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Original Article

Safety and timing of early therapeutic anticoagulation therapy after craniotomy

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ABSTRACT

Background: To date, there are few guidelines and studies to guide the timing of initiation of therapeutic anticoagulation (AC) after craniotomy. The goal of this study was to assess the timing, safety, and outcomes of patients following the administration of therapeutic AC after craniotomy.

Methods: A retrospective case–control study was performed evaluating all craniotomy patients from August 2017 to July 2021. Cases were selected if they received therapeutic AC within ten days of craniotomy. Nineteen out of 1013 craniotomy patients met the inclusion criteria. Indications for therapeutic AC were diverse, including deep venous thrombosis, pulmonary embolism, dural venous sinus thrombosis, mechanical heart valve, and left ventricular thrombus.

Results: The mean and median time to therapeutic AC were 5.35 and 5 days, respectively. Three patients developed intracerebral hemorrhage (ICH) that was stable on repeat imaging and did not require any surgical intervention or result in new neurologic deficits. There was no significant association between therapeutic AC and postoperative ICH ($P = 0.067$).

Conclusion: This study demonstrated that the initiation of therapeutic AC in postoperative craniotomy patients from postoperative days 2 to 10 did not result in any major complications. A prospective study is warranted to clarify the indications and safety of therapeutic AC after craniotomy.

Keywords: Anticoagulation therapy, Craniotomy, Intracranial hemorrhage, Mechanical heart valves, Venous thromboembolism

INTRODUCTION

Therapeutic anticoagulation (AC) is essential to the management of many diseases, in particular venous thromboembolism (VTE). The incidence of postoperative VTE after craniotomy ranges from 3% to 60% in the literature.[1,4] VTE carries significant morbidity and up to 30% mortality in the case of an untreated pulmonary embolism (PE).[13] Additional risk factors for VTE after craniotomy include diabetes mellitus, increased age, presence of motor deficit, prolonged intubation/reintubation, history of VTE, and high-grade gliomas.[6,10,12,15,17]

Intracerebral hemorrhage (ICH) at the surgical site in patients who undergo a craniotomy can result in devastating complications, including reoperation, permanent neurological deficit, and death.[16] One large retrospective study of 5520 patients found that 1.5% of patients

required reoperation for hematoma evacuation following craniotomy without therapeutic AC.[2] Negotiating the risk of thromboembolic complications to ICH development in these patients is difficult in the absence of robust evidence-based guidelines for therapeutic AC post-craniotomy.[11,14,16]

Whereas earlier studies had investigated therapeutic AC for mechanical heart valves or VTE several weeks after craniotomy, few studies have examined the outcomes of early therapeutic AC.[3,6] In a recent retrospective study of therapeutic AC after craniotomy, "ultra-early" therapeutic AC was defined as within ten days of craniotomy, and only one of 18 patients developed a postoperative ICH that required surgical intervention.[14] Likewise, our retrospective study aims to expand the evidence for the indications, safety, and outcomes of therapeutic AC within ten days after craniotomy.

MATERIALS AND METHODS

Study design

This protocol was approved by the Institutional Review Board (IRB) at Louisiana State University Health Sciences Center-New Orleans (IRB #2071). This is a single-center retrospective review of neurosurgical patients between August 2017 and July 2021. Inclusion criteria were craniotomy or craniectomy and therapeutic AC in <10 days postoperatively. No exclusion criteria were specified.

Study collection and clinical methods

A total of 1013 underwent craniotomy or craniectomy at our institution in the study period. Ninety-six patients were retrospectively identified in Epic SlicerDicer as possible study candidates. Subsequent chart review identified 40 patients started on therapeutic AC post craniotomy during their hospitalization. Of this number, 19 patients were started on therapeutic AC within ten days. These patients were matched by age (±2 years) and gender in a 1:2 ratio to control craniotomy subjects. Therapeutic AC was defined as therapeutic doses of AC with heparin, enoxaparin, fondaparinux, warfarin, apixaban, rivaroxaban, or dabigatran. Demographics and clinical data included age, gender, reason for admission, date of surgery, type of surgery, disposition, and mortality. Specific AC data included prophylactic measures, therapeutic agents, indication, time from surgery to initiation, complications, and interventions.

