Journal of Neuro-Oncology (2022) 156:341–352
https://doi.org/10.1007/s11060-021-03916-2

CLINICAL STUDY

The role of anticoagulation for superior sagittal sinus thrombosis following craniotomy for resection of parasagittal/parafalcine meningiomas

Adrian E. Jimenez[1] · Adham M. Khalafallah[2] · David Botros[1] · Melanie A. Horowitz[1] · Omar Azmeh[1] · Shravika Lam[3] · Leonardo A. P. Oliveira[1] · Sachiv Chakravarti[1] · Sophie Liu[1] · Esther Wu[1] · Oren Wei[1] · Jose L. Porras[1] · Chetan Bettegowda[1] · Rafael J. Tamargo[1] · Henry Brem[1] · Debraj Mukherjee[1]

Received: 11 October 2021 / Accepted: 27 November 2021 / Published online: 2 December 2021

Abstract
Objective The safety and efficacy of anticoagulation in managing superior sagittal sinus (SSS) thrombosis remains unclear. The present study investigated the relationship between anticoagulation and cerebrovascular complications in parasagittal/parafalcine meningioma patients presenting with post-surgical SSS thrombosis.
Methods We analyzed 266 patients treated at a single institution between 2005 and 2020. Bivariate analysis was conducted using the Mann–Whitney U test and Fisher's exact test. Multivariate analysis was conducted using a logistic regression model. Blood thinning medications investigated included aspirin, warfarin, heparin, apixaban, rivaroxaban, and other novel oral anticoagulants (NOACs). A symptomatic SSS thrombosis was defined as a radiographically apparent thrombosis with new headaches, seizures, altered sensorium, or neurological deficits.
Results Our patient cohort was majority female (67.3%) with a mean age (± SD) of 58.82 ± 13.04 years. A total of 15 (5.6%) patients developed postoperative SSS thrombosis and 5 (1.9%) were symptomatic; 2 (0.8%) symptomatic patients received anticoagulation. None of these 15 patients developed cerebrovascular complications following observation or anticoagulative treatment of asymptomatic SSS thrombosis. While incidence of any other postoperative complications was significantly associated with SSS thrombosis in bivariate analysis ($p = 0.015$), this association was no longer observed in multivariate analysis ($OR = 2.15$, $p = 0.16$) when controlling for patient age, sex, and anatomical location of the tumor along the SSS.
Conclusions Our single-institution study examining the incidence of SSS thrombosis and associated risk factors highlights the need for further research efforts better prognosticate this adverse outcome. Conservative management may represent a viable treatment strategy for patients with SSS thrombosis.

Keywords Anticoagulation · Meningioma · Neuro-oncology · Outcomes · Thrombosis

Introduction

Surgical resection of extra-axial brain tumors including meningiomas has been associated with the development of cerebral venous sinus thrombosis (CVT) [1, 2]. Though often considered a relatively infrequent postoperative complication, improvements in imaging techniques have likely been a major cause of the rising incidence of CVT in recent years [3–5]. CVT symptoms vary and can include headaches, seizures, or mental status changes, though the majority of patients develop asymptomatic thrombi [6, 7]. Though CVT is often treated with anticoagulation, numerous studies examining patients with postoperative CVT have found that anticoagulation in the postoperative setting can lead to

Adrian E. Jimenez and Adham M. Khalafallah both contributed equally to this study

✉ Debraj Mukherjee
dmukher1@jhmi.edu

[1] Department of Neurosurgery, Johns Hopkins University School of Medicine, 1800 Orleans St, Baltimore, MD 21287, USA

[2] Department of Neurological Surgery, University of Miami School of Medicine, Miami, FL 33136, USA

[3] Department of Neurological Surgery, Vanderbilt University Medical Center, Nashville, TN 37232, USA

an increased risk of complications including intracerebral hemorrhage [6–10]. Asymptomatic post-operative CVT have been found to carry a more benign course compared to symptomatic CVT and may be safely observed and managed conservatively, avoiding the risks associated with postoperative anticoagulation [7, 11, 12].

Surgical resection of parasagittal and parafalcine meningiomas likely promotes SSS thrombus development via direct pressure to venous structures during the removal of these tumors [13]. Research into the role of anticoagulation in patients who develop SSS thrombi is limited [7]. The present study therefore aims to (1) determine risk factors for the development of postoperative SSS thrombosis in patients with parasagittal/parafalcine meningiomas and (2) examine subsets of patients with symptomatic versus asymptomatic SSS thrombosis to determine whether conservative management (observation), in lieu of anticoagulation, is associated with adverse postoperative outcomes. Our results may be useful for optimizing the postoperative management of patients with SSS thrombosis following parasagittal/parafalcine meningioma resection.

Methods

Patient selection and recorded variables

Our study analyzed data from 266 patients who underwent surgical resection for parasagittal/parafalcine meningiomas at a single academic medical institution between January 1st 2005 and August 5th 2020. Our Institutional Review Board (IRB), acting as a Health Insurance Portability and Accountability Act (HIPAA) Privacy Review Board, reviewed and approved the waiver of informed consent for this retrospective, HIPAA-compliant study (IRB00181593). Manual chart review of electronic medical records was conducted to obtain patient demographic and surgical information. Race was dichotomized into two categories due to limited sample size: White and Other. Other included African-American, Asian, and otherwise non-specified patients. Insurance status was analyzed as a binary variable consisting of (1) patients who had private insurance or (2) patients on Medicare, Medicaid, and those who were uninsured. Frailty was measured using the 5-factor modified frailty index (mFI-5) due to previous research demonstrating its association with postoperative outcomes following brain tumor surgery [14–17]. mFI-5 scores were manually calculated by tracking the presence or absence of the following five medical comorbidities: "functional status," "history of diabetes," "history of chronic obstructive pulmonary disease," "congestive heart failure," and "hypertension." Functional status was defined as either independently performing activities of daily living (1) or requiring assistance (0) with these activities. The presence of each comorbidity corresponded to one-point, for a minimum score of 0 and a maximum score of 5.

