoperative evacuation of chronic subdural hematoma.

Some sources indicate a beneficial effect, other authors speak of non-measurable differences. It generally crystallized quickly that authors and researchers disagree on many aspects of chronic subdural hematoma.

In my opinion, it is essential to weigh the risks of complications and to consider the best surgical technique for each patient individually. The additional insertion of a drainage tube should also be determined individually for each patient, since the insertion of a foreign body always carries the risk of infection.

One should develop a increased sensitivity for one's fellow human beings, which would allow one to notice changes in character more quickly and thus make a diagnosis more quickly. It is better to be medically examined once too often when symptoms appear, than to overlook a chronic bleeding.

11. REFERENCES

1. Edlmann E, Giorgi-Coll S, Whitfield PC, Carpenter KLH, Hutchinson PJ. Pathophysiology of chronic subdural haematoma: inflammation, angiogenesis and implications for pharmacotherapy. J Neuroinflammation. 2017 Dec;14(1):108.
2. Rohde V, Graf G, Hassler W. Complications of burr-hole craniostomy and closed-system drainage for chronic subdural hematomas: a retrospective analysis of 376 patients. Neurosurg Rev. 2002 Mar;25(1–2):89–94.
3. Karibe H, Kameyama M, Kawase M, Hirano T, Kawaguchi T, Tominaga T. [Epidemiology of chronic subdural hematomas]. No Shinkei Geka. 2011 Dec;39(12):1149–53.
4. Rust T, Kiemer N, Erasmus A. Chronic subdural haematomas and anticoagulation or anti-thrombotic therapy. Journal of Clinical Neuroscience. 2006 Oct;13(8):823–7.
5. Juratli TA, Klein J, Schackert G. Das chronische Subduralhämatom im Alter. Chirurg. 2017 Feb;88(2):131–5.
6. Gelabert-González M, Iglesias-Pais M, García-Allut A, Martínez-Rumbo R. Chronic subdural haematoma: surgical treatment and outcome in 1000 cases. Clinical Neurology and Neurosurgery. 2005 Apr;107(3):223–9.
7. Fogelholm R, Waltimo O. Epidemiology of chronic subdural haematoma. Acta neurochir. 1975 Sep;32(3–4):247–50.