In our practice, therapeutic AC with heparin was preferred over other agents due to its short half-life and ready reversibility in patients at risk of postoperative ICH. Our heparin nomogram started at 14 units/kg/hour without boluses and targeted anti-Xa assays of 0.4–0.6 units/mL. Other dosing regimens for therapeutic AC were based on manufacturer recommendations. Surveillance imaging was performed when the anti-Xa level reached the target range or a day after the start of other agents. Subsequent imaging was repeated based on new neurological symptoms.

Statistical analysis

Descriptive statistics were calculated on categorical, discrete, and continuous variables. The chi-square test was calculated to detect an association between therapeutic AC and postoperative ICH in the case versus control groups. Statistical analysis was performed in Excel 2023 (Microsoft) and Statistical Package for the Social Sciences Statistics version 29 (IBM).

RESULTS

Nineteen patients started therapeutic AC within ten days after craniotomy, as detailed in Table 1. All subjects survived hospitalization. Indications for craniotomy varied. Six patients (31%) needed decompressive craniectomy (DC), of which five were for traumatic brain injury (TBI) and one was for a large spontaneous ICH. Five patients (26%) underwent craniotomy for tumor resection. Three patients (16%) underwent craniotomy for treatment of a vascular lesion, of which two were for ruptured aneurysms, and one was for a hemorrhagic cavernous malformation. Three patients (16%) required craniotomy for the drainage of a cerebral abscess. Two patients (11%) had posterior fossa decompressions; one was for a Chiari malformation, and the other was for a gunshot wound causing herniation.

Seven patients received AC preoperatively. Three patients were on warfarin for mechanical heart valves. Two patients were on apixaban; one patient was on apixaban for atrial fibrillation, while the other was on apixaban for an inferior vena cava (IVC) thrombus. One patient was on unfractionated heparin due to a PE that was found in the hospital before surgery. One patient had metastatic cancer and was on enoxaparin for a deep venous thrombosis (DVT). In preparation for craniotomy, the reversal of AC varied by the urgency of the surgery. In two patients, surgery was elective, and therapeutic AC was held for at least five half-lives without bridging AC before surgery. Of the remaining cases, reversal was performed emergently with prothrombin complex concentrate (PCC) and Vitamin K for warfarin, protamine for heparin, and PCC for apixaban.

In the postoperative period, prophylactic AC was specified by each neurosurgeon. All patients received mechanical prophylaxis with sequential compression devices. Of the remainder, most were started on subcutaneous heparin or enoxaparin. This choice was unit-specific and reflected a concern for rapid reversibility with heparin as compared to increased efficacy with enoxaparin. Prophylactic AC was

Table 1: Anticoagulated cohort demographics.

Patient	Age	Gender	Previous AC	Reason for craniotomy
1	42	Female	Enoxaparin	Tumor resection: R temporal metastatic ovarian cancer
2	31	Female	Warfarin	DC: L ICH
3	60	Female	None	Aneurysm clipping: L peri callosal aneurysm
4	68	Male	Apixaban	Drainage of abscess: R temporal
5	44	Female	None	Drainage of abscess: Pons
6	58	Female	None	Tumor resection: R cerebellar metastatic lung adenocarcinoma
7	41	Female	None	Tumor resection: Petroclival meningioma
8	17	Male	None	Drainage of abscess: R epidural empyema
9	60	Female	Apixaban	Tumor resection: L parietal metastatic non-small cell lung cancer
10	56	Female	None	Aneurysm clipping and DC: L MCA
11	43	Male	Heparin	Cavernous malformation resection: Pons
12	77	Male	None	Tumor resection: L cerebellopontine angle meningioma
13	33	Female	None	Chiari decompression: Suboccipital craniectomy
14	16	Male	None	Trauma: Posterior fossa decompression secondary to GSW
15	59	Male	Warfarin	Trauma: Bifrontal DC secondary to SDH
16	58	Male	None	Trauma: R DC
17	41	Male	Warfarin	Trauma: L DC
18	47	Male	None	Trauma: Bifrontal DC
19	24	Female	None	Trauma: L craniotomy EDH evacuation

AC: Anticoagulation, DC: Decompressive craniectomy, EDH: Epidural hematoma, GSW: Gunshot wound, ICH: Intracerebral hemorrhage, L: Left, MCA: Middle cerebral artery, R: Right, SDH: Subdural hematoma

started on postoperative day (POD) 1–2 in 14 (74%) and POD 1–3 in 17 patients (89%). Of the two other patients, one patient started therapeutic heparin on POD 2, whereas the other patient started therapeutic enoxaparin on POD 3 to treat a DVT.

