

**The management and outcome of patients with chronic subdural
hematoma: a prospective, multi-center, observational cohort study in the
United Kingdom**

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ABSTRACT

OBJECT

Symptomatic chronic subdural haematoma (CSDH) will become an increasingly common presentation in neurosurgical practice as the population ages, but quality evidence remains lacking to guide the optimal management of these patients. The British Neurosurgical Trainee Research Collaborative (BNTRC) was established by neurosurgical trainees in 2012 to improve research by combining the efforts of trainees in each of the UK and Ireland's Neurosurgical Units. We present the first study by the BNTRC that describes current management and outcomes for patients with CSDH throughout the UK and Ireland. This provides a resource both for current clinical practice and future clinical research of CSDH.

METHODS

Data on management and outcomes for patients with CSDH referred to UK and Ireland Neurosurgical Units were collected prospectively over an 8-month period and audited against criteria predefined from the literature; NSU mortality <5%, NSU morbidity <10%, symptomatic recurrence within 60 days requiring repeat surgery <20%, and unfavourable functional status (mRS 4-6) at NSU discharge <30%.

RESULTS

Data from 1205 patients in 26 NSUs were collected. Burr hole craniostomy was the most common procedure (89%) and symptomatic recurrence requiring repeat surgery within 60 days was observed in 9%. Criteria on mortality (2%), rate of recurrence (9%) and unfavourable functional outcome (22%) were met, but morbidity was greater than expected (14%). Multivariate analysis

demonstrated that failure to leave a drain intra-operatively independently predicted recurrence and unfavourable functional outcome ($p=0.011$, $p=0.048$, respectively). Increasing patient age ($p<0.00001$), post-operative bed rest ($p=0.019$) and use of a single burr hole ($p=0.020$) independently predicted unfavourable functional outcomes, but prescription of high flow oxygen or pre-operative use of anti-platelet medications did not.

CONCLUSIONS

This is the largest prospective CSDH study and helps establish national standards. It has confirmed in a real-world setting the effectiveness of placing a subdural drain. Our study identified a number of modifiable prognostic factors, but questions the necessity of some common aspects of CSDH management, such as enforced post-operative bed rest. Future studies should seek to establish how we can optimise peri-operative care of patients with CSDH to reduce morbidity as well as minimize CSDH recurrence. The BNTRC is unique worldwide, conducting multi-centre trainee-led research and audit. This study demonstrates that collaborative research networks are powerful tools to interrogate clinical research questions.

Keywords: Chronic subdural haematoma, neurosurgery, outcomes,

INTRODUCTION

Chronic subdural haematoma (CSDH) is a collection of liquefied blood between the dura and arachnoid layer of the brain. The incidence is 8.2/100,000/year after 70 years of age.² With an ageing population a rise in CSDH prevalence is anticipated. Spontaneous resolution can occur, but surgical evacuation is indicated in patients who deteriorate or do not improve. However, there is little Class I evidence describing optimal surgical and peri-operative management strategies.

The three most common surgical techniques to treat CSDH are twist-drill craniostomy (TDC), burr-hole craniostomy (BHC), and craniotomy. Whilst all three techniques have approximately the same mortality (2-4%), craniotomy has significantly higher morbidity, and TDC has a higher rate of recurrence, suggesting BHC is the preferred technique.²⁵ In contrast, a more recent meta-analysis concluded TDC should be first-line treatment, with craniotomy reserved for symptomatic recurrence.⁸

Other aspects of peri-operative and post-operative management may also influence outcome. A randomised controlled trial (RCT) demonstrated that subdural drains left in-situ after BHC reduced CSDH recurrence requiring re-drainage (9.3 vs. 24.0% recurrence with/without drain).²¹ The benefit of drains was confirmed in a recent meta-analysis.³ However, conflicting evidence for other aspects of CSDH management leads to considerable variation in practice. For example, the optimal number of burr holes (one vs. two) or the benefit of using intra-operative irrigation is uncertain.^{12,19,23} Post-operatively there is contradictory advice about the relative risks and benefits of bed rest versus early mobilization.^{1,15,17} The benefit of corticosteroids as either a primary treatment or an adjunct to surgery remains unclear.^{6,26} Opinions also vary regarding the need to administer agents to mitigate the biological effects of anti-platelets (e.g. platelet transfusion for aspirin). Observational studies

suggest anti-platelet and anti-coagulant use pre-operatively is associated with higher rates of CSDH recurrence.^{4,9,22} Conversely, a retrospective study of 58 patients suggested that early surgery for patients taking anti-platelets without drug cessation or platelet infusion may be safe.¹⁸

Patients with CSDH would benefit from a stronger evidence base for their management. The present study aims to present the clinical, management and outcome characteristics of patients with CSDH across the UK and Ireland. From this data we aimed to identify variables independently associated with symptomatic CSDH recurrence and unfavourable outcomes that could be interrogated in future studies. This was the first study to be conducted by the British Neurosurgical Trainee Research Collaborative (BNTRC).

