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Pathogenesis of Chronic Subdural Hematoma: A Cohort Evidencing De Novo and Transformational Origins

Ellie Edlmann,1,2,* Peter C. Whitfield,1 Angelos Kolias,3 and Peter J. Hutchinson3

Abstract

Chronic subdural hematoma (CSDH) is a common neurosurgical pathology, yet conflicting opinions exist concerning the pathophysiological processes involved. Many consider CSDH a product of an aged acute subdural hematoma (ASDH) secondary to trauma. Serial imaging, however, has demonstrated CSDH formation in patients without any initial ASDH. To understand the relevance of acute hemorrhage in a cohort of patients with CSDH, transformation from an ASDH were categorized as CSDH-acute transformed (CSDH-AT) and those without any acute hemorrhage at the outset as CSDH-de-novo (CSDH-DN). A cohort of 41 eligible patients with CSDH were included, with baseline imaging after trauma (or spontaneous ASDH) available for assessment of acute hemorrhage. Volumetric analysis of all subdural collections and measurements of baseline atrophy were performed. In 37% of cases, there was an ASDH present on baseline imaging (CSDH-AT), whereas 63% had no acute hemorrhage at baseline (CSDH-DN). The CSDH-ATs developed more rapidly (mean 16 days from baseline to diagnosis) and were smaller in volume than the CSDH-DNs, which developed at a mean delay of 57 days. In 54% of the CSDH-DNs, a subdural hygroma was present on baseline imaging, and there was a wide range of baseline cerebral atrophy. This study provides radiological evidence for two distinct pathways in the formation of CSDH, with CSDH-DN occurring more commonly and often involving subdural hygroma. Further work is needed to understand whether the pathological origin has implications for patient outcome.

Keywords: chronic subdural hematoma; imaging; pathology; subdural hygroma

Introduction

Chronic subdural hematoma (CSDH) is generally assumed to represent maturation of a preceding traumatic acute subdural hematoma (ASDH) from weeks to months earlier. More recently, progression from an established hygroma is discussed as a potential source.1 Experimental animal studies have questioned the pathogenesis, showing that acute subdural blood alone is not always sufficient to initiate the formation of a CSDH.2,3 Further, the majority of untreated ASDHs do not progress to CSDHs, and in many CSDH cases, there is no preceding trauma reported.4,5 Biochemical data support the role of inflammation and angiogenesis occurring in the subdural space as a pathogenic mechanism of a CSDH formation not requiring acute hemorrhage at onset.6,7

This study reviews a cohort of patients with CSDH who had baseline and delayed diagnostic imaging to increase our understanding of the radiological formation of CSDH. We hypothesize that two distinct pathophysiological processes can occur, defined as:

1. Acute transformed chronic subdural hematoma (CSDH-AT), where an ASDH precedes the formation of a CSDH.
2. De-novo chronic subdural hematoma (CSDH-DN), where a CSDH develops without evidence of a preceding ASDH.

To investigate this hypothesis, baseline imaging, nearly always undertaken in the context of trauma, was evaluated and compared with imaging at the time of subsequent...
CSDH diagnosis. Evidence that a CSDH can develop without a preceding ASDH is important so that patients with a “normal” trauma scan are still vigilant to later development of CSDH symptoms and prompt investigation occurs in such cases. Identification of different subtypes of CSDH aids understanding of why CSDHs occur at different time points after trauma, which has the potential to influence patient outcome.

Methods
The study cohort was selected from the 205 participants recruited to the Dex-CSDH trial (ISRCTN80782810) in Cambridge between 2015 and 2017.8 This trial was ethically approved by North West Haydock Research and Ethics Committee, and consent was obtained before participation. All recruited trial participants had been admitted to a neurosurgical unit with symptomatic CSDH.

For the purpose of this study, all trial participants with a symptomatic CSDH who had a previous hospital attendance with trauma (and in one case spontaneous headache) and underwent previous “baseline” brain imaging, in the preceding six months, were included. This time period was selected because 95% of Dex-CSDH trial participants who reported previous head trauma said it occurred within six months of presentation. None of the patients in this series sustained trauma of sufficient severity to warrant any further trauma-initiated scans in the interval between the baseline scan and the diagnostic scan that led to recruitment into the Dex-CSDH trial. This led to a cohort of 41 patients.

Baseline data on demographics and clinical information were collected on all patients. Follow-up data were Glasgow Coma Scale (GCS) at discharge and modified Rankin scale (mRS) scores at three and six months post-treatment for CSDH. The latter was dichotomized into favorable (0–3) and unfavorable (4–6) outcome.