Routine discharge disposition was defined as discharge to home (self-care) or home with healthcare service assistance. Nonroutine discharge disposition was defined as discharge to a rehabilitation facility, a skilled nursing facility, or a hospice facility, a definition that has been used in prior studies [18]. Tumor size was calculated using post-contrast magnetic resonance images; volume was measured using dimensions in the axial (x), coronal (y), and sagittal (z) planes and was calculated using the following formula: $\frac{x \cdot y \cdot z}{2}$. WHO grade was analyzed as a dichotomized variable (grade I vs. grade II/III), as was tumor invasion of the SSS (full occlusion vs. none/partial involvement as determined via blinded review of pre-operative MRI imaging by author A.E.J.) and Simpson grade (grade I/II/III vs. IV). Simpson grade was determined using surgeon operative report findings. Anticoagulation was defined as use of any of the following medications post-operatively as documented in the electronic medical record: aspirin, warfarin, therapeutic heparin, apixaban, rivaroxaban, or other novel oral anticoagulants. At our institution, all brain tumor patients receive 5,000 units/mL of subcutaneous heparin postoperatively (until hospital discharge) for deep vein thrombosis/pulmonary embolism (DVT/PE) prophylaxis.

A postoperative complication was defined as occurrence of any one of the following: wound infection, hematoma, deep vein thrombosis/pulmonary embolism, myocardial infarction, meningitis, seizure, dysphagia, new language deficit, new motor deficit, new visual deficit, new sensory deficit, or new cognitive deficit. Occurrence of a postoperative SSS thrombosis was tracked and analyzed separately from the aforementioned postoperative complications. Imaging reports by independent neuroradiologists were reviewed to identify patients with SSS thrombosis, and three co-authors (A.E.J., A.M.K., and D.M.) independently confirmed whether thrombi were present within the SSS using post-operative MR venograms. At our institution, postoperative MR venograms are only ordered for meningioma patients if there was preoperative imaging demonstrated substantial tumor involvement with the SSS, if there was suspicion for SSS damage intraoperatively, or if there is otherwise any concern for reduced sinus patency after surgery. While anticoagulation use at our institution is not standardized, the decision to start a patient on blood thinners to treat SSS thrombosis involves multidisciplinary collaboration between our neurosurgery team and our neurocritical care team, along with discussion of risks and benefits with the patient and/or family members. The decision depends on patient-specific and operative-specific risk factors, and mainly involves treatment with a low goal, no bolus heparin drip. In the present study, cerebrovascular complications were defined specifically as intracerebral hemorrhage, ischemic stroke, or transient ischemic events (TIAs).

Patients who developed SSS thromboses were stratified into those who developed asymptomatic or symptomatic thrombi. In line with previous research detailing symptoms of cerebral venous thrombosis, a symptomatic SSS thrombosis was defined as a postoperative thrombus in the presence of one or more of the following symptoms: new headaches, seizures, altered sensorium, or neurological deficits [4, 11, 19–21]. At our institution, conservative management of SSS thrombosis consisted of observation only (i.e. no aggressive hydration, hyperventilation, or medication protocols).

Statistical analysis

Data was collected using Microsoft Excel (version 2016, Microsoft Corp.), and statistical analyses were conducted using R Statistical Software (version 3.3.2., r-project.org). The Mann–Whitney U test was used for bivariate analysis of continuous variables and Fisher's exact test was used for bivariate analysis of categorical variables. Multivariate analysis was conducted using logistic regression.

Data was analyzed in two phases. First, bivariate analysis was used to identify statistically significant associations between patient demographics/clinical characteristics and SSS thrombus development. Second, multivariate analysis was performed using the dependent variable of postoperative SSS thrombosis. Covariates in this analysis included all variables that approached statistical significance in bivariate analysis ($p < 0.10$). Post-operative anticoagulation was excluded from multivariate analysis given its role as a treatment following SSS thrombus development rather than a risk factor predisposing patients to thrombosis. Patient age and sex were forced into the logistic regression model due to prior studies demonstrating their role as risk factors for CVT development [2, 22, 23]. Values of $p < 0.05$ were considered statistically significant, and p-values were reported as two-sided.

Results

Patient demographics and clinical characteristics

Our patient cohort had a mean age (± SD) of 58.82 ± 13.04 years. Our cohort was majority female (67.3%), containing 197 (74.1%) Caucasian patients. The majority of patients in our cohort were not Hispanic/Latino (98.1%) and were married (65.8%). A total of 147 (55.3%) patients had private insurance, while 107 (40.2%), 7 (2.6%), and 5 (1.9%) patients had Medicare, Medicaid, or were uninsured, respectively. Our cohort had a mean mFI-5 score of 0.52 with a standard deviation of 0.76. The mean BMI among our patient cohort was 28.72 ± 5.77 kg/m^2. A total of 69 (25.9%) patients were past or current smokers while 22 (8.3%) patients were taking hormonal contraceptives prior to surgery.