In every case, the need for AC was determined to be urgent to emergent, either due to new VTE, large clot burden (IVC clot, subacute DVT), new left ventricular thrombus, or highly thrombogenic mechanical heart valve. The initial AC agent was heparin in 13 patients (68%), enoxaparin in three patients (16%), apixaban in two patients (11%), and warfarin in one patient (5%). The average time to start AC after craniotomy was 5.35 days. The fastest time to start AC post craniotomy was two days, while the slowest time was ten days. The most common indication for therapeutic AC was VTE in 13 patients (68%).

Table 2 illustrates the postoperative course of each patient included in the study. Four complications occurred after starting therapeutic AC. Three patients (17%) developed ICH, which was stable on repeat imaging [Supplemental Figure 1]. None of these patients required further surgery or developed focal neurologic deficits due to the ICH.

In one case, an ICH was detected after a right cerebellar tumor resection on POD 9 following four days of AC. Her new neurologic deficits were headache and lethargy, and the volume of the hemorrhage was 16 mL. Protamine was given to reverse therapeutic enoxaparin, an IVC filter was placed for her right leg DVT, and further, therapeutic AC was withheld despite a small PE. The patient was restarted on prophylactic AC 5 days after ICH and did not develop any further complications from the VTE or ICH.

The second patient developed a left frontal ICH and intraventricular hemorrhage after a bifrontal DC for TBI. The patient had a mechanical heart valve, and therapeutic heparin as a bridge to warfarin was started on POD 2. The ICH was detected due to new lethargy on POD 16 after 14 days of therapeutic AC and stable imaging twice before. The ICH had a volume of 35 mL in the context of known bifrontal contusions. The patient's anti-Xa was 0.35, and INR was 1.7 at that time. After reversal with protamine and PCC, repeat imaging was stable, and therapeutic AC was restarted one week later without further complication.

The final patient had a left DC for TBI and demonstrated a small right tentorial subdural hematoma on POD 15. The patient was started on therapeutic heparin as a bridge to warfarin for a mechanical heart valve on POD 5. Repeat imaging was stable, and therapeutic AC was not interrupted.

The only complication of therapeutic AC outside of ICH occurred in a patient on therapeutic heparin who developed heparin-induced thrombocytopenia and thrombosis. The

Table 2: Postoperative AC.

Patient	POD VTE PPX	VTE PPX	POD AC	Indication for AC	Initial AC	Complications due to AC	Disposition	Long-term AC
1	1	Heparin 5000 units SC q8h	6	Subacute DVT	Enoxaparin	No	Home	Enoxaparin
2	2	Heparin 5000 units SC q8h	7	Chronic MV	Warfarin	No	IPR	Warfarin
3	1	Heparin 5000 units SC q8h	5	Acute LV thrombus	Heparin	No	IPR	Warfarin
4	1	Heparin 5000 units SC q8h	7	Acute PE	Apixaban	No	IPR	Apixaban
5	1	Heparin 5000 units SC q8h	9	Acute PE	Heparin	No	IPR	Apixaban
6	2	Enoxaparin 40 mg SC daily	5	Acute PE	Heparin	Right cerebellar ICH	IPR	Enoxaparin
7	1	Heparin 5000 units SC q8h	8	Acute PE	Heparin	No	SNF	Apixaban
8	N/A	None	3	Acute L subclavian DVT	Enoxaparin	No	Home	Enoxaparin
9	1	Heparin 5000 units SC q8h	7	Chronic IVC thrombosis	Apixaban	No	Home	Apixaban
10	2	Heparin 5000 units SC q8h	4	Acute DVT	Heparin	No	IPR	Rivaroxaban
11	N/A	None	3	Acute DVT/PE	Heparin	No	LTCH	Apixaban
12	1	Heparin 5000 units SC q8h	3	Acute PE	Heparin	No	Home	Apixaban
13	2	Heparin 5000 units SC q8h	7	Acute DVT	Heparin	No	Home	Apixaban
14	3	Enoxaparin 30 mg SC q12h	8	Acute DVT	Enoxaparin	No	IPR	Enoxaparin
15	N/A	None	2	Chronic MV	Heparin	Left frontal ICH/IVH	SNF	Warfarin
16	2	Heparin 5000 units SC q8h	4	Acute PE	Heparin	No	IPR	Apixaban
17	2	Heparin 5000 units SC q12h	5	Chronic MV	Heparin	Right tentorial SDH	Home	Warfarin
18	3	Heparin 5000 units SC q8h	5	Acute DVT	Heparin	HITT	LTCH	Apixaban
19	2	Enoxaparin 30 mg SC q12h	7	Acute DVT	Heparin	No	IPR	Enoxaparin