Imaging assessments
All baseline imaging was analyzed for presence of ASDH ipsilateral to subsequent CSDH development, and, if present, the patient was classified as a CSDH-AT. Given that an interval head injury of sufficient severity to warrant further trauma-initiated brain imaging had not occurred in any case, we made a pragmatic assumption that a de novo CSDH had developed (CSDH-DN) without the initial formation of an ASDH. Volumetric measurements of all ASDHs and CSDHs were performed using ITK-snap software.9 Density and midline shift (MLS) measurements were made.

Measures of atrophy
Baseline imaging for CSDH-DN patients was assessed for cerebral atrophy and hygroma, because these have been implicated in CSDH formation.10–12 We did not conduct this analysis on the CSDH-AT group of patients because of the confounding effects of mass effect caused by the hematoma. We measured the following indices:

1. The bicaudate ratio (BCR), calculated as the distance between the two caudate nuclei apices at the level they make the greatest indentation on the lateral ventricles, divided by the maximum width of the skull at the same level (Fig. 1A).13
2. The subdural space depth (SSD), measured as the maximum distance from the cortex to the inner skull on any slice (Fig. 1B).
3. Subdural hygroma presence or absence; a hygroma was considered present if the cortical surface was flattened and sulci obliterated, or if there was clear asymmetry between sides (Fig. 1C).14
4. The cortical atrophy scale (CAS) assessment as adapted by Jeong and associates10 was scored as per Figure 2.15

![FIG. 1. (A) Example of bicaudate ratio measurements (yellow line/blue line); (B) example of subdural space depth measurements as per greatest depth at blue lines; (C) example of subdural hygroma (arrow), with no hygroma on contralateral side.](image-url)
Statistical analysis
GraphPad Prism 7 was used for all statistical analysis. A $p$ value of <0.05 was considered significant. Continuous data (e.g., age) were compared using an unpaired t test if parametrical and Mann-Whitney if nonparametrical. Categorical data (e.g., gender) were tested with the Fisher exact or chi-square test; the chi-square test for trend was used for multiple categories (such as GCS and mRS). There were no missing data points or patients lost to follow-up to cause bias.

Results
All 41 eligible patients had data available at baseline and follow-up. In 40/41 patients, the baseline CSDH imaging was performed acutely after head trauma. One patient experienced severe, sudden-onset headache prompting hospital attendance, and baseline imaging revealed an idiopathic spontaneous ASDH (angiographic imaging was normal). Interim imaging between initial trauma and CSDH diagnosis was performed on 13 patients (10 with ASDH) as part of routine follow-up.

In 26/41 (63%) patients, there was no evidence of ASDH on baseline imaging, and these patients were classified as developing a CSDH-DN. In 15/41 (37%) patients, there was presence of ASDH on baseline imaging, and these patients were classified as CSDH-AT.

The CSDH-DN case examples are shown in Figure 3.

Three patients had serial imaging with evidence of progression from normal imaging to presence of hygroma and eventual CSDH formation (as shown in Fig. 3C). Despite the presence of bilateral hygromas in Figure 3C,
only one side progressed to a CSDH-DN. Case examples of CSDH-AT (Fig. 4) show progressive changes in haematoma density and expansion to CSDH.

**Baseline data**

In 31/41 (76%) patients, the baseline scan was on the same day as the trauma/spontaneous ASDH, while the remaining patients had a baseline scan within 10 days of trauma (Table 1). Two of the 41 patients underwent initial magnetic resonance imaging (MRI) rather than computed tomography (CT): CSDH-DN developed in both patients. There were no significant differences between the demographics for the CSDH subtypes, including age, gender, and antithrombotic use. The baseline characteristics of patients in this study were comparable to those seen across the entire Dex-CSDH trial cohort.16 The time interval from initial event to CSDH diagnosis was significantly longer for CSDH-DN (median 57 days) than CSDH-AT (median 16 days) ($p \leq 0.0001$, Fig. 5).

**Diagnostic CSDH imaging characteristics**

Significantly more patients had bilateral CSDH-DN (9/26) than CSDH-AT (0/15) ($p = 0.0154$, Table 2). Only five bilateral CSDH-DNs had both sides treated, however, with just the largest side treated in four cases. Volumes were compared between subtypes for all treated CSDHs (excluding untreated sides), with the sides combined in bilaterally treated cases. This showed CSDH-DNs were significantly larger in combined volume than CSDH-ATs ($p = 0.0111$), and remained significant if only unilateral CSDHs were included ($p = 0.05$)—see Figure 6.