METHODS

We conducted a nationwide, multi-center, prospective cohort study to describe the clinical characteristics of patients with CSDH, variation in operative and peri-operative strategies, and to ascertain short-term outcomes evaluated against 'best-practice' criteria determined from review of the published literature. The *Strengthening the Reporting of Observational studies in Epidemiology* (STROBE) checklist was used in preparation of this manuscript.

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PARTICIPANTS AND STUDY SETTINGS

Study participants were identified and enrolled at 26 of the 33 UK and Ireland neurosurgical units (NSUs) between May 2013 and January 2014. Eligibility criteria were age over 16, presentation with a primary or recurrent CSDH confirmed on cranial imaging, and referral to a participating NSU. CSDH was defined radiologically as a predominantly hypodense, isodense or mixed density subdural collection. Patients with other pathologies identified at

operation or during subsequent management were excluded (e.g. vascular malformations, subdural empyema). The study protocol was approved by the Academic Committee of the Society of British Neurological Surgeons (SBNS) and has been published previously.⁷ The study was supported by the SBNS and formed part of the Neurosurgical National Audit Programme (NNAP).

OUTCOME MEASURES AND AUDIT STANDARDS

Audit standards were determined from the literature as described previously;⁷ NSU mortality <5%, NSU morbidity <10%, symptomatic recurrence within 60 days requiring repeat surgery <20% and unfavourable functional status (mRS 4-6) at NSU discharge <30%.

DATA COLLECTION

The BNTRC is a network of neurosurgical trainees and supervising consultants in each Neurosurgical Unit (NSU) in the UK and Ireland. Local trainee investigators identified patients at the time of admission to the NSU from on-call referral databases or theatre operative logbooks. Patient demographics, baseline characteristics including medical co-morbidities and relevant medication history, and details of pre-, intra- and post-operative management were collected. A minimum data set including baseline characteristics and proposed management were collected for patients referred to but not transferred into the NSU. Re-operation within 60 days of index admission was identified and recorded. The modified Rankin Scale (mRS) score at discharge from the NSU, morbidity and mortality in the NSU, destination at discharge from the NSU, and length of stay in the NSU, were also recorded.

Data were submitted to a secure online database maintained by the Outcome Registry Intervention and Operation Network (ORION) at the University of Cambridge. The ORION database complies with Department of Health Information Governance policies and with standards for secure processing of

patient healthcare data set out in the Information Governance Toolkit of the Health and Social Care Information Centre. Each NSU was the data controller for its own data. Local governance approvals were in place in each participating NSU.

DATA ANALYSIS

Anonymised data were collated and checked for errors prior to analysis. Patients with missing data sets were excluded if the missing data was relevant to that particular analysis. Data were analysed according to the pre-defined audit standards using one-sample tests. Multivariable logistic regression models were used to assess the impact of variables on outcome and odds ratios are reported. Data were analysed using IBM SPSS Statistics 21.

RESULTS

DEMOGRAPHICS

Data was collected on 1205 patients with CSDH referred to 26 NSUs; recruitment per unit ranged from 4-175 patients (mean 46 patients). Of 1205 patients referred, 823 (68.3%) were accepted for NSU admission. The remaining 382 patients were managed at their referring hospital; twenty-four of these patients were subsequently transferred to the NSU, but have been excluded from the outcome analysis because of incomplete data. The commonest reason for not being transferred was that the subdural collection was considered small and insufficient to explain a patient's symptoms, or that the patient was asymptomatic (Table 1).

BASELINE CLINICAL CHARACTERISTICS OF TRANSFERRED PATIENTS

The median age of patients admitted was 77 years (range 20-99). Sixty-eight percent were male. 62% (514/823) had a documented history of head injury in

the preceding 3 months. Demographic and baseline characteristics of patients are listed in Table 2.

Cognitive impairment was the most frequent presenting symptom of transferred patients (58%), followed by hemiparesis (41%) and headache (41%) (Table 2). The majority of patients had a GCS of 13-15 (88%), not significantly different to non-transferred patients (89%). Patient's functional status on admission was determined using the mRS and the median score was 3.