Most patients (88.3%) were not admitted through the emergency room, and most (84.2%) had a WHO Grade I tumor. The mean tumor size (± SD) in our cohort was 24.06 ± 35.81 cm^3. A total of 79 (29.7%), 125 (47.0%), and 62 (23.3%) patients had tumors that did not invade the SSS, had partial involvement with the SSS, and fully occluded the SSS, respectively. Most patients (81.2%) received a Simpson grade I/II/III resection. Within our study cohort, 45 (72.6%) of the 62 patients with tumors that fully occluded the SSS had gross total resection of their tumors (i.e. Simpson grade IV resection). Among the 199 patients with tumors that did not occlude the SSS, 171 (85.9%) had gross total resection of their tumors. While patients with tumors that fully occluded the SSS had lower odds of a gross total resection relative to patients with tumors that did not fully occlude the SSS, this association did not attain statistical significance (OR = 0.51, p = 0.062). Among the patients in our cohort, 2 (0.8%) had surgical ligation of the SSS during tumor resection and 2 (0.8%) patients had SSS reconstruction. Among the 2 SSS ligation patients, 1 patient had partial tumor involvement with the SSS preoperatively, while the other patient had no tumor involvement with the SSS. Among the 2 SSS reconstruction patients, both had tumors that partially occluded the SSS. A total of 19 (7.1%) patients received postoperative anticoagulation (excluding subcutaneous heparin received for routine DVT/PE prophylaxis) for the following indications: 2 patients (0.8%) received anticoagulation for postoperative SSS thrombosis, 5 (1.9%) received anticoagulation for prior DVT/PE, 4 (1.5%) for an unknown/undocumented indication, 1 (0.4%) for anticoagulation in the setting of recent coronary stent placement, 1 (0.4%) for atrial fibrillation, and 1 (0.4%) for unspecified heart disease. A total of 78 (29.3%) patients had at least one postoperative complication (excluding SSS thrombosis), and the top three most common complications were new motor deficit (9.0%), new cognitive deficit (7.9%), and seizure (6.8%). The majority of patients (85.3%) had a routine discharge following surgery. The mean LOS and mean ICU LOS were 1.54 ± 1.94 days and 4.95 ± 7.06 day, respectively.

Factors associated with SSS thrombosis

Tables 1, 2, 3 stratify patient demographics, tumor characteristics, and postoperative outcomes (respectively) by SSS thrombosis occurrence, with the aim of identifying common factors among the 15 (5.6%) patients in our study who developed SSS thrombi. In bivariate analysis, the only factor that was significantly associated with increased odds of SSS thrombus development was occurrence of any

Table 1 Parasagittal/parafalcine meningioma patient demographics, N (%)

Characteristic	SSSVT (n = 15)	No SSSVT (n = 251)	p-value
Mean age ± SD	54.93 ± 14.76	59.05 ± 12.93	0.37
Sex			
Male	5 (33.3)	82 (48.5)	1.00
Female	10 (66.7)	169 (67.3)	
Race			
White	12 (80.0)	185 (73.7)	0.77
Other	3 (20.0)	66 (26.3)	
Ethnicity			
Hispanic/Latino	1 (6.7)	4 (1.6)	0.25
Not Hispanic/Latino**	14 (93.3)	247 (98.4)	
Marital status			
Married	10 (66.7)	165 (65.7)	1.00
Not Married	5 (33.3)	86 (34.3)	
Insurance status			
Private	9 (60.0)	138 (55.0)	0.79
Other†	6 (40.0)	113 (45.0)	
Mean mFI-5 ± SD	0.60 ± 0.91	0.51 ± 0.75	0.83
Hypertension	5 (33.3)	74 (29.5)	–
Diabetes	2 (13.3)	31 (12.4)	–
Chronic obstructive pulmonary disease	1 (6.7)	11 (4.4)	–
Functional status ‡	0 (0.0)	10 (4.0)	–
Heart failure	1 (6.7)	3 (1.2)	–
Mean BMI ± SD (kg/m^2)‡‡	27.26 ± 4.43	28.81 ± 5.83	0.33
Past or current smoker			
Yes	4 (26.7)	65 (25.9)	1.00
No	11 (73.3)	186 (74.1)	
Hormonal contraceptive use			
Yes	3 (20.0)	19 (7.6)	0.12
No	12 (80.0)	232 (92.4)	

ASA American Society of Anesthesiologists physical status classification system, *BMI* body mass index, *mFI-5* modified 5-factor frailty index, *SSSVT* superior sagittal sinus venous thrombosis

*Statistically significant ($p < 0.05$)

**Includes patients who refused to answer

†Patients with Medicare or Medicaid, or who are uninsured

‡Functional status is defined as requiring assistance with activities of daily living

‡‡BMI data was only available for 13 SSSVT patients and for 210 Non-SSSVT patients

other postoperative complication (odds ratio [OR] = 3.93, p = 0.015). Importantly, the association between tumor location along the posterior 1/3rd of the SSS vs. anterior 1/3rd of the SSS and thrombus development approached but did not attain statistical significance (OR = 3.46, p = 0.088). Tumor histology as assessed by the WHO grading scale was not significantly associated with SSS thrombosis development (p = 0.71). Alongside postoperative complications and SSS tumor localization, age and sex were forced into a logistic regression model as covariates due to prior studies demonstrating their utility as risk factors for predicting SSS thrombosis [2, 22, 23]. As shown in Table 4, when controlling for age, sex, and tumor location along the SSS in multivariate analysis, occurrence of any postoperative complication was no longer significantly associated with SSS thrombosis development (OR = 2.15, p = 0.16).

SSS thrombosis patient cohorts

Table 5 lists specific demographic and clinical characteristics for 10 (3.8%) patients who developed asymptomatic SSS thrombosis. Three of these patients (30.0%) received anticoagulation therapy following surgical resection. Four of these patients (40.0%) had a thrombus that was fully occluding the SSS, with the remainder having a thrombus that only partially occluded flow through the sinus. Notably, none of the

Table 2 Parasagittal/parafalcine meningioma patient tumor characteristics, N (%)