**Table 1. Summary of Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>CSDH-DN</th>
<th>CSDH-AT</th>
<th>$p$ (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>26 (63%)</td>
<td>15 (37%)</td>
<td>0.7197 (NS)</td>
</tr>
<tr>
<td>Scanned on same day as baseline injury</td>
<td>19 (76%)</td>
<td>12 (75%)</td>
<td>0.2836 (NS)</td>
</tr>
<tr>
<td>Mean age</td>
<td>78</td>
<td>75</td>
<td>0.4818 (NS)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male (77%)</td>
<td>Male (53%)</td>
<td>0.4818 (NS)</td>
</tr>
<tr>
<td></td>
<td>Female (23%)</td>
<td>Female (47%)</td>
<td></td>
</tr>
<tr>
<td>Patients on AP or AC</td>
<td>14 (54%)</td>
<td>9 (60%)</td>
<td>0.7021 (NS)</td>
</tr>
<tr>
<td>Median time interval to CSDH diagnosis</td>
<td>57 days</td>
<td>16 days</td>
<td>$&lt; 0.0001$ (S)</td>
</tr>
<tr>
<td></td>
<td>(range 32–145 days)</td>
<td>(range 7–45 days)</td>
<td></td>
</tr>
</tbody>
</table>

CSDH-DN, chronic subdural hematoma-*de novo*; CSDH-AT, chronic subdural hematoma-acute transformed; AP, antiplatelet; AC, anticoagulant; NS, not significant; S, significant.
Bilateral cases were excluded from MLS assessments, because of the potential interaction between sides. There was no significant difference in MLS, mean density, or density subtype (homogenous or mixed) between CSDH-DN and CSDH-AT. This suggests that although they may have different pathological beginnings, each CSDH evolves into a similar pathological product by diagnosis.

Table 2. Diagnostic Chronic Subdural Hematoma Imaging

<table>
<thead>
<tr>
<th></th>
<th>All CSDHs</th>
<th>CSDH-DN</th>
<th>CSDH-AT</th>
<th>p (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laterality: all patients (n)</td>
<td>41</td>
<td>26</td>
<td>15</td>
<td>0.0154 (S)</td>
</tr>
<tr>
<td>i. Patients with unilateral CSDH</td>
<td>32</td>
<td>17</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>ii. Patients with bilateral CSDH</td>
<td>9</td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>All treated CSDH volume (cm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>113</td>
<td>125.6</td>
<td>85.5</td>
<td></td>
</tr>
<tr>
<td>Min.</td>
<td>49.8</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>246.5</td>
<td>137.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral CSDH volume (cm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>113</td>
<td>121.2</td>
<td>85.5</td>
<td>0.05 (S)</td>
</tr>
<tr>
<td>Min.</td>
<td>49.8</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>179.7</td>
<td>137.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral CSDH MLS (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.3</td>
<td>9.9</td>
<td>10.7</td>
<td>0.4968 (NS)</td>
</tr>
<tr>
<td>Min.</td>
<td>5.2</td>
<td>3.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>15.8</td>
<td>16.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean density of all treated CSDHs (HU)</td>
<td>41.3</td>
<td>40.5</td>
<td>43.1</td>
<td>0.3239 (NS)</td>
</tr>
<tr>
<td>No. of all CSDHs by density type</td>
<td>&gt; 0.9999 (NS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homogenous</td>
<td>23</td>
<td>16</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Mixed Density</td>
<td>23</td>
<td>15</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

CSDH-DN, chronic subdural hematoma-de novo; CSDH-AT, chronic subdural hematoma-acute transformed; S, significant; MLS, midline shift; NS, not significant; HU, Hounsfield unit.

ASDH imaging

The majority of the CSDH-AT cohort had an isolated ASDH on baseline imaging (13/15), while additional underlying brain injury was present in two patients (as seen in Fig. 4D). There was a significant negative correlation between ASDH volume and time from trauma to CSDH-AT (Spearman r = -0.6811, p = 0.0174) suggesting larger ASDHs form a CSDH-AT more rapidly than smaller ASDHs (Fig. 7). Despite this, there was no significant correlation between original ASDH volume and CSDH-AT volume (Spearman r = 0.3536, p = 0.1964).

