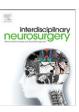
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Technical Note & Surgical Technique

Chronic anticoagulation with warfarin is associated with decreased functional outcome and increased length of stay following craniotomy for acute subdural hematoma



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ABSTRACT

Introduction: With the continued rise of the aging population, the incidence of acute subdural hematoma (ASDH) in the setting of chronic oral anticoagulation with warfarin is expected to increase. No study has directly addressed the risks of poorer outcomes in chronically anticoagulated patients after ASDH evacuation.

Methods: We reviewed retrospectively 94 consecutive cases of ASDH at a single institution with fresh frozen plasma and craniotomy. The outcomes of patients with ASDH in the setting of chronic oral anticoagulation were compared to those of patients with ASDH not taking oral anticoagulation.

Results: There were 22 patients receiving chronic anticoagulation (11 male, 11 female, mean age 63.7 ± 4 years) with ASDH requiring craniotomy for evacuation. These patients had significantly lower mean discharge Glasgow Outcome Scores (GOS) when compared to control subjects $(2.3 \pm 0.3 \text{ versus } 3.0 \pm 0.2)$. Despite presentation with higher Glasgow Coma Scores (GCS), ASDH size tended to be larger in anticoagulated patients, although not significant. Overall mortality was nearly double, that is 55% in anticoagulated patients compared to 29% in those without anticoagulation. Of previously anticoagulated patients alive at discharge, hospital length of stay was longer compared to controls (31.9 \pm 8.5 days versus 21.1 \pm 2.4 days).

Conclusions: These data suggest that ASDH evacuation in chronically anticoagulated patients is associated with higher mortality rates, decreased likelihood of independent function, and increased length of hospital stay. Further research is needed to determine if the effect of chronic anticoagulation on outcome is independent of cofounders, such as age and medical comorbidities. These data may help practitioners and families create treatment plans and furthermore serve as the gold standard for the future evaluation of novel anticoagulation reversal agents such as factor VIIa.

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1. Introduction

Of all the types of intracranial injuries, traumatic acute subdural hematoma (ASDH) is one of the most lethal lesions and most challenging problems with its high mortality rates and limited functional recovery. The initial rates of mortality from this injury were reported between 72% and 96% from the first attempts at surgical treatment for ASDH in the 1930's and 1940's [20]. Despite major advances in the management of head injuries with more rapid diagnosis, computerized tomography (CT) scanning and aggressive neurosurgical interventions, the mortality rate continues to range from 50% to 90% [9,22,24,26,28].

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Several factors have been well documented to significantly correlate with the morbidity and mortality from ASDH. These variables include: age, mechanism of injury, neurological condition on admission, postoperative intracranial pressure (ICP), and time of injury to surgical evacuation of the ASDH [4,9–11,14,20,22,26]. Only two of these—the time between injury to surgical evacuation and postoperative ICP—are controllable factors that may affect improved survival and long-term recovery from ASDH [5,22,24,26].

The concurrence of subdural hematoma and anticoagulant therapy has been well established; however a paucity of data exists on whether anticoagulant therapy negatively affects the mortality in ASDH. In a retrospective study on the role of anticoagulant therapy in the development of subdural hematomas, Wintzen and Tijssen found no correlation between anticoagulant-related subdural hematoma and an increased mortality but did not provide specific data on the mortality rate associated with each type of subdural hematoma [27]. By contrast,

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in an analysis by Kawamata et al. of warfarin-related intracranial hemorrhages in 27 patients with cardiac diseases, fatal outcomes were found in all three patients with ASDH, despite surgical evacuation in two [13].

With the aging of the population and the well-established indications of anticoagulation increasing in prevalence with age [21], exposure to anticoagulant therapy is becoming increasingly common. Furthermore, with at least 12% of ASDH patients reportedly on anticoagulant therapy [25], the effect of anticoagulation on the morbidity and mortality of ASDH is an important question to be answered. Control of anticoagulant therapy may be a potential modifiable factor influencing the outcome of ASDH.

In the present paper, we conducted a retrospective case series review to assess whether pre-existing anticoagulant therapy significantly affects the morbidity and mortality of patients treated for ASDH. Furthermore, we sought to determine what, if any, characteristics contribute to the observed variable outcomes of ASDH in anticoagulated patients compared to non-anticoagulated controls.

2. Patients and methods

In order to assess the effect of pre-existing chronic anticoagulation therapy with Warfarin in acute subdural hematoma (ASDH) we performed a single-institution retrospective cases series review. Operative records were used to identify all patients who underwent craniotomy for evacuation of an ASDH over a seven-year period at a single institution. Patient demographics, clinical presentation, radiological records, operative notes, and clinical outcomes were obtained retrospectively and were available for review in all cases. Pre-existing anticoagulation therapy was defined as knowledge of the patient being on a regimen of warfarin regardless of the admission international normalized ratio (INR). Patients with an elevated INR (>1.4) at the time of presentation were administered fresh frozen plasma (FFP). No patient was refractory to FFP therapy and no patients received recombinant INR reversal agents. Patients were considered to have a supratherapeutic INR if it exceeded the recommended treatment range for the condition for which they were receiving treatment (atrial fibrillation, artificial valve, deep venous thrombosis, etc.).