8. Gazzeri R, Laszlo A, Faiola A, Colangeli M, Comberiati A, Bolognini A, et al. Clinical investigation of chronic subdural hematoma: Relationship between surgical approach, drainage location, use of antithrombotic drugs and postoperative recurrence. Clinical Neurology and Neurosurgery. 2020 Apr;191:105705.
9. Mehta V, Harward SC, Sankey EW, Nayar G, Codd PJ. Evidence based diagnosis and management of chronic subdural hematoma: A review of the literature. Journal of Clinical Neuroscience. 2018 Apr;50:7–15.
10. Kitya D, Punchak M, Abdelgadir J, Obiga O, Harborne D, Haglund MM. Causes, clinical presentation, management, and outcomes of chronic subdural hematoma at Mbarara Regional Referral Hospital. Neurosurgical Focus. 2018 Oct;45(4):E7.
11. Vega RA, Valadka AB. Natural History of Acute Subdural Hematoma. Neurosurgery Clinics of North America. 2017 Apr;28(2):247–55.
12. Yadav Y, Parihar V, Namdev H, Bajaj J. Chronic subdural hematoma. Asian J Neurosurg. 2016;11(4):330.
13. Feghali J, Yang W, Huang J. Updates in Chronic Subdural Hematoma: Epidemiology, Etiology, Pathogenesis, Treatment, and Outcome. World Neurosurgery. 2020 Sep;141:339–45.
14. Markwalder T-M. Chronic subdural hematomas: a review. Journal of Neurosurgery. 1981 May;54(5):637–45.
15. K A, Yarnell O. SUBDURAL HÆMATOMA AFTER WHIPLASH INJURY. The Lancet. 1969 Aug;294(7614):237–9.
16. Kolias AG, Chari A, Santarius T, Hutchinson PJ. Chronic subdural haematoma: modern management and emerging therapies. Nat Rev Neurol. 2014 Oct;10(10):570–8.
17. Munro D. SURGICAL PATHOLOGY OF SUBDURAL HEMATOMA: BASED ON A STUDY OF ONE HUNDRED AND FIVE CASES. Arch NeurPsych. 1936 Jan 1;35(1):64.
18. Sato S, Suzuki J. Ultrastructural observations of the capsule of chronic subdural hematoma in various clinical stages. Journal of Neurosurgery. 1975 Nov;43(5):569–78.
19. Ito H, Yamamoto S, Saito K, Ikeda K, Hisada K. Quantitative estimation of hemorrhage in chronic subdural hematoma using the 51Cr erythrocyte labeling method. Journal of Neurosurgery. 1987 Jun;66(6):862–4.
20. Jones N, Iljin K, Dumont DJ, Alitalo K. Tie receptors: new modulators of angiogenic and lymphangiogenic responses. Nat Rev Mol Cell Biol. 2001 Apr;2(4):257–67.
21. Helmy A, De Simoni M-G, Guilfoyle MR, Carpenter KLH, Hutchinson PJ. Cytokines and innate inflammation in the pathogenesis of human traumatic brain injury. Progress in Neurobiology. 2011 Nov;95(3):352–72.
22. Hohenstein A, Erber R, Schilling L, Weigel R. Increased mRNA Expression of VEGF within the Hematoma and Imbalance of Angiopoietin-1 and -2 mRNA within the Neomembranes of Chronic Subdural Hematoma. Journal of Neurotrauma. 2005 May;22(5):518–28.
23. Hoeben A, Landuyt B, Highley MS, Wildiers H, Van Oosterom AT, De Bruijn EA. Vascular Endothelial Growth Factor and Angiogenesis. Pharmacol Rev. 2004 Dec;56(4):549–80.
24. Hara M, Tamaki M, Aoyagi M, Ohno K. Possible role of cyclooxygenase-2 in developing chronic subdural hematoma. J Med Dent Sci. 2009 Sep;56(3):101–6.
25. Shono T, Inamura T, Morioka T, Matsumoto K, Suzuki SO, Ikezaki K, et al. Vascular endothelial growth factor in chronic subdural haematomas. Journal of Clinical Neuroscience. 2001 Sep;8(5):411–5.
26. Nanko N, Tanikawa M, Mase M, Fujita M, Tateyama H, Miyati T, et al. Involvement of Hypoxia-Inducible Factor-1.ALPHA. and Vascular Endothelial Growth Factor in the Mechanism of Development of Chronic Subdural Hematoma. Neurol Med Chir(Tokyo). 2009;49(9):379–85.