DVT: Deep venous thrombosis, MV: Mechanical heart valve, LTCH: Long-term care hospital, LV: Left ventricular, HITT: Heparin-induced thrombocytopenia and thrombosis, ICH: Intracerebral hemorrhage, IPR: Inpatient rehabilitation, PE: Pulmonary embolism, POD: Postoperative day, PPX: Prophylaxis, SNF: Subacute nursing facility, VTE: Venous thromboembolism, AC: Anticoagulation, SC: Subcutaneous, N/A: Not applicable, IVH: Intraventricular hemorrhage, SDH: Subdural hematoma

patient was switched to argatroban and then transitioned to apixaban without any further complication.

The therapeutic AC cohort was compared to a control cohort of 38 patients who were not anticoagulated in 10 days of craniotomy, as detailed in Supplemental Tables 1 and 2. Overall, the control cohort was significantly less ill than the therapeutic AC cohort, as shown by a length of stay of 9.2 versus 23.5 days and discharge to home in 20 (52%) versus 6 (32%) patients. Only one control displayed a worsening hemorrhage postoperatively, which occurred after leaving DC for a large ICH and ended in death. No association was demonstrated between therapeutic AC and postoperative ICH ($P = 0.067$).

DISCUSSION

As the most common fatal postoperative complication of neurosurgery is VTE, it is imperative to identify the safe timing of therapeutic AC after surgery.[8,13] Additional

vascular and cardiac comorbidities, such as mechanical heart valves or atrial fibrillation, may further argue for early therapeutic AC post-craniotomy. Starting therapeutic AC on patients in most situations is safe, with a major bleeding risk of 1.6% after three months of AC for VTE and 2.3% yearly for AC for atrial fibrillation.[5,7] Instead, neurosurgeons are routinely asked to decide between the risk of postoperative ICH and the benefit of therapeutic AC in high-risk situations and without strong guidelines.[11] Although this decision should be informed by consultation with hematology, cardiology, or critical care specialists, it often falls to neurosurgeons to make the call based on scant data.

Preliminary evidence to inform this decision is mounting. Prophylactic AC is routinely started after craniotomy and has been shown to reduce the incidence of VTE in 1087 patients after craniotomy.[4] In a retrospective series of 83 patients with VTE within 30 days after craniotomy, three patients (3.6%) developed subclinical ICH while on AC.[9] Of these patients, therapeutic AC was stopped and reversed in two patients, with progression and death in one patient and progression of DVT to PE in another patient. Another retrospective series of 53 patients after craniotomy who needed therapeutic AC for VTE concluded that there was no increased incidence of ICH when AC was started between POD 2 and 29, except for the use of warfarin.[6] In the latest retrospective series of therapeutic AC after craniotomy before POD 10, there was one case (5.6%) that led to reoperation.[14]

Our series adds to the evidence that therapeutic AC within ten days post-craniotomy can be safe. The indications for craniotomy in our population included elective and emergent conditions. The indications for therapeutic AC were similarly diverse, reflecting the complexity of contemporary practice. Our institution primarily performed therapeutic AC with a heparin nomogram without boluses and with a conservative anti-Xa goal. This strategy was conservative, designed to prolong the time from heparin initiation to therapeutic AC to avoid periods of supratherapeutic AC and related complications. While therapeutic enoxaparin is acknowledged to have a lower bleeding risk than heparin in many conditions, this has not yet been established in the neurosurgical literature. With its short half-life and easy reversibility, heparin AC may be preferable in patients at high risk for postoperative ICH. Sixteen percent of subjects developed ICH after therapeutic AC in our study. None resulted in reoperation, morbidity, or mortality, and therapeutic AC was either continued or restarted shortly after that. This outcome compares favorably