Characteristic	SSSVT (n = 15)	No SSSVT (n = 251)	p-value
Symptomatic presentation			
Yes	14 (93.3)	210 (83.7)	0.48
No	1 (6.7)	41 (16.3)	
Specific presenting symptoms			
Headache	8 (53.3)	118 (47.0)	–
Seizures	5 (33.3)	66 (26.3)	–
Motor deficit	3 (20.0)	46 (18.3)	–
Sensory deficit	1 (6.7)	32 (12.7)	–
Cognitive deficit	4 (26.7)	30 (12.0)	–
Visual deficit	3 (20.0)	26 (10.4)	–
Vertigo	3 (20.0)	24 (9.6)	–
Decreased hearing	3 (20.0)	23 (9.2)	–
Gait deficit	3 (20.0)	22 (8.8)	–
Confusion	0 (0.0)	16 (6.4)	–
Nausea/vomiting	4 (26.7)	13 (5.2)	–
Language deficit	0 (0.0)	8 (3.2)	–
Dysphagia	1 (6.7)	7 (2.8)	–
Diplopia	1 (6.7)	6 (2.4)	–
Bladder incontinence	0 (0.0)	4 (1.6)	–
Dysarthria	0 (0.0)	1 (0.4)	–
Emergency admission			
Yes	1 (6.7)	30 (12.0)	1.00
No	14 (93.3)	221 (88.0)	
WHO Grade			
I	12 (80.0)	212 (84.5)	0.71
II/III	3 (20.0)	39 (15.5)	
Mean tumor size $cm^3 \pm SD$	47.74 ± 99.82	22.65 ± 27.66	0.27
Tumor laterality			
Right	6 (40.0)	113 (45.0)	Reference
Left	9 (60.0)	114 (45.4)	0.60
Bilateral	0 (0.0)	24 (9.6)	0.59
SSS tumor localization			
Anterior 1/3rd	3 (20.0)	63 (25.1)	Reference
Middle 1/3rd	6 (40.0)	152 (60.6)	0.73
Posterior 1/3rd	6 (40.0)	36 (14.3)	0.088
Tumor invasion of SSS			
Full Occlusion	4 (26.7)	78 (31.1)	1.00
Partial Involvement/No Occlusion	11 (73.3)	173 (68.9)	

SSS superior sagittal sinus, *SSSVT* superior sagittal sinus venous thrombosis

*Statistically significant ($p < 0.05$)

10 patients with asymptomatic SSS thrombosis developed postoperative cerebrovascular-related complications. Table 6 lists the 5 (1.9%) symptomatic SSS thrombosis patients. Two of these five patients (60.0%) were treated with postoperative anticoagulation, and all 5 patients were found to have a thrombus completely occluding the SSS. Regarding the postoperative course of the symptomatic patients who received anticoagulation, Patient 11 was discharged 4 days after surgery without anticoagulation, though a SSS thrombosis was noted on postoperative MRI. She was readmitted 4 days after discharge due to progressing SSS thrombosis symptoms (persistent headaches accompanied by nausea) and was managed with a heparin drip which was then transitioned to rivaroxaban (20 mg twice daily). Patient 13 was advised to begin taking aspirin (81 mg daily) after hospital discharge on postoperative day 15. None of the symptomatic patients developed postoperative cerebrovascular-related complications. Figure 1A, B displays post-contrast MRI and MR

Table 3 Parasagittal/parafalcine meningioma patient postoperative outcomes, N (%)

Characteristic	SSSVT (n = 15)	No SSSVT (n = 251)	p-value
Simpson grade			
I/II/III	10 (66.7)	206 (82.1)	0.17
IV	5 (33.3)	45 (17.9)	
SSS ligation			
Yes	1 (6.7)	1 (0.4)	0.11
No	14 (93.3)	250 (99.6)	
SSS reconstruction			
Yes	0 (0.0)	2 (0.8)	1.00
No	15 (100.0)	249 (99.2)	
Postoperative anticoagulation			
Yes	2 (13.3)	13 (5.2)	0.20
No	13 (86.7)	238 (94.8)	
Any postoperative complications**			
Yes	9 (60.0)	69 (27.5)	***0.015****
No	6 (40.0)	182 (72.5)	
Type of postoperative complications			
New motor deficit	2 (13.3)	22 (8.8)	–
New cognitive deficit	4 (26.7)	17 (6.8)	–
Seizure	2 (13.3)	16 (6.4)	–
Surgical site infection	3 (20.0)	11 (4.4)	–
New sensory deficit	0 (0.0)	11 (4.4)	–
Dysphagia	0 (0.0)	7 (2.8)	–
New language deficit	0 (0.0)	6 (2.4)	–
New visual deficit	0 (0.0)	6 (2.4)	–
DVT/PE	0 (0.0)	5 (2.0)	–
Hematoma	0 (0.0)	1 (0.4)	–
Routine discharge disposition			
Yes	12 (80.0)	215 (85.7)	0.47
No	3 (20.0)	36 (14.3)	
Mean days in ICU ± SD	3.00 ± 4.99	1.45 ± 1.56	0.15
Mean LOS in days ± SD	8.20 ± 11.58	4.76 ± 6.69	0.14

SSS superior sagittal sinus

*Statistically significant ($p < 0.05$)

**Excluding SSSVT, *SSSVT* superior sagittal sinus venous thrombosis

venogram images for patients who developed symptomatic and asymptomatic SSS thrombosis.

Discussion

Prior research

Previous research has described the use of anticoagulation to treat postoperative CVT. A 2002 systematic review by Stam et al. detailed the results of two randomized controlled clinical trials examining a total of 79 postoperative CVT patients [24–26]. The first trial by Einhaupl and Villringer studied 20 patients with CVT who were randomized into two groups of 10 and received either therapeutic heparin or placebo. The heparin and placebo groups were well-matched for age and gender. After 8 months, 8 patients in the heparin group had complete clinical recovery while only 1 patient in the placebo group completely recovered ($p < 0.01$) [25]. The second trial by de Bruijn et al. studied a cohort of 59 patients who were randomized to either nadroparin followed by 3 months of oral anticoagulants (30 patients) or to placebo (29 patients). The nadroparin and placebo groups were well-matched for age and gender. "Poor outcome" was defined as either death or a Barthel Index Score of < 15. The authors found that patients in the placebo group had a greater number of poor outcomes compared to patients in the heparin group, though these differences were not statistically significant [24]. Reviewing the results of these two clinical trials, Stam et al. concluded that anticoagulation for CVT