27. Weigel R, Schilling L, Schmiedek P. Specific Pattern of Growth Factor Distribution in Chronic Subdural Hematoma (CSH): Evidence for an Angiogenic Disease. Acta Neurochirurgica. 2001 Aug 1;143(8):811–9.
28. Kalamatianos T, Stavrinou LC, Koutsarnakis C, Psachoulia C, Sakas DE, Stranjalis G. PlGF and sVEGFR-1 in chronic subdural hematoma: implications for hematoma development: Clinical article. JNS. 2013 Feb;118(2):353–7.
29. Hua C, Zhao G, Feng Y, Yuan H, Song H, Bie L. Role of Matrix Metalloproteinase-2, Matrix Metalloproteinase-9, and Vascular Endothelial Growth Factor in the Development of Chronic Subdural Hematoma. Journal of Neurotrauma. 2016 Jan;33(1):65–70.
30. Funai M, Osuka K, Usuda N, Atsuzawa K, Inukai T, Yasuda M, et al. Activation of PI3 Kinase/Akt Signaling in Chronic Subdural Hematoma Outer Membranes. Journal of Neurotrauma. 2011 Jun;28(6):1127–31.
31. Burbridge MF. [No title found]. Angiogenesis. 2002;5(3):215–26.
32. Manicone A, Mcguire J. Matrix metalloproteinases as modulators of inflammation. Seminars in Cell & Developmental Biology. 2008 Feb;19(1):34–41.
33. Moskała M, Gościński I, Kałuża J, Polak J, Krupa M, Adamek D, et al. Morphological Aspects of the Traumatic Chronic Subdural Hematoma Capsule: SEM Studies. Microsc Microanal. 2007 Jun;13(3):211–9.
34. Sarkar C, Lakhtakia R, Gill SS, Sharma MC, Mahapatra AK, Mehta VS. Chronic Subdural Haematoma and the Enigmatic Eosinophil. Acta Neurochir (Wien). 2002 Oct;144(10):983–8.
35. M□ller W, Firsching R. Significance of eosinophilic granulocytes in chronic subdural hematomas. Neurosurg Rev. 1990;13(4):305–8.
36. Stanisic M, Lyngstadaas SP, Pripp AH, Aasen AO, Lindegaard K-F, Ivanovic J, et al. Chemokines as markers of local inflammation and angiogenesis in patients with chronic subdural hematoma: a prospective study. Acta Neurochir. 2012 Jan;154(1):113–20.
37. Pripp AH, Stanišić M. The Correlation between Pro- and Anti-Inflammatory Cytokines in Chronic Subdural Hematoma Patients Assessed with Factor Analysis. Kaderali L, editor. PLoS ONE. 2014 Feb 27;9(2):e90149.
38. Iliescu IA, Constantinescu AI. Clinical evolutional aspects of chronic subdural haematomas - literature review. J Med Life. 2015;8 Spec Issue:26–33.
39. Lee K-S. ReviewNatural history of chronic subdural haematoma. Brain Injury. 2004 Apr;18(4):351–8.
40. Putnam TJ. CHRONIC SUBDURAL HEMATOMA: ITS PATHOLOGY, ITS RELATION TO PACHYMENINGITIS HEMORRHAGICA AND ITS SURGICAL TREATMENT. Arch Surg. 1925 Sep 1;11(3):329.
41. Kotwica Z, Brzeziński J. A long course of chronic subdural haematomas. Acta neurochir. 1987 Mar;85(1–2):44–5.
42. Liliang P-C, Tsai Y-D, Liang C-L, Lee T-C, Chen H-J. Chronic subdural haematoma in young and extremely aged adults: a comparative study of two age groups. Injury. 2002 May;33(4):345–8.
43. Ito H, Komai T, Yamamoto S. Fibrinolytic enzyme in the lining walls of chronic subdural hematoma. Journal of Neurosurgery. 1978 Feb;48(2):197–200.
44. Nakagawa T, Kodera T, Kubota T. Expression of Matrix Metalloproteinases in the Chronic Subdural Haematoma Membrane. Acta Neurochirurgica. 2000 Jan 12;142(1):61–6.
45. Chapin JC, Hajjar KA. Fibrinolysis and the control of blood coagulation. Blood Reviews. 2015 Jan;29(1):17–24.
46. Park S-H, Kang D-H, Park J, Hwang J-H, Hwang S-K, Sung J-K, et al. Fibrinogen and D-dimer analysis of chronic subdural hematomas and computed tomography findings: A prospective study. Clinical Neurology and Neurosurgery. 2011 May;113(4):272–6.
47. Heula A-L, Ohlmeier S, Sajanti J, Majamaa K. Characterization of Chronic Subdural