Each patient underwent a standard fronto-temporal-parietal craniotomy (Fig. 1) for clot evacuation followed by admission to an intensive care unit. All patients received the institutional standard of care post-operative treatment. Mortality and functional outcome were retrospectively assessed using discharge summaries and a modified Glasgow Outcome Scale (GOS). Independent functional outcome was defined as a GOS score of 4 or 5 points. Hospital length of stay was defined as the length in days from the time of presentation until the final disposition of the patient was achieved (death, rehab, home, etc.).

3. Results

3.1. Patient population

A total of 94 craniotomies for ASDH evacuation were performed at our institution during the seven-year period of study. Twenty-two of these patients were on a regimen of chronic oral anticoagulation with warfarin, where as the remaining 74 patients (control) had no such documented history (see Table 1). The mean \pm SEM age for warfarin patients was 63 \pm 5 years versus 47 \pm 5 years for controls. Fifty percent of anticoagulated patients were male compared to 73% of controls. The medical comorbidities of hypertension, diabetes mellitus, or coronary artery disease were present in 11 (50%) of warfarin patients and 21 (29%) of controls. The mechanism of injury was a fall in 77% of warfarin patients, but only 33% of controls. Of patients receiving anticoagulation, 45% presented <4 h from last witnessed baseline condition and 41% with pupillary defects (unilateral or bilateral) compared to 52% and 50% of controls respectively. Mean \pm SEM Glasgow coma scale (GCS)

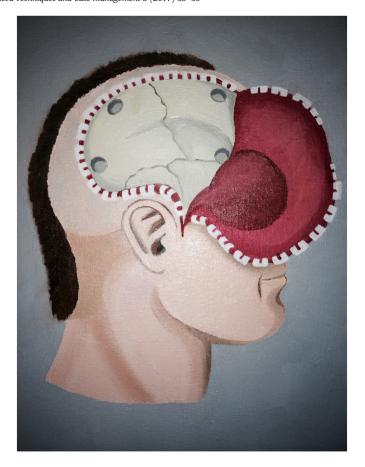


Fig. 1. Standard fronto-temporal-parietal craniotomy opening for evacuation of acute subdural hematoma.

scores at presentation were 10 \pm 0.9 in warfarin patients, compared to 8.5 \pm 0.5 in controls. Radiographically, other brain injury such as contusion or traumatic subarachnoid hemorrhage was present on CT scanning in 9 (41%) of subjects receiving warfarin versus 26 (36%) of controls. Mean \pm SEM maximum ASDH thickness and midline shift as measured by computerized tomography were 19.5 \pm 1.8 and 11.8 \pm

Table 1 Comparison of patients on a regimen of oral anticoagulation with warfarin versus those not (controls) who underwent craniotomy for acute subdural hematoma (aSDH) evacuation. The cohort that was anticoagulated was older and presented with higher Glasgow coma scores (GCS) despite having slightly larger aSDH thicknesses when compared to controls. Data reported as number (%) unless otherwise specified. All means reported as mean \pm SEM. Abbreviations: SAH = subarachnoid hemorrhage, HTN = hypertension, DM = diabetes mellitus, CAD = coronary artery disease.

| | Warfarin | Control | |
|------------------------------------|----------------|----------------|---------|
| Variable | (n = 22) | (n = 72) | p-value |
| Mean age (years) | 63 ± 5 | 47 ± 5 | 0.004 |
| Gender male | 11 (50%) | 53 (73%) | 0.07 |
| Medical comorbidities (HTN, DM, or | 11 (50%) | 21 (29%) | 0.12 |
| CAD) | | | |
| Clinical characteristics | | | |
| Mechanism of injury fall | 17 (77%) | 24 (33%) | 0.0007 |
| Present under 4 h | 10 (45%) | 38 (52%) | 0.72 |
| Mean GCS presentation | 10 ± 0.9 | 8.5 ± 0.5 | 0.06 |
| Pupillary defect at presentation | 9 (41%) | 36 (50%) | 0.61 |
| Radiographic characteristics | | | |
| Other brain injury (contusion or | 9 (41%) | 26 (36%) | 0.88 |
| SAH) | | | |
| Mean aSDH thickness by CT scan | 19.5 ± 1.8 | 16.5 ± 0.9 | 0.06 |
| (mm) | | | |
| Mean midline shift by CT scan (mm) | 11.8 ± 1.6 | 13.1 ± 0.9 | 0.64 |

^{*} Statistically significant difference

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