Table 4 Multivariate analysis of superior sagittal sinus thrombosis development (N = 266)

Characteristic	Odds ratio	95% CI	p-value
Greater age	0.98	0.94–1.02	0.26
Sex			
Male	1.06	0.31–3.18	0.92
Female			
SSS tumor localization			
Anterior 1/3rd	Reference	Reference	Reference
Middle 1/3rd	0.86	0.22–4.23	0.84
Posterior 1/3rd	3.32	0.81–16.67	0.11
Any postoperative complications**			
Yes	2.15	0.71–6.36	0.16
No			

*Statistically significant ($p < 0.05$)

**Excluding SSSVT; *SSSVT* superior sagittal sinus venous thrombosis

appeared safe and trended toward a reduced risk of death or dependency. [24, 26].

Within the neurosurgical literature, additional retrospective studies have supported the use of anticoagulation in treating CVT [6, 27]. Medel et al. reviewed 34 studies on the interventional management of CVT and concluded that systemic anticoagulation was a reasonable initial strategy for the treatment of CVT even in the setting of preexisting intracerebral hemorrhage [6]. Moore et al. conducted a retrospective review of 43 patients with cerebellopontine angle tumors, 5 of whom developed transverse and/or sigmoid sinus thrombosis following tumor resection. The authors found that patients with larger tumors were significantly more likely to develop postoperative thrombosis ($p < 0.001$), and they also noted that all patients with thrombosis were treated with intravenous heparin with none developing complications. The authors concluded that early postoperative initiation of anticoagulation was safe and effective and in preventing the progression of CVT. [27].

Given that numerous studies have reported severe hemorrhagic complications resulting from postoperative anticoagulant use, more recent work has focused on the safety of conservative, observational therapy in treating asymptomatic cases of CVT [6–10, 12]. A retrospective study by Benjamin and colleagues analyzed a cohort 74 patients of whom 24 (32.4%) developed asymptomatic CVT. All thrombosis patients were managed conservatively, with one patient receiving intravenous hydration and the remaining being observed only. No complications were associated with either observation or hydration, and the authors concluded that their conservative management provided a safe, alternative strategy in the care of asymptomatic CVT patients, avoiding the risk of hemorrhage associated with anticoagulation therapy [7]. A recent retrospective case series by Orlev et al. similarly examined transverse/sigmoid thrombosis following posterior fossa surgery. The authors retrospectively examined 538 patients, 26 (4.8%) of whom developed sinus thrombosis. The authors found that the thrombosis group had a significantly greater postoperative complication rate compared to the non-thrombosis group ($p = 0.02$), but they noted that complications resolved without anticoagulation in most patients (88%). Therefore, taking into consideration the greater risks of intracerebral hemorrhage associated with postoperative anticoagulation, the authors concluded that it may be reasonable to manage this specific patient population conservatively. [12].

Current study

Our results emphasize the importance of closely monitoring patients during their postoperative hospital course, and they suggest an association between SSS thrombosis development and other postoperative complications. Patients who experience any postoperative complications are perhaps more likely to have experienced excessive manipulation of critical venous structures, potentially raising their risk of developing thrombi within the SSS. Conversely, it is also possible that the association we observed in our study is due to SSS thrombosis leading to the development of additional postoperative complications such as seizures, a well-known known complication of CVT [28]. Importantly, the fact that the association between SSS thrombosis and postoperative complications was no longer significant when controlling for SSS tumor location, age, and sex suggests that SSS thrombosis risk is multifactorial and that anatomical location of parasagittal/parafalcine tumors may play a role in SSS thrombosis development. While WHO grade has been shown to correlate well with meningioma recurrence rate and overall survival, the fact that our study did not observe a significant association between WHO grade and SSS thrombus development suggests that a higher tumor histological grade is not necessarily a risk factor for thrombotic complications in patients with parasagittal/parafalcine meningiomas [29–31]. Given our limited sample size, further research studying perioperative variables not examined in our present study could yield additional predictive factors that may be helpful in stratifying patients at greater risk of developing thromboses. Elucidating the role of age and sex in SSS thrombosis development and determining whether they affect prognosis in parasagittal/parafalcine meningioma patients specifically will also be an important avenue for future research when larger patient cohorts are available.

Additionally, among the 10 patients in our study who developed asymptomatic SSS thrombi and did not receive anticoagulation therapy (aside from subcutaneous heparin for DVT/PE prophylaxis), none developed cerebrovascular

Table 5 Patients who developed asymptomatic venous thrombosis of the superior sagittal sinus following parasagittal meningioma resection (N = 10)

Case Number	Age (Years)	Sex	Presenting Symptoms	Pre-op mFI-5 Score	WHO Grade	Simpson Resection Grade	Postoperative Anticoagulation	Postoperative Complications	LOS	Readmit within 30 days	Recurrence
1	29	F	Headache, nausea/vomiting, visual deficit	0	I	IV	HSQ	None	3	No	Yes (4 months)
2	59	F	Headache, nausea/vomiting, visual deficit, gait deficit	0	I	II	HSQ	Surgical site infection	3	No	No
3	69	M	Nausea/vomiting, vertigo, cognitive deficit	1	II	I	HSQ	None	6	Yes	No
4	68	F	Seizures, headaches, decreased hearing, vertigo, dysphagia, motor deficit, gait deficit	3	I	I	HSQ	None	21	No	No
5	65	F	Seizures, sensory deficit, cognitive deficit	0	I	IV	HSQ	None	2	No	Yes (19 months)
6	47	F	Seizures, headaches	0	II	II	HSQ	Surgical site infection	2	Yes	No
7	39	M	Headaches, diplopia	0	I	II	HSQ	None	3	No	Yes (29 months)
8	74	M	Motor deficit	0	I	II	HSQ	None	2	No	Yes (23 months)
9	66	F	Headaches	0	II	II	HSQ	None	3	No	No
10	45	F	None	1	I	I	HSQ	None	3	No	No