Hematoma Fluid Proteome: Neurosurgery. 2013 Aug;73(2):317–31.
48. Ito H, Yamamoto S, Komai T, Mizukoshi H. Role of local hyperfibrinolysis in the etiology of chronic subdural hematoma. Journal of Neurosurgery. 1976 Jul;45(1):26–31.
49. Nomura S, Kashiwagi S, Fujisawa H, Ito H, Nakamura K. Characterization of local hyperfibrinolysis in chronic subdural hematomas by SDS-PAGE and immunoblot. Journal of Neurosurgery. 1994 Dec;81(6):910–3.
50. Luxon LM, Harrison MJ. Chronic subdural haematoma. Q J Med. 1979 Jan;48(189):43–53.
51. Adhiyaman V, Asghar M, Ganeshram KN, Bhowmick BK. Chronic subdural haematoma in the elderly. Postgrad Med J. 2002 Feb 1;78(916):71.
52. Potter JF, Fruin AH. Chronic subdural hematoma--the 'great imitator'. Geriatrics. 1977 Jun;32(6):61–6.
53. Cameron MM. Chronic subdural haematoma: a review of 114 cases. Journal of Neurology, Neurosurgery & Psychiatry. 1978 Sep 1;41(9):834–9.
54. Henderson MJ. A difficult psychiatric patient. Postgraduate Medical Journal. 2000 Sep 1;76(899):585–6.
55. Fogelholm R, Heiskanen O, Waltimo O. Chronic subdural hematoma in adults: Influence of patient's age on symptoms, signs, and thickness of hematoma. Journal of Neurosurgery. 1975 Jan;42(1):43–6.
56. Welsh JE, Tyson GW, Winn HR, Jane JA. Chronic subdural hematoma presenting as transient neurologic deficits. Stroke. 1979 Sep;10(5):564–7.
57. Rozzelle CJ, Wofford JL, Branch CL. Predictors of Hospital Mortality in Older Patients with Subdural Hematoma. Journal of the American Geriatrics Society. 1995 Mar;43(3):240–4.
58. Ashkenazi E, Pomeranz S. Nystagmus as the presentation of tentorial incisure subdural haematoma. Journal of Neurology, Neurosurgery & Psychiatry. 1994 Jul 1;57(7):830–1.
59. Phookan G, Cameron M. Bilateral chronic subdural haematoma: an unusual presentation with isolated oculomotor nerve palsy. Journal of Neurology, Neurosurgery & Psychiatry. 1994 Sep 1;57(9):1146–1146.
60. Sandyk R. Isolated failure of upward gaze as a sign of chronic subdural haematoma. S Afr Med J. 1982 Jan 9;61(2):32.
61. Sunada I, Inoue T, Tamura K, Akano Y, Fu Y. Parkinsonism Due to Chronic Subdural Hematoma —Case Report—. Neurol Med Chir(Tokyo). 1996;36(2):99–101.
62. Abdulla A. Reversible akinetic-rigid syndrome due to bilateral subdural haematomas. Age and Ageing. 1999 Oct 1;28(6):582–3.
63. Y. Okumura, K. Nakai, T. Itakura, N MS. Case Study: Gerstmann's syndrome associated with chronic subdural haematoma: a case report. Brain Injury. 1998 Jan;12(8):697–701.
64. Lesoin F, Destee A, Jomin M, Warot P, Wilson SG. Quadriparesis as an unusual manifestation of chronic subdural haematoma. Journal of Neurology, Neurosurgery & Psychiatry. 1983 Aug 1;46(8):783–5.
65. Markwalder T-M, Steinsiepe KF, Rohner M, Reichenbach W, Markwalder H. The course of chronic subdural hematomas after burr-hole craniostomy and closed-system drainage. Journal of Neurosurgery. 1981 Sep;55(3):390–6.
66. Fujisawa H, Nomura S, Kajiwara K, Kato S, Fujii M, Suzuki M. Various Magnetic Resonance Imaging Patterns of Chronic Subdural Hematomas: Indicators of the Pathogenesis? Neurol Med Chir(Tokyo). 2006;46(7):333–9.
67. Stanišić M, Pripp AH. A Reliable Grading System for Prediction of Chronic Subdural Hematoma Recurrence Requiring Reoperation After Initial Burr-Hole Surgery. Neurosurgery. 2017 Nov 1;81(5):752–60.