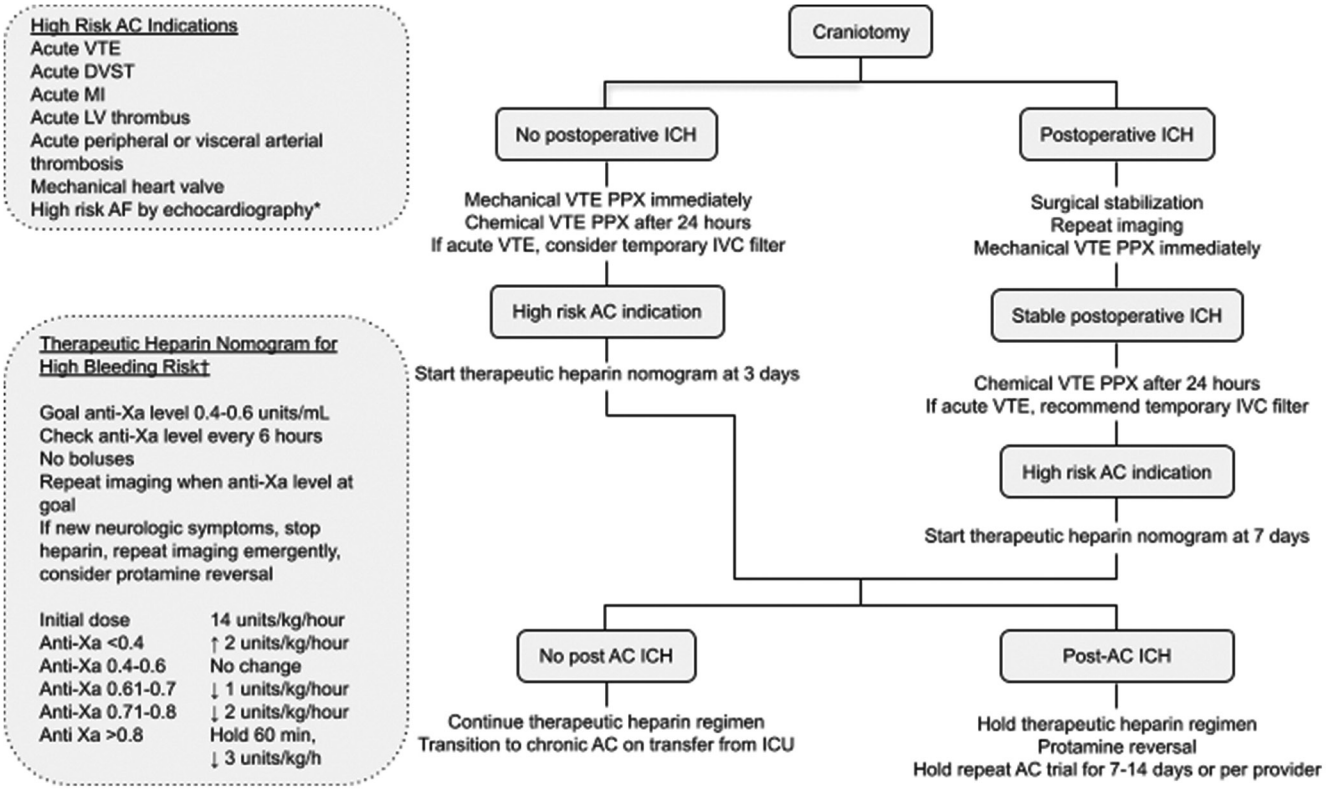

Figure 1: Proposed therapeutic AC algorithm after craniotomy *As determined by consultation with cardiology with features to include left atrial appendage thrombus, left atrial spontaneous echocardiographic contrast, and LV ejection fraction <40%. †Based on institutional and departmental interpretation of common heparin nomograms. AC: Anticoagulation, AF: Atrial fibrillation, DVST: Dural venous sinus thrombosis, ICH: Intracerebral hemorrhage, IVC: Inferior vena cava, LV: Left ventricle, MI: Myocardial infarction, PPX: Prophylaxis. VTE: Venous thromboembolism.

with other recent series. A larger randomized trial is indicated to clarify the timing, protocol, and safety of therapeutic AC against the risk of ICH after craniotomy.