HSQ subcutaneous heparin

Table 6 Patients who developed symptomatic venous thrombosis of the superior sagittal sinus following parasagittal meningioma resection (N = 5)

Case Number	Age (Years)	Sex	Presenting Symptoms	Pre-op mFI-5 Score	WHO Grade	Simpson Resection Grade	Postoperative Anticoagulation	Postoperative Complications	LOS (days)	Readmit within 31 days	Recurrence
11	40	F	Headache, nausea/vomiting	0	I	IV	HSQ, IV heparin, rivaroxaban	Seizures	4	Yes	No
12	32	F	Seizures, headaches, visual deficit	0	I	I	HSQ	Seizures	2	Yes	Yes (3 months)
13	61	F	Seizures, decreased hearing, cognitive deficit	2	I	IV	HSQ, aspirin	New onset cognitive deficit	15	No	No
14	65	M	Decreased hearing	1	I	I	HSQ	New onset motor deficit	9	No	Yes (8 months)
15	65	M	Vertigo, motor deficit, cognitive deficit, gait deficit	1	I	IV	HSQ	Surgical site infection, new onset motor deficit	45	No	No

HSQ subcutaneous heparin

complications. Our results support the notion that conservative observation of patients who develop asymptomatic SSS thrombi may represent a viable treatment strategy, especially among patients with contraindications to anticoagulation. Our findings are in line with prior work suggesting that conservative observation can provide a safe alternative to postoperative anticoagulation in the management of CVT [7, 11, 12]. It is important to note that while conservative management for SSS thrombosis at our institution consists of observation only (in addition to repeat cranial imaging while the patient's symptoms persist), other conservative management strategies discussed in the neurosurgical literature include aggressive hydration or prolonged ICU stay [7]. Research has yet to demonstrate a reduction in morbidity or mortality attributable to the use of these treatments in the management of SSS thrombosis, but additional investigations with larger patient cohorts may be helpful in definitively establishing the safety and efficacy of these strategies. Regarding intravenous fluids during observation, the normal practice at our institution is to keep patients well-hydrated with normal saline at approximately 1.5 times their normal maintenance fluid volume if there are no concerns regarding their kidney function.

While 2 of our patients with symptomatic CVT received anticoagulation in the form of IV heparin, rivaroxaban, and aspirin, their postoperative course was not markedly different from the 3 symptomatic patients who were observed and did not receive anticoagulation (aside from subcutaneous heparin for DVT/PE prophylaxis). Studies with larger patient cohorts will be necessary to confirm our findings and to determine if they generalize to other meningioma subtypes. Given that all patients in our study cohort received subcutaneous heparin for DVT/PE prophylaxis, it remains unclear what the effect of this anticoagulation dose is on the risk of developing an SSS thrombus. Addition of an anticoagulant to a patient's postoperative medication regime should intuitively reduce their risk of developing a cerebral venous clot. However, we are unaware of any research quantifying this effect within the neurosurgical literature, likely due to the fact that many institutions administer heparin postoperatively for DVT/PE prophylaxis, limiting the number of patients available to serve a control group. Future research efforts will be necessary to understand the effect of prophylactic heparin on the occurrence of clinical and subclinical sinus thrombosis.

An interesting finding in our study was that the majority of patients with SSS thrombosis in our study cohort (66.7%) were asymptomatic, which raises the question as to why certain patients are able to tolerate impaired cerebral venous flow. An important finding to note is that while all 5 patients with symptomatic SSS thromboses had a thrombus that was fully occluding the SSS on MR venogram, only four (40.0%) asymptomatic patients had fully occluded sinuses, with the

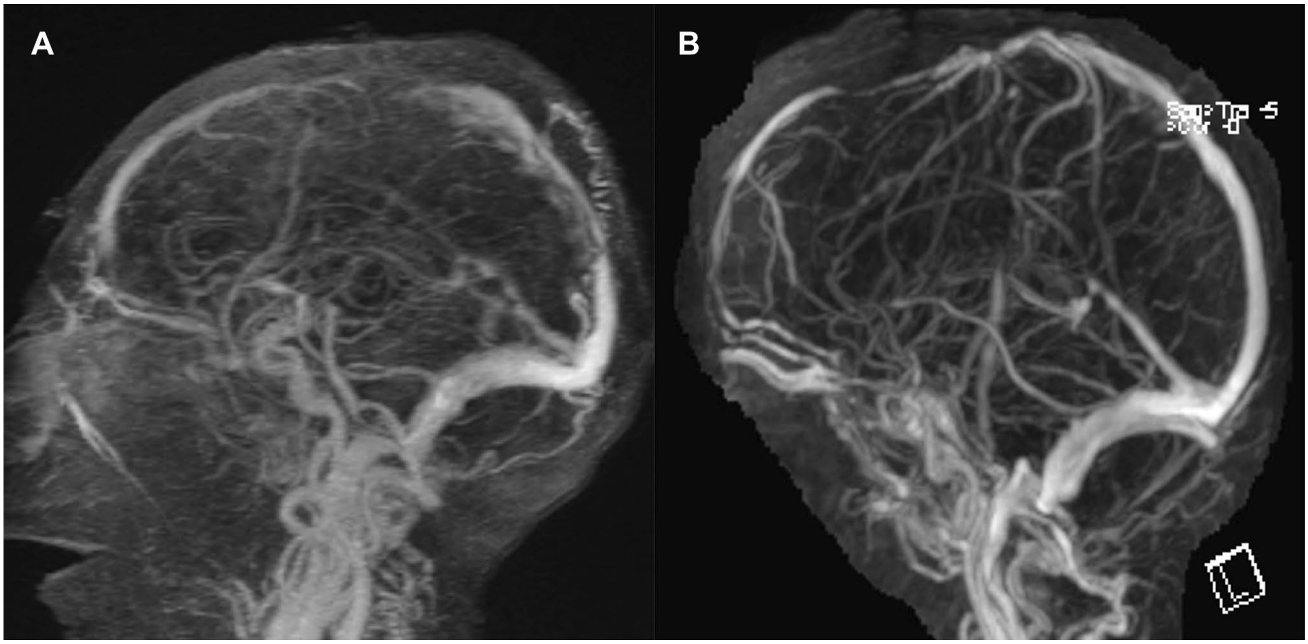

Fig. 1 **A** (left), Sagittal section of MR venogram displaying SSS occlusion in an asymptomatic patient. **B** (right), Sagittal section of MR venogram displaying SSS occlusion in a symptomatic patient