CSDH-DN and the subdural space

A hygroma was found (as per methodology definition) in 14/26 (54%) patients in whom a CSDH-DN developed. Four patients had unilateral hygromas ipsilateral to the CSDH-DN. The remaining 10 hygromas were bilateral; five of these had a unilateral CSDH-DN, three had a bilateral CSDH-DN where only one side necessitated treatment, and two developed a bilateral CSDH-DN where both sides were treated. Counting all sides individually,
two-thirds of hygromas (16/24) developed into a CSDH-DN necessitating treatment. The time delay from trauma to baseline imaging was significantly longer in patients who had a hygroma than those without, suggesting hygroma formation is not immediate (mean 3.2 days versus 0.5 days, \( p = 0.0451 \)). There was also no significant difference in the CSDH-DN volume between patients with or without a hygroma.

Atrophy assessments were performed on 25/26 CSDH-DN patients, with one patient excluded because of an abnormal gantry angle prohibiting BCR calculation. Results are summarized in Table 3. The median BCR for all patients was 0.14, and there was no difference in BCR between patients with a hygroma present or absent (\( p = 0.6867 \)). No correlation was found between the BCR and the total SSD (Spearman \( r = 0.07043 \), \( p = 0.7436 \)). The BCR, however, did correlate with the CAS grade, with significant increases in BCR across the four grades (\( p = 0.0018 \), Fig. 8A). Although there appeared to be a trend between BCR and CSDH-DN volume (Fig. 8B), this was not significant (\( p = 0.0931 \)).

The SSD was significantly greater on sides with a hygroma present than those without (\( p < 0.0001 \)). This suggests the SSD could be used as an objective measure for reporting the presence of hygroma (e.g., SSD > 5 mm is likely to represent hygroma).

There was no correlation between CSDH-DN volumes and the time interval from trauma (\( r = -0.0835 \), \( p = 0.6552 \)).

**Outcome data**

Patients with CSDH-AT had significantly lower GCS scores when admitted to the neurosurgical unit (NSU) compared with CSDH-DN patients (\( p = 0.0358 \)) (Fig. 9A). The “GCS ≤12” group included scores of 7, 8, and 9 in the CSDH-AT group, whereas the lowest GCS score in the CSDH-DN group was 12, in only one patient. This difference in GCS score had resolved by the time of discharge from NSU (Fig. 9B). Two patients in this series were treated conservatively with medical treatment—both CSDH-DNs. The remaining 39 patients with CSDHs were treated surgically, at a median of two days (range 0–12 days) from the diagnostic CSDH imaging. There were two recurrences: one CSDH-DN and one CSDH-AT.

There was no significant difference between the dichotomized three-month or six-month mRS scores for the CSDH subtypes, with good outcome (mRS 0–3) at six months in 85% of CSDH-DN and 80% CSDH-AT.

**Discussion**

This study provides evidence that supports the hypothesis that in some patients (37% in this cohort) an ASDH is transformed into a CSDH (CSDH-AT). In contrast, in 63% of our cohort, a CSDH appeared to develop de novo (CSDH-DN) with no radiological signs of a primary ASDH at the time of trauma presentation and no episodes

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**Table 3. Baseline Trauma Imaging Measurement for Chronic Subdural Hematoma-De Novo Patients**

<table>
<thead>
<tr>
<th></th>
<th>All CSDH-DNs</th>
<th>No SHG</th>
<th>SHG present</th>
<th>( p ) (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>25</td>
<td>11</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Median bicaudate ratio (range)</td>
<td>0.14 (0.09-0.26)</td>
<td>0.14 (0.09-0.26)</td>
<td>0.13 (0.09-0.18)</td>
<td>0.6867 (NS)</td>
</tr>
<tr>
<td>Cortical Atrophy Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>BCR: 0.10 (1)</td>
<td>N/A</td>
<td>N/A</td>
<td>0.0020 (S) on one-way ANOVA correlating BCR and CAS.</td>
</tr>
<tr>
<td>B</td>
<td>0.12 (10)</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.14 (8)</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>0.17 (6)</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Mean unilateral SSD (mm)</td>
<td>8.3</td>
<td>4.6</td>
<td>9.1</td>
<td>0.0001 (S)</td>
</tr>
<tr>
<td>Mean time from trauma to baseline imaging (range)</td>
<td>2 days (0-10)</td>
<td>0.5 days (0-5)</td>
<td>3.2 days (0-10)</td>
<td>0.0451 (S)</td>
</tr>
<tr>
<td>Median CSDH-DN volume (cm(^3))*</td>
<td>104.7</td>
<td>116.8</td>
<td>103.6</td>
<td>No (0.5196)</td>
</tr>
</tbody>
</table>

CSDH-DN, chronic subdural hematoma-de novo; SHG, subdural hygroma; NS, not significant; BCR, bicaudate ratio; S, significant; ANOVA, analysis of variance; CAS, cortical atrophy scale; SSD, subdural space depth.