MANAGEMENT OF PATIENTS TRANSFERRED TO A NSU

Steroid Use

Twenty-six patients (3%) received a course of dexamethasone. Sixteen (2%) as the primary treatment modality for a median of 6.5 days (range 3-21 days) with a median dose of 4mg per day (range 4-16mg). Ten patients (1%) as adjuvant treatment peri-operatively for a median of 6 days (range 1-40) with a median dose of 8mg per day (range 4-12mg). Of the 382 patients not transferred steroid therapy was recommended in 39 cases (10%).

Perioperative clotting

Of the patients transferred, 356/823 (43%) were prescribed anticoagulant or antiplatelet medication at the time of referral: 171 aspirin (21%), 160 warfarin (19%), 36 clopidogrel (4%), 6 dipyridamole (1%) and 12 'other' medications not listed (1%). Aspirin was discontinued a median of 3 days prior to surgery (range 0-44 days). Of the patients taking aspirin, 49/171 (28.7%) received a transfusion of platelets preoperatively. For patients taking warfarin (n=160), the most common reversal strategies were vitamin K + clotting factors (82), vitamin K alone (28) or clotting factors alone (20). Reversal treatment was not reported in 22 patients (14%).

Surgical treatment

Surgical procedures were performed on 787 of 823 patients (94%); 76% by registrars, 21% by senior house officers, 3% by consultants. Most operations were performed under general anaesthesia (93%).

Burr hole craniostomy (BHC) was the most frequent procedure (700/787; 89%), followed by craniotomy (72/787; 9%) and TDC in just one case (<1%); the remaining 14 patients had a craniectomy, or BHC and craniotomy on different sides. Unilateral BHC was most commonly performed using two-burr holes (89%); 10% had a single burr hole. Burr holes were irrigated intraoperatively to remove the collection in 99% of cases and a drain was used in 85% of cases, most often sited subdurally (92%) rather than subgaleally. Drains were left in-situ for 48 hours (68%) or 24-hours (28%).

Postoperative management

Postoperative bed rest was prescribed in 61% of patients after BHC (median 12-24 hours). Only 10% of patients undergoing BHC were prescribed high-flow oxygen postoperatively. Post-operative cranial imaging was performed in 380 (48%) patients after surgery, of which the investigation was described as routine in 58%.

PATIENT OUTCOMES

Outcomes were determined against the previously described criteria.

Mortality (*Audit standard – all cause mortality in NSU <5%*)

Mortality and morbidity data was reported for 798/823 transferred patients. Eighteen patients (2%) died during the study (18/798). Causes of death included pneumonia (10), other sepsis (2) and stroke (3).

Morbidity (*Audit standard – all cause morbidity in NSU <10%*)

The NSU morbidity rate was 14% (111/798), mainly from respiratory tract infection (8%) (Table 3).

Symptomatic recurrence requiring surgery (*Audit standard – rate <20%*)

Follow-up data was available for all 787 patients who underwent surgery. Recurrence occurred within 60 days of primary surgery in 73 patients (9%). The median duration of time to re-operation was 12 days (range 0-57). There was no significant difference in recurrence between patients who had BHC or craniotomy ($p=0.831$).

We determined variables associated with symptomatic recurrence in the 684 patients who underwent de novo BHC for whom data was available, using logistic regression (Table 4). Sixteen patients for whom BHC was for a CSDH recurrence were excluded from analysis.

Drain insertion after BHC, ($p=0.011$, odds ratio-0.414) and a higher preoperative GCS ($p=0.008$, OR=0.859) were predictive of reduced recurrence after controlling for the variables shown in Table 4. These same variables remained predictive of recurrence when all 772 BHC and craniotomy patients were considered together ($p=0.0003$, OR=0.347 and $p=0.002$, OR=0.855, respectively).

We dichotomized the 684 BHC patients according to whether they had unilateral or bilateral CSDH. 157 of 202 patients documented to have bilateral CSDH underwent bilateral BHC. In patients with unilateral BHC a higher pre-operative GCS ($p=0.006$, OR=0.839) and drain insertion after BHC ($p=0.004$, OR=0.317) were still predictive of reduced recurrence. In the bilateral BHC group none of the variables reach statistical significance (Supplementary

Table 1). Bilateral BHC was not an independent risk factor for recurrence ($p=0.867$).