remainder having a thrombus that only partially impaired venous flow (i.e. reduced signal on MR venogram). However, given that there were still 6 patients with a thrombus that was fully occluded the SSS who did not present with any symptoms, degree of venous flow impairment only partially explains our study findings. One interesting possibility is the notion of collateral venous circulation bypassing thrombosed SSS segments. Within the MR venogram imaging reports of one of our asymptomatic patients, a radiologist noted that while there was a short segment on the patient's SSS where flow was occluded (i.e. lacked signal), there were prominent venous channels surrounding this area which extended to regions of normal flow in the more posterior SSS, suggesting the possibility of collateral venous circulation. Further research will be necessary to quantify the relationship between SSS venous flow impairment and presenting symptoms, as well as the possible role of collateral venous circulation in bypassing thrombosed SSS segments.

Limitations

There are a number of limitations to our study. First, our study was retrospective in nature, and therefore we cannot comment on the possible causal relationships between variables analyzed. Additionally, our study would benefit from validation with a prospective cohort examining risk factors and outcomes among conservatively managed, post-operative SSS thrombosis patients. Second, our data was collected from surgeries conducted at a single academic institution over a limited time period, and our findings would be strengthened by further studies examining CVT development among post-operative parasagittal/parafalcine meningioma patients at many different hospitals. Third, our sample size was limited, possibly restricting our statistical power to identify associations that may have otherwise appeared in larger cohort studies. Fourth, our definition of "symptomatic SSS thrombosis" is subjective, and while we based our criteria of "symptomatic" using criteria defined in prior research, it is important to note that a "symptomatic presentation" depends largely on each patient's unique thrombosis risk factors as well as operative factors such as manipulation or damage to the SSS [4, 11, 19–21]. Nevertheless, we hope that the definitions of symptomatic and asymptomatic SSS thrombosis used at our institution may prove useful in aiding surgeons to determine patients' thrombosis risk postoperatively, even if there may be some variability in what constitutes a symptomatic presentation between institutions. Acknowledging these limitations, we believe this study yields clinically useful results that can be used to help guide the management of post-operative parasagittal/parafalcine meningioma patients with SSS thrombosis.

Conclusion

Our study found that SSS thrombosis development among patients undergoing surgical resection of parasagittal/parafalcine meningiomas was significantly associated with incidence of other postoperative complications in bivariate analysis, but this relationship did not hold in multivariate analysis when controlling for age, sex, and tumor location along the SSS. Our results suggest that SSS thrombosis risk is multifactorial and that anatomical location of parasagittal/parafalcine tumors may contribute to SSS thrombosis development. Additionally, we found no increased incidence of cerebrovascular complications among patients treated conservatively for SSS thrombosis within our single-institution cohort, suggesting conservative management may be a viable treatment strategy for SSS thrombosis after surgical resection of parasagittal/parafalcine meningioma.

Acknowledgements We thank Robert M. Romano for his editorial support in the preparation of this manuscript

Author contributions AJ, AK, and DM contributed to the study conception and design. Material preparation, data collection and analysis were performed by AJ, AM, DB, MH, OA, SL, LO, SC, SL, EW, and OW. The first draft of the manuscript was written by AJ and AM, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding The authors received no funding for the research, authorship, and/or publication of this article. The authors acknowledge assistance for clinical data coordination and retrieval from the Core for Clinical Research Data Acquisition, supported in part by the Johns Hopkins) Institute for Clinical and Translational Research (UL1TR001079).

Data availability The authors have full control of all primary data and agree to allow the journal to review their data if requested.

Code availability Not applicable.

Declarations

Conflict of interest AJ declares that he has no conflict of interest. AM declares that he has no conflict of interest. DB declares that she has no conflict of interest. MH declares that she has no conflict of interest. OA declares that he has no conflict of interest. Shravika Lam declares that she has no conflict of interest. LO declares that he has no conflict of interest. SC declares that he has no conflict of interest. Sophie Liu declares that he has no conflict of interest. EW declares that she has no conflict of interest. OW declares that he has no conflict of interest. JP declares that he has no conflict of interest. CB is a consultant for Depuy-Synthes and Bionaut Labs. RT declares that he has no conflict of interest. HB is a consultant for AsclepiX Therapeutics, StemGen, InSightec, Accelerating Combination Therapies, NexImmune, Camden Partners, LikeMinds Inc., Galen Robotics Inc., and Nurami Medical, and he receives support from Arbor Pharmaceuticals, Bristol-Myers Squibb, and AcuityBio Corp. for non–study-related clinical or research effort. DB declares that he has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent The Institutional Review Board (IRB), acting as a Health Insurance Portability and Accountability Act (HIPAA) Privacy Board, reviewed and approved the waiver of informed consent for this retrospective study (IRB00181593).