There are several limitations to our study. The control group was matched by age and gender but not the severity of illness. This weakness would have only supported the alternative conclusion that there was a significantly higher rate of postoperative ICH than without therapeutic AC. Although most patients were started on heparin for therapeutic AC first, there was some heterogeneity. This variation reflects the retrospective nature of our research, which included multiple neurosurgeons with different training and experience. The heterogeneity of indications for craniotomy and AC was even greater and certainly limited the generalizability of our findings, particularly given its small sample size from a single institution. Despite this limitation, the study nonetheless reflects the low current level of evidence in the field and adds to preliminary evidence to inform further investigation. In the future, it will be beneficial to collaborate with other institutions to execute a prospective study that standardizes the AC protocol, increases sample size, and controls for bias and confounding variables. The algorithm in Figure 1 represents our recommendation for therapeutic AC after craniotomy and may be viewed as a representation of our current practice and the foundation for a subsequent study.

CONCLUSION

This retrospective study demonstrated the safety of starting therapeutic AC in postoperative craniotomy patients. Approximately 16% of patients developed ICH after starting therapeutic AC, but none of these cases required surgery or resulted in a permanent neurological deficit. A future study should aim to develop a specific protocol and time to initiate therapeutic AC on postoperative craniotomy patients safely.

Ethical approval

This protocol was approved by the Institutional Review Board (IRB) at Louisiana State University Health Sciences Center-New Orleans (IRB #2071 September 22nd, 2021)

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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SUPPLEMENTAL TABLES

Supplemental Table 1: Control cohort demographics.

Patient	Age	Gender	Previous AC	Reason for craniotomy
20	15	Male	None	Trauma: R DC due to GSW
21	16	Male	None	Tumor resection: R temporal pleomorphic xanthoastrocytoma
22	17	Male	None	Cavernous malformation resection: L frontal
23	18	Male	None	Trauma: Bifrontal decompressive craniectomy due to GSW
26	24	Female	None	AVM resection: Ruptured L frontal
27	24	Female	None	Tumor resection: Intraventricular neurocytoma
28	31	Female	None	Aneurysm clipping: Ruptured R MCA
29	31	Female	None	Tumor resection: Intraventricular neurocytoma
30	32	Female	None	Tumor resection: L temporal astrocytoma
31	34	Female	None	Tumor resection: R parietal glioblastoma multiforme
32	40	Male	None	SDH evacuation: Suboccipital
37	43	Female	None	Tumor resection: R occipital ependymoma
38	43	Female	None	Wound revision and pseudomeningocele marsupialization
39	44	Female	None	SDH evacuation: R hemispheric
40	44	Female	None	Tumor resection: L parasagittal meningioma
41	46	Female	None	Tumor resection: R parasagittal meningioma
42	47	Male	None	Trauma: R DC due to GSW
43	47	Male	None	Trauma: L parietal depressed skull fracture
44	55	Female	None	Aneurysm clipping: Ruptured L PCom
45	55	Female	None	Tumor resection: L frontal anaplastic astrocytoma
46	57	Male	None	Trauma: L SDH
47	57	Female	None	Aneurysm clipping: Unruptured R ACA
48	57	Male	None	DC: L ICH
49	58	Female	None	Tumor resection: L cerebellar metastatic ovarian cancer
50	58	Female	None	DC: R MCA stroke
51	59	Male	None	Trauma: Bifrontal DC
52	59	Male	None	Trauma: Frontal cranialization due to GSW
53	61	Female	None	Tumor resection: L parasagittal meningioma
54	61	Female	None	Tumor resection: R sphenoid wing meningioma
55	62	Female	None	Tumor resection: L frontal metastatic colon cancer
56	67	Male	None	SDH evacuation: R hemispheric
57	69	Male	None	SDH evacuation: Bilateral hemispheric
58	77	Male	None	Tumor resection: L parasagittal meningioma
59	77	Male	None	Tumor resection: L frontal meningioma

AC: Anticoagulation, ACA: Anterior communicating artery, ICH: Intracerebral hemorrhage, DC: Decompressive craniectomy, L: Left, MCA: Middle cerebral artery, PCom: Posterior communicating artery, R: Right, SDH: Subdural hematoma, GSW: Gunshot wound, AVM: Arteriovenous malformation

Supplemental Table 2: Control cohort postoperative AC and case matching.