There was no significant difference in recurrence rates between patients having one burr hole (10%) or more than one burr hole (8%) for unilateral CSDH ($p=0.875$) when controlling for the other variables. Antiplatelet medication use preoperatively, the administration of high flow oxygen in the post-operative period and bed rest did not independently significantly affect recurrence, ($p=0.266$, $p=0.811$, $p=0.586$, respectively), even when the BHC cohort was divided into unilateral and bilateral CSDH groups (Table 4, Supplementary Tables 1 and 2). The pre-operative appearance on CT imaging of a mixed density subdural collection, rather than a homogeneously isodense or hypodense clot, did not predict recurrence ($p=0.293$) (Table 4).

Functional outcome (*Audit standard – unfavourable mRS (4-6) at discharge from NSU <30%*)

Modified Rankin Score (mRS) data was available for 798 patients at the point of discharge. An unfavourable mRS (4-6) occurred in 176 patients (22%). The Median mRS score was 2, compared to 3 preoperatively (Figure 1). Factors predicting unfavourable mRS were determined in the 684 patients who had de novo BHC using logistic regression; 148 of these patients had an unfavorable mRS (Table 5).

In the BHC group a favourable pre-operative mRS (equal to or less than 3) was independently predictive of a favourable mRS at discharge ($p<0.00001$, $OR=2.13$), as was drain insertion ($p=0.048$), good pre-operative GCS ($p=0.01$) and lower age ($p=<0.00001$); the average age of patients with a favourable mRS was 76 years (range 65-83), compared to 84 years (76-88) for those with an unfavorable mRS. Prescribed post-operative bed rest predicted a poor outcome ($p=0.019$). Interestingly, although the number of burr holes for BHC

did not predict recurrence, more than one burr hole did predict a favourable functional outcome ($p=0.020$). Pre-operative mid-line shift did not significantly correlate with functional outcome ($p=0.857$).

The same factors remained significant predictors of poor outcome when the BHC patients were considered along with the craniotomy patients. When patients with unilateral or bilateral CSDH were examined separately, age and initial MRS remained significant in both groups ($p<0.0001$) (Supplementary Tables 3 and 4). In the unilateral BHC only group bedrest ($p=0.001$, OR=2.637), drain insertion ($p=0.002$, OR=0.320), increased in significance, multiple burr holes was unchanged ($p=0.030$, OR=0.407), and pre-operative GCS became almost non-significant ($p=0.054$, OR=0.887).

Length of stay and Discharge destination

The median length of NSU stay was 7 days (range 1-179); there was no statistical difference between BHC and craniotomy. At NSU discharge, 47% of patients (358) were transferred to a local hospital for ongoing care whilst 49% were discharged home, one sixth of whom required carers.

DISCUSSION

This was the BNTRC's first study and represents the largest prospective, observational, multi-centre study of CSDH management, NSU outcomes and 60-day recurrence rates.

The BNTRC was established by neurosurgical trainees in 2012 to improve research by combining the efforts of trainees in each of the UK and Ireland's NSUs. ¹⁴ The collaborative provides a semi-formal structure to support

individuals; study leads devise the project protocol and invite collaborative members to join a steering group. Individual trainees in each NSU volunteer as data collectors. Both authorship and collaborator status on publications is defined in advance. Upon project completion the data becomes available to all collaborating members to permit further analysis.

This study provides valuable insights into current management of patients with CSDH. It will inform contemporary practice. It validates in a real world setting the 2009 randomized controlled trial that demonstrated the effectiveness of subdural drain insertion.²¹ Other key observations should be validated in prospective trials. The study defines the current standard of care for patients with symptomatic CSDHs as burr-hole drainage with insertion of a subdural drain for 24-48 hours. There was no clear preference for prescribed bed rest or high flow oxygen in the postoperative period; bed rest was actually associated with unfavourable functional outcome.

Current practice exceeded pre-defined audit standards for functional outcome at discharge, in-NSU mortality and 60-day post-operative symptomatic CSDH recurrence. However, the 14% incidence of postoperative morbidity was greater than the audit standard of less than 10%. This may reflect better data collection in our prospective study compared to existing retrospective studies. Interestingly, the previously largest series (retrospective) of operated cases of CSDH reported 19.6% morbidity.¹⁰ There is nevertheless an opportunity to optimise care for CSDH patients, many of whom are elderly with multiple co-morbidities. There may be parallels to achieving this in the way that changes to peri-operative care of patients with neck of femur fractures reduced mortality in that vulnerable population.¹³ The BNTRC is therefore collaborating on a prospective study to examine how to optimise peri-operative factors in CSDH patient management.