*Excludes any untreated sides of bilateral CSDH.
of additional trauma warranting imaging in the period between the post-trauma scan and the diagnostic scan leading to recruitment into the Dex-CSDH trial.

A potential criticism is the reliability of the baseline CT to rule out hemorrhage entirely. It must be accepted that there may be “microscopic” hemorrhage at baseline even in CSDH-DN. This is not clinically significant, however, because CT is recognized to have a high sensitivity for detecting acute intracranial blood and is the first-line modality in trauma. The purpose of the distinction is also clinical rather than purely pathological, because even if there is microhemorrhage in CSDH-DN, this is not recognizable on CT and as such, these patients will have a diagnosis of having no acute hemorrhage.

Further, this absence of obvious hemorrhage clearly leads to a specific, slower process of CSDH formation that differs from those with diagnosed ASDH at baseline. It is possible for patients in the CSDH-DN group to have had an interim trauma incurring an ASDH between the normal baseline scan and CSDH diagnosis. Several of our CSDH-DN patients had serial imaging that did not show an ASDH, providing evidence again this contention. Further, none of the patients in this series sustained an interval head injury of sufficient severity to warrant a repeat, trauma-initiated brain scan.

Time intervals were calculated using the date of CSDH diagnostic imaging, rather than symptom onset, because the latter is much more difficult to define. This could potentially introduce bias, because patients with an ASDH on original imaging may be more likely to present earlier for follow-up imaging than those who have been told they have a normal baseline scan. The highly significant difference in time interval between CSDH-AT and CSDH-DN diagnosis (median 16 vs. 57 days), however, supports the hypothesis that the timeline of the pathophysiological processes is different.

In eight patients, baseline imaging was delayed (up to 10 days) after trauma, and in three patients, interval scans were performed (Fig. 3C), without any sign of ASDH, refuting the theory of delayed acute SDH causing CSDH. Instead, our findings lend support to the extensively investigated theory of formation of an inflammatory subdural membrane encapsulating a growing collection of fluid, blood, and inflammatory cells that is self-perpetuating and expands over time.

All CSDH-ATs occurred one to three weeks after trauma, apart from one outlier (the smallest ASDH was
diagnosed on day 45). Others report a similar time frame of ASDH transformation into CSDH. It is logical that a CSDH-AT forms more rapidly than CSDH-DN, because there is potentially greater disruption of the dural border cells layer and a larger volume of acute blood to act as a stimulus for CSDH transformation. It took a median of eight weeks for CSDH-DNs to be seen, with significantly larger volumes than CSDH-ATs. There was no correlation between the time and CSDH-DN volume, with two of the largest CSDH-DNs forming in the shortest time intervals. We suggest that the CSDH expansion rate is related to variations in post-traumatic inflammatory responses rather than time, but this requires further investigation.

The minimal difference in MLS between the CSDH sub-types, despite CSDH-DNs being significantly larger, suggests either CSDH-DN patients have greater baseline atrophy to tolerate a larger CSDH, or the longer delay from trauma allows more cerebral compensation.

Pathophysiology of CSDH-DN
Pathophysiologically, disruption to the cells lining the dura (dural border cells) is likely to be essential in initiating the cascade of events resulting in a CSDH. As demonstrated in this case series, however, this need not involve any visible acute hemorrhage, although it may result in an arachnoid tear and subsequent hygroma. Because the trauma initiating this process is too minor to cause hemorrhage, this may explain why up to 39% of patients do not report preceding trauma. Thus, the dural border cells could be injured by seemingly innocuous processes, such as sudden brief changes in intracranial pressure or cerebrospinal fluid dynamics, particularly in an older patient with pre-existing atrophy.

Previous studies have reported findings of atrophy measures correlating to CSDH risk. In this study, several measures were assessed, with some concordance between BCR and the CAS. There was no significant correlation between BCR and CSDH-DN volume, suggesting that while brain atrophy is a risk factor, it has minimal impact on the final volume of CSDH-DN.