Patient	POD VTE PPX	VTE PPX	POD AC	Indication for AC	Initial AC	New or enlarged ICH	VTE	Disposition	Long-term AC	Match
20	2	Enoxaparin 40 mg SC daily	NA	NA	NA	No	No	IPR	None	14
21	NA	None	NA	NA	NA	No	No	Home	None	8
22	NA	None	NA	NA	NA	No	No	Home	None	8
23	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	14
26	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	19
27	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	19
28	3	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	2
29	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	2
30	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	13
31	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	13
32	2	Enoxaparin 40 mg SC daily	NA	NA	NA	No	No	Home	None	17
33	2	Enoxaparin 30 mg SC q12h	NA	NA	NA	No	No	LTCH	None	17
34	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	7
35	2	Enoxaparin 30 mg SC q12h	NA	NA	NA	No	No	IPR	None	11
36	4	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	11
37	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	7
38	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	1
39	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	1
40	NA	None	NA	NA	NA	No	No	Home	None	5
41	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	5
42	4	Enoxaparin 40 mg SC daily	NA	NA	NA	No	No	LTCH	None	18
43	3	Enoxaparin 30 mg SC q12h	NA	NA	NA	No	No	Home	None	18
44	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	10
45	3	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	10
46	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	16
47	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	6
48	1	Enoxaparin 40 mg SC daily	NA	NA	NA	Yes	No	Expired	None	16

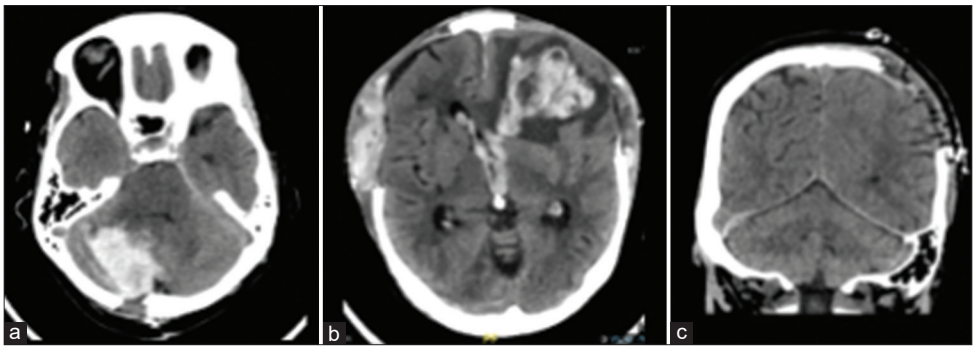
(Contd...)

Supplemental Table 2: *(Continued).*

Patient	POD VTE PPX	VTE PPX	POD AC	Indication for AC	Initial AC	New or enlarged ICH	VTE	Disposition	Long-term AC	Match
49	2	Enoxaparin 40 mg SC daily	NA	NA	NA	No	No	Home	None	6
50	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	3
51	2	Enoxaparin 30 mg SC q12h	NA	NA	NA	No	No	IPR	None	15
52	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	15
53	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	3
54	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	9
55	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	9
56	5	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	4
57	3	Heparin 5000 units SC q8h	NA	NA	NA	No	No	Home	None	4
58	1	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	12
59	2	Heparin 5000 units SC q8h	NA	NA	NA	No	No	IPR	None	12

AC: Anticoagulation, IPR: Inpatient rehabilitation, LTCH: Long-term care hospital, POD: Postoperative day, PPX: Prophylaxis, SC: Subcutaneous, VTE: Venous thromboembolism, ICH: Increcerebral hemorrhage, NA: Not applicable

SUPPLEMENTAL FIGURE



Supplemental Figure 1: Postoperative intracranial hemorrhage after therapeutic AC Patient 6 in (a) suffered a 16 mL ICH in the resection bed of her right cerebellar metastasis. Patient 15 in (b) developed a 35 mL ICH with intraventricular hemorrhage in the context of bifrontal contusions and bifrontal DC after TBI. Patient 17 in (c) had a minimal right tentorial subdural hematoma after leaving DC for TBI. AC: Anticoagulation, DC: Decompressive craniectomy, ICH: Intracerebral hemorrhage, TBI: Traumatic brain injury.