The decision to proceed with revision surgery was as the discretion of the

patient's Consultant neurosurgeon, based on clinical symptoms, correlated with imaging. The 9% rate of symptomatic recurrence we observed at 60 days may have underestimated the true rate if there were late recurrences, but previous studies suggested recurrence is most likely within this timeframe.¹⁶ The median time to recurrence in the present study agrees with that reported previously.⁴ Our study demonstrated that only 48% of operative patients underwent post-operative imaging, so there may have been incidences of recurrence that did not reach clinical significance, but would have been detected radiologically. Since the need for re-do surgery is based on symptomatic recurrence, radiological recurrence alone is of less importance.

We observed that the number of burr holes was not an independent risk factor for CSDH recurrence after BHC, but single burr holes were associated with poorer functional outcomes at discharge. Pre-operative mRS was not predictive of the number of burr holes used in BHC, and the reason for the poorer functional outcomes is not clear. Previous retrospective studies have suggested that a single burr hole is as effective as two in selected cases.^{11,12} Future studies should interrogate this further. A single burr hole may be preferential if associated with reduced operative length and in turn post-operative morbidity, but this has yet to be demonstrated.

More than one burr hole may traditionally be preferred where there is a mixed density subdural collection (mixed between hyperdense and isodense/hypodense material). This is because the hyperdense material represents more acute blood that is thicker than isodense/hypodense blood and does not discharge as easily from a single burr hole. However, our study identified that the radiological appearance of the subdural collection was not predictive of symptomatic recurrence. This may be because the goal of surgery is to reduce the mass effect from the CSDH, not necessarily to remove the haematoma altogether; the residual subdural collection can resolve spontaneously. A single burr hole may be adequate to achieve this and

interestingly we observed no correlation between subdural density and the number of burr holes used for BHC.

Evidence for the benefit of corticosteroids in CSDH management remains scarce. Our study documented steroid use in only a small proportion of patients. The effect of dexamethasone on reduction in reoperation rate of CSDH is the focus of a several ongoing studies, including a RCT comparing dexamethasone to placebo after BHC supported by the BNTRC.

Anticoagulant and antiplatelet use have been implicated in both the development and recurrence of CSDH.⁵ In our study 43% of the patients transferred to a NSU for treatment were taking an antiplatelet or anticoagulant medication. Strategies for the preoperative optimisation of platelet function and coagulation in these patients varied greatly, but the pre-operative prescription of antiplatelet agents was not an independent risk factor for recurrence. The impact of anti-coagulant agents was not examined, as all patients on these agents had their INR corrected pre-operatively. Although the use of antiplatelet agents was not observed to be associated with recurrence, the heterogeneity of timing of discontinuing medication and of reversal strategies suggests this observation should be interpreted cautiously. Nevertheless, it remains feasible that some patients may not need to discontinue their medication for the traditional '7 days' before burr-hole surgery. This could be important, because delay in recommencing these therapies is associated with thromboembolic risk and delay to surgery whilst managing anticoagulant and antiplatelet therapies may also be associated with increased morbidity.

Although our observations are based on UK and Ireland data the results will be of interest internationally, because CSDH is common worldwide. There will undoubtedly be variations between countries in the preference for some aspects of CSDH management that were not well represented in UK practice, such as prescription of steroids or use of Twist Drill Craniostomy. The design of prospective

studies to develop an evidence base to CSDH management should include all these factors.

There are some limitations to our study. For example, we captured data from patients managed in NSUs so do not know the natural history of patients with CSDH managed in hospitals without NSUs. We examined relatively short-term outcome measures and longer-term outcome measures such as 6-month functional status and mortality rate would be valuable. Our patient cohort was skewed to management with BHC, so we could not make a meaningful analysis of variables predicting outcome in the craniotomy subgroup. In addition, our study demonstrated that surgical drainage of CSDH is performed almost exclusively by trainee neurosurgeons and senior house officers. This is clearly standard practice in the UK and a previous study has found no association between seniority of surgeon and post-operative recurrence of CSDH.²⁰ It should also be noted that it is our experience that a Consultant neurosurgeon is always the person to make a decision to proceed to surgery and is available if needed. The question may nevertheless be raised as to whether patient outcomes would be different if Consultant surgeons were the primary surgeon. This is an important question for future study.

CONCLUSIONS

We have defined the preferred strategy for treating symptomatic CSDH as burr hole drainage with post-operative closed drainage system. We have observed that many variations in practice do not significantly impact outcome. Further research is required to examine these relationships in more detail and to determine whether standardisation of management can improve patient outcomes.

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Appendix

Collaborators

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COMPETING INTERESTS

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Figure 1. A comparison of proportion of all patients with a given modified Rankin Score (mRS) in the pre and post-operative patient cohorts. The graph demonstrates the shift to better functional status on discharge compared to status on admission to NSU.