68. Chon K-H, Lee J-M, Koh E-J, Choi H-Y. Independent predictors for recurrence of chronic subdural hematoma. Acta Neurochir. 2012 Sep;154(9):1541–8.
69. Shen J, Xin W, Li Q, Gao Y, Zhang J. A Grading System For The Prediction Of Unilateral Chronic Subdural Hematoma Recurrence After Initial Single Burr Hole Evacuation. RMHP. 2019 Nov;Volume 12:179–88.
70. Structural Imaging Using Magnetic Resonance Imaging and Computed Tomography - ClinicalKey [Internet]. [cited 2022 Mar 12]. Available from: https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323642613000401
71. Rasuli B, Gaillard F. Subdural haemorrhage. In: Radiopaedia.org [Internet]. Radiopaedia.org; 2008 [cited 2022 Mar 21]. Available from: http://radiopaedia.org/articles/2121
72. Nakaguchi H, Tanishima T, Yoshimasu N. Factors in the natural history of chronic subdural hematomas that influence their postoperative recurrence. Journal of Neurosurgery. 2001 Aug;95(2):256–62.
73. Soleman J, Taussky P, Fandino J, Muroi C. Evidence-Based Treatment of Chronic Subdural Hematoma. In: Sadaka F, editor. Traumatic Brain Injury [Internet]. InTech; 2014 [cited 2021 Dec 2]. Available from: http://www.intechopen.com/books/traumatic-brain-injury/evidence-based-treatment-of-chronic-subdural-hematoma
74. Naganuma H, Fukamachi A, Kawakami M, Misumi S, Nakajima H, Wakao T. Spontaneous Resolution of Chronic Subdural Hematomas: Neurosurgery. 1986 Nov;19(5):794–8.
75. Lee K-S. How to Treat Chronic Subdural Hematoma? Past and Now. J Korean Neurosurg Soc. 2019 Mar 1;62(2):144–52.
76. Weigel R. Outcome of contemporary surgery for chronic subdural haematoma: evidence based review. Journal of Neurology, Neurosurgery & Psychiatry. 2003 Jul 1;74(7):937–43.
77. Cenic A, Bhandari M, Reddy K. Management of Chronic Subdural Hematoma: A National Survey and Literature Review. Can j neurol sci. 2005 May;32(4):501–6.
78. Abecassis IJ, Kim LJ. Craniotomy for Treatment of Chronic Subdural Hematoma. Neurosurgery Clinics of North America. 2017 Apr;28(2):229–37.
79. Ducruet AF, Grobelny BT, Zacharia BE, Hickman ZL, DeRosa PL, Anderson K, et al. The surgical management of chronic subdural hematoma. Neurosurg Rev. 2012 Apr;35(2):155–69.
80. Taussky P, Fandino J, Landolt H. Number of burr holes as independent predictor of postoperative recurrence in chronic subdural haematoma. British Journal of Neurosurgery. 2008 Jan;22(2):279–82.
81. Han H-J, Park C-W, Kim E-Y, Yoo C-J, Kim Y-B, Kim W-K. One vs. Two Burr Hole Craniostomy in Surgical Treatment of Chronic Subdural Hematoma. J Korean Neurosurg Soc. 2009;46(2):87.
82. Kansal R, Nadkarni T, Goel A. Single versus double burr hole drainage of chronic subdural hematomas. A study of 267 cases. Journal of Clinical Neuroscience. 2010 Apr;17(4):428–9.
83. Hennig R, Kloster R. Burr Hole Evacuation of Chronic Subdural Haematomas Followed by Continuous Inflow and Outflow Irrigation. Acta Neurochirurgica. 1999 Feb 17;141(2):171–6.
84. Aoki N. Subdural Tapping and Irrigation for the Treatment of Chronic Subdural Hematoma in Adults. Neurosurgery. 1984 May 1;14(5):545–8.
85. Berghauser Pont LME, Dirven CMF, Dippel DWJ, Verweij BH, Dammers R. The role of corticosteroids in the management of chronic subdural hematoma: a systematic review. Eur J Neurol. 2012 Nov;19(11):1397–403.
86. Holl DC, Volovici V, Dirven CMF, Peul WC, van Kooten F, Jellema K, et al.