Hygroma has been reported as an important intermediary in some cases of CSDH formation and was observed in 54% (14/26) of patients in this cohort. In clinical practice, hygromas are often not reported, which may be because of the overlap with cerebral atrophy. The SSD appeared to be a useful objective measure of hygroma presence in this cohort, and further investigation of this metric in elderly patients with trauma may aid prediction of CSDH risk.

Pathophysiology of CSDH-AT
It is well recognized that conservatively managed ASDHs can either resolve or transform into a CSDH over time, the latter occurring in approximately 18–21% of ASDHs. This is likely to be even higher in older patients as reported by Laviv and Rappaport, where, in patients with a mean age of 78 years, 43/95 (45%) low velocity ASDHs developed into a subsequent CSDH. The time interval from ASDH to CSDH is often reported to be within two to three weeks, supported by the median of 16 days in this study, but can be as late as three months. The size of baseline ASDHs transforming into CSDH-ATs was small (median volume 60.7 cm³) in comparison with reports of operated ASDHs (mean volume 146.1 cm³) in a similar age-group.

Notably, Benedetto and colleagues reported that 85.7% of patients with an ASDH volume more than 200 cm³ died within 10 days; thus, there is a pre-selection of smaller ASDHs in those that survive and do not need surgical evacuation. There is also evidence, however, that larger ASDHs managed conservatively are more likely to develop a CSDH necessitating treatment.

In our series, the ASDHs increased by more than a third in volume to form CSDH-AT (from 60.7 cm³ to 85.5 cm³), demonstrating rapid growth in a mean time of only 16 days. There was a significant inverse correlation between the volume of the ASDH and the time interval to CSDH-AT diagnosis. Thus, larger volume ASDHs transformed more quickly, suggesting either a larger original blood load, or perhaps a more significant trauma, provides a greater stimulus for rapid conversion to CSDH. The CSDH-AT volume did not correlate with the original ASDH volume, suggesting small ASDHs have the capacity to expand to the same extent as larger ASDHs, doing so more slowly.

Outcome
Recurrence rates were too low to make any comment in relation to the pathogenic pathways, and there were no significant differences in discharge GCS or mRS scores at three and six months. Small cohort size and mRS dichotomization, however, may mean small differences in outcome have been overlooked. A previous study has suggested patients with a known history of trauma have a better outcome than those without reported trauma, possibly because of differences in baseline morbidity. The CSDH-DN may well be synonymous with nontraumatic CSDH, because trauma was too insignificant or too long ago to recall, and may occur in frailer or more comorbid patients, thus influencing outcome.

Baseline cerebral atrophy, which was severe (CAS D) in several CSDH-DN patients, may also be relevant to long-term outcome. It has already been demonstrated that CSDH is likely to contribute to accelerated cerebral volume loss, even greater than that seen in patients with dementia. The underlying mechanisms are not
Fully understood, but the more prolonged formation of CSDH-DN may put these patients at greater risk than CSDH-AT and warrants further investigation.

Previous studies have shown that larger CSDHs, with more midline shift, are associated with higher recurrence rates and unfavorable outcome.\(^{45,46}\) As CSDHs expand with time, this would seem to suggest that earlier diagnosis could improve outcome. Further, lower presentation with time, this would seem to suggest that earlier diagnosis and treatment timeline to help further understand the distinction between these subtypes and whether this impacts long-term outcome.

The main limitation to this study is that only 41/205 patients had available baseline imaging. Larger case series are required to provide sufficient numbers to compare the pathological subgroups more reliably. Even if baseline imaging is not available, the time from recent trauma to CSDH development may be a helpful indicator of CSDH pathological subtype, which should be considered in future studies. There is selection bias because of patients only coming from the Dex-CSDH trial population; however, all patients had symptomatic CSDH, and only one patient was aged under 59, representing a typical neurosurgical CSDH population.

**Conclusion**

This study supports the hypothesis of two pathophysiological processes forming CSDHs, either after ASDH (CSDH-AT) or without acute hemorrhage (CSDH-DN). In the latter, we suggest that an injury causing dural bor-
der cell damage results in a transition through a hygroma phase in many cases and takes significantly longer to form than CSDH-AT.

We advocate careful observation of the CSDH formation timeline to help further understand the distinction between these subtypes and whether this impacts long-term outcome.

**Author Contributions**

EE developed study protocol and performed data collection, analysis, and writing of the manuscript; PW assisted in data interpretation and manuscript editing; AK assisted in manuscript editing; PH assisted in concept of study and manuscript editing.

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**Author Disclosure Statement**

No competing financial interests exist.

**References**

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