References

1. Wong JM, Panchmatia JR, Ziewacz JE et al (2012) Patterns in neurosurgical adverse events: Intracranial neoplasm surgery. Neurosurg Focus 33(5):1–3
2. Gessler F, Bruder M, Duetzmann S et al (2018) Risk factors governing the development of cerebral vein and dural sinus thrombosis after craniotomy in patients with intracranial tumors. J Neurosurg 128(2):373–379
3. Dmytriw AA, Song JSA, Yu E, Poon CS (2018) Cerebral venous thrombosis: state of the art diagnosis and management. Neuroradiology 60(7):669–685
4. Silvis SM, De Sousa DA, Ferro JM, Coutinho JM (2017) Cerebral venous thrombosis. Nat Rev Neurol 13(9):555–565
5. Coutinho JM, Zuurbier SM, Aramideh M, Stam J (2012) The incidence of cerebral venous thrombosis: a cross-sectional study. Stroke 43(12):3375–3377
6. Medel R, Monteith SJ, Crowley RW, Dumont AS (2009) A review of therapeutic strategies for the management of cerebral venous sinus thrombosis. Neurosurg Focus. https://doi.org/10.3171/2009.8.FOCUS09154
7. Benjamin CG, Sen RD, Golfinos JG et al (2019) Postoperative cerebral venous sinus thrombosis in the setting of surgery adjacent to the major dural venous sinuses. J Neurosurg 131(4):1317–1323
8. Apra C, Kotbi O, Turc G et al (2017) Presentation and management of lateral sinus thrombosis following posterior fossa surgery. J Neurosurg 126(1):8–16
9. Keiper GL, Sherman JD, Tomsick TA, Tew JM (1999) Dural sinus thrombosis and pseudotumor cerebri: unexpected complications of suboccipital craniotomy and translabyrinthine craniectomy. J Neurosurg 91(2):192–197
10. Sader N, de Lotbinière-Bassett M, Tso MK, Hamilton M (2018) Management of venous sinus thrombosis. Neurosurg Clin N Am 29(4):585–594
11. Brahimaj BC, Beer-Furlan A, Crawfrod FC et al (2019) Dural venous sinus thrombosis after vestibular schwannomaa surgery: the anticoagulation dilemma. J Neurol Surg B Skull Base. https://doi.org/10.1093/neuros/nyz310_156
12. Orlev A, Jackson CM, Luksik A et al (2019) Natural history of untreated transverse/sigmoid sinus thrombosis following posterior fossa surgery: case series and literature review. Oper Neurosurg 0(0):1–8
13. Raza SM, Gallia GL, Brem H et al (2010) Perioperative and long-term outcomes from the management of parasagittal meningiomas invading the superior sagittal sinus. Neurosurgery 67(4):885–893
14. Subramaniam S, Aalberg JJ, Soriano RP, Divino CM (2018) New 5-Factor modified frailty index using American College of surgeons NSQIP data. J Am Coll Surg 226(2):173-181.e8
15. Huq S, Khalafallah AM, Jimenez AE et al (2020) Predicting postoperative outcomes in brain tumor patients with a 5-factor modified frailty index. Neurosurgery 0(0):1–8
16. Khalafallah AM, Huq S, Jimenez AE et al (2020) The 5-factor modified frailty index: an effective predictor of mortality in brain tumor patients. J Neurosurg. https://doi.org/10.3171/2020.5.JNS20766
17. Khalafallah AM, Shah PP, Huq S et al (2020) The 5-factor modified frailty index predicts health burden following surgery for pituitary adenomas. Pituitary 26(6):630–640

18. Brandel MG, Rennert RC, Wali AR et al (2018) Impact of preoperative endovascular embolization on immediate meningioma resection outcomes. Neurosurg Focus 44(4):1–7
19. Goyal G, Charan A, Singh R (2018) Clinical presentation, neuroimaging findings, and predictors of brain parenchymal lesions in cerebral vein and Dural sinus thrombosis: a retrospective study. Ann Indian Acad Neurol 21(3):203–208
20. Shew M, Kavookjian H, Dahlstrom K et al (2018) Incidence and risk factors for sigmoid venous thrombosis following CPA tumor resection. Otol Neurotol 39(5):e376–e380
21. Coutinho JM (2015) Cerebral venous thrombosis. J Thromb Haemost 13(S1):S238–S244
22. Pan L, Ding J, Ya J et al (2019) Risk factors and predictors of outcomes in 243 Chinese patients with cerebral venous sinus thrombosis: a retrospective analysis. Clin Neurol Neurosurg. 183:105384
23. Silvis SM, Middeldorp S, Zuurbier SM et al (2016) Risk factors for cerebral venous thrombosis. Semin Thromb Hemost 42(6):622–631
24. de Bruijn S, Stam J (1999) Randomized, placebo-controlled trial of anticoagulant treatment with low-molecular-weight heparin for cerebral sinus thrombosis. Stroke 30:484–488
25. Einhäupl K, Villringer A, Meister W et al (1991) Heparin treatment in sinus venous thrombosis. Lancet 338(8767):597–600
26. Stam J, De Bruijn SF, DeVeber G (2002) Anticoagulation for cerebral venous sinus thrombosis. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD002005
27. Moore J, Thomas P, Cousins V, Rosenfeld JV (2014) Diagnosis and management of Dural sinus thrombosis following resection of cerebellopontine angle tumors. J Neurol Surg B Skull Base 75(6):402–408
28. Bousser MG, Ferro JM (2007) Cerebral venous thrombosis: an update. Lancet Neurol 6(2):162–170
29. Palma L, Celli P, Franco C et al (1997) Long-term prognosis for atypical and malignant meningiomas: a study of 71 surgical cases. J Neurosurg 86(5):793–800
30. Modha A, Gutin PH (2005) Diagnosis and treatment of atypical and anaplastic meningiomas: a review. Neurosurgery 57(3):538–549
31. Yang SY, Park CK, Park SH et al (2008) Atypical and anaplastic meningiomas: prognostic implications of clinicopathological features. J Neurol Neurosurg Psychiatry 79(5):574–580