Pathophysiology and Nonsurgical Treatment of Chronic Subdural Hematoma: From Past to Present to Future. World Neurosurgery. 2018 Aug;116:402-411.e2.
87. Berghauser Pont LME, Dammers R, Schouten JW, Lingsma HF, Dirven CMF. Clinical Factors Associated With Outcome in Chronic Subdural Hematoma: A Retrospective Cohort Study of Patients on Preoperative Corticosteroid Therapy. Neurosurgery. 2012 Apr;70(4):873–80.
88. Zhang Y, Chen S, Xiao Y, Tang W. Effects of Dexamethasone in the Treatment of Recurrent Chronic Subdural Hematoma. World Neurosurgery. 2017 Sep;105:115–21.
89. Chan DYC, Chan DTM, Sun TFD, Ng SCP, Wong GKC, Poon WS. The use of atorvastatin for chronic subdural haematoma: a retrospective cohort comparison study. British Journal of Neurosurgery. 2017 Jan 2;31(1):72–7.
90. Pichert G, Henn V. [Conservative therapy of chronic subdural hematomas]. Schweiz Med Wochenschr. 1987 Nov 21;117(47):1856–62.
91. Xu M, Chen P, Zhu X, Wang C, Shi X, Yu B. Effects of Atorvastatin on Conservative and Surgical Treatments of Chronic Subdural Hematoma in Patients. World Neurosurgery. 2016 Jul;91:23–8.
92. Huang J, Tian Y, Song Y, Hu R, Zhang S, Gong Z, et al. Effect of Different Factors on the Short-Term Outcome of Chinese Patients With Primary Chronic Subdural Hematoma at Different Age Groups: A Two-Center Retrospective Study. Front Aging Neurosci. 2019 Nov 29;11:325.
93. Ishihara H, Ishihara S, Kohyama S, Yamane F, Ogawa M, Sato A, et al. Experience in Endovascular Treatment of Recurrent Chronic Subdural Hematoma. Interv Neuroradiol. 2007 Mar;13(1_suppl):141–4.
94. Smely C, Madlinger A, Scheremet R. Chronic subdural haematoma ? a comparison of two different treatment modalities. Acta neurochir. 1997 Sep;139(9):818–26.
95. Lega BC, Danish SF, Malhotra NR, Sonnad SS, Stein SC. Choosing the best operation for chronic subdural hematoma: a decision analysis: Clinical article. JNS. 2010 Sep;113(3):615–21.
96. Kamenova M, Wanderer S, Lipps P, Marbacher S, Mariani L, Soleman J. When the Drain Hits the Brain. World Neurosurgery. 2020 Jun;138:e426–36.
97. Markwalder TM, Seiler RW. Chronic Subdural Hematomas: To Drain or Not to Drain? Neurosurgery. 1985 Feb 1;16(2):185–8.
98. Bellut D, Woernle CM, Burkhardt J-K, Kockro RA, Bertalanffy H, Krayenbühl N. Subdural Drainage versus Subperiosteal Drainage in Burr-Hole Trepanation for Symptomatic Chronic Subdural Hematomas. World Neurosurgery. 2012 Jan;77(1):111–8.
99. Wakai S, Hashimoto K, Watanabe N, Inoh S, Ochiai C, Nagai M. Efficacy of closed-system drainage in treating chronic subdural hematoma: a prospective comparative study. Neurosurgery. 1990 May;771.
100. Tsutsumi K, Maeda K, Iijima A, Usui M, Okada Y, Kirino T. The relationship of preoperative magnetic resonance imaging findings and closed system drainage in the recurrence of chronic subdural hematoma. Journal of Neurosurgery. 1997 Dec;87(6):870–5.
101. Weir B, Gordon P. Factors affecting coagulation: fibrinolysis in chronic subdural fluid collections. Journal of Neurosurgery. 1983 Feb;58(2):242–5.
102. Almenawer SA, Farrokhyar F, Hong C, Alhazzani W, Manoranjan B, Yarascavitch B, et al. Chronic Subdural Hematoma Management: A Systematic Review and Meta-analysis of 34829 Patients. Annals of Surgery. 2014 Mar;259(3):449–57.

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