Postoperative cerebral venous sinus thrombosis in the setting of surgery adjacent to the major dural venous sinuses

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OBJECTIVE Cerebral venous sinus thrombosis (CVST) is a known complication of surgeries near the major dural venous sinuses. While the majority of CVSTs are asymptomatic, severe sinus thromboses can have devastating consequences. The objective of this study was to prospectively evaluate the true incidence and risk factors associated with postoperative CVST and comment on management strategies.

METHODS A prospective study of 74 patients who underwent a retrosigmoid, translabyrinthine, or suboccipital approach for posterior fossa tumors, or a supratentorial craniotomy for parasagittal/falcine tumors, was performed. All patients underwent pre- and postoperative imaging to evaluate sinus patency. Demographic, clinical, and operative data were collected. Statistical analysis was performed to identify incidence and risk factors.

RESULTS Twenty-four (32.4%) of 74 patients had postoperative MR venograms confirming CVST, and all were asymptomatic. No risk factors, including age ($p = 0.352$), BMI ($p = 0.454$), sex ($p = 0.955$), surgical approach ($p = 0.909$), length of surgery ($p = 0.785$), fluid balance ($p = 0.943$), mannitol use ($p = 0.136$), tumor type ($p = 0.46$, $p = 0.321$), or extent of resection ($p = 0.253$), were statistically correlated with thrombosis. All patients were treated conservatively, with only 1 patient receiving intravenous fluids. There were no instances of venous infarctions, hemorrhages, or neurological deficits. The rate of CSF leakage was significantly higher in the thrombosis group than in the nonthrombosis group ($p = 0.01$).

CONCLUSIONS This prospective study shows that the radiographic incidence of postoperative CVST is higher than that previously reported in retrospective studies. In the absence of symptoms, these thromboses can be treated conservatively. While no risk factors were identified, there may be an association between postoperative CVST and CSF leak.

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KEYWORDS cerebral venous sinus thrombosis; venous sinus thrombosis; sinus thrombosis; lateral sinus thrombosis; skull base tumors; parasagittal tumors; vascular disorders

CEREBRAL venous sinus thrombosis (CVST), first described in 1825 by Ribes, has remained a difficult condition to diagnose and manage.¹³ There are multiple risk factors that can lead to spontaneous CVST, including trauma, infection, hematological disorders, oral contraceptives, malignancy, and dehydration.^{8,18,22} CVST of varying degrees is also a well-documented complication of neurosurgical operations that are adjacent to the major dural sinuses. Current literature estimates a 5%–12% incidence of postoperative CVST.^{4,14} Although rare,

CVST can have devastating sequelae, and management in the postoperative setting is particularly challenging.

This condition is often clinically silent, with only a small number of patients becoming symptomatic. The presence and severity of symptoms depend on the extent of thrombosis and, importantly, on the collateral venous drainage supply.¹³ Typically, symptoms arise when venous outflow obstruction leads to increased intracranial pressure. Therefore, headache is the most common presenting symptom. Other symptoms include nausea with or with-

ABBREVIATIONS CTV = CT venography; CVST = cerebral venous sinus thrombosis; MRV = MR venography.

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FIG. 1. Noncontrast CT scan of the head, demonstrating a tubular hyperdensity (arrow) that contours the shape of the distal right transverse and sigmoid sinuses and is suggestive of sinus thrombosis. This is referred to as the “cord sign.” Figure is available in color online only.

out emesis, altered mental status, visual changes, seizures, pseudotumor cerebri, and, less commonly, focal neurological deficit.^{10,13,14} More severe symptoms arise when CVST leads to a hemorrhagic stroke, which can be catastrophic.⁹

Historically, CVST was difficult to diagnose and often went untreated due to limitations in imaging modalities. Although there are some cases of CVST that can be detected by the presence of a tubular hyperdensity within a venous structure, known as “the cord sign,” overall, the sensitivity of noncontrast CT is low (Fig. 1).^{3,21} CT venography (CTV) is more sensitive and can be performed to facilitate the diagnosis of CVST. This modality is limited by radiation exposure and the possibility of confounding results due to artifact from the surrounding bone. Recent advances in MRI provide higher resolution evaluation of cerebral sinuses (Fig. 2). The most sensitive sequences for diagnosis of CVST are noncontrast MR venography (MRV), such as 2D and 3D time-of-flight and phase-contrast MRV, as well as contrast-enhanced MRV.^{1,17} These sequences are useful in the diagnosis of CVST and also to monitor the thrombosis over time when present (Fig. 3). Cerebral angiography, although more invasive, remains the gold standard. The improved ability to diagnose CVST has shifted the focus to management and treatment of this condition.

Current guidelines provide class IIA, level B evidence supporting anticoagulation with heparin on diagnosis for spontaneous sinus thrombosis.^{6,16} There is also documentation of thrombolytics being used as a salvage maneuver

FIG. 2. Axial MR venogram after contrast administration, revealing a filling defect in the right transverse sigmoid junction (arrow), indicating a venous thrombosis. This patient was noted to have a thrombosis in the right transverse sinus just to the right to the midline, extending through the right sigmoid sinus, right jugular bulb, and into the proximal right internal jugular vein just below the skull base. Figure is available in color online only.

if anticoagulation with heparin fails.^{7,13,15,16} Systemic heparinization carries a 40% risk of hemorrhage in the setting of spontaneous CVST.^{7,13} For immediate postcraniotomy patients with CVST, systemic heparinization is a relative contraindication given the postoperative bleeding risk.

Although sinus thrombosis can be a major cause of morbidity and mortality, its incidence and factors that contribute to its formation postoperatively remain unclear. The goals of this study were to 1) identify the true incidence of postoperative sinus thrombosis, 2) elucidate potential risk factors, 3) comment on clinical outcomes, and 4) recommend management guidelines.

Methods

Patients

An IRB-approved, HIPAA-compliant prospective study was conducted at NYU Langone Medical Center. All patients with a planned surgery involving a dural venous sinus were approached for enrollment. If enrolled, patients underwent the addition of MRV to standard preoperative MRI if there was no plan for preoperative angiography for other purposes. Seventy-four consecutive patients who underwent surgery between July 1, 2015, and August 9, 2016, were included. Inclusion criteria were patients 18 years or older who underwent a retrosigmoid, translabyrinthine, or suboccipital resection of a posterior fossa tumor or a supratentorial craniotomy for resection of a parasagittal/falcine tumor and had preoperative MRV or cerebral angiography and postoperative MRV within the same hospital admis-

FIG. 3. **Left:** Coronal MR venogram after contrast administration, revealing venous thrombosis of the right transverse and sigmoid sinuses, right jugular bulb, and into the proximal right internal jugular vein just below the skull base. **Right:** Coronal MR venogram after contrast administration revealing interval resolution of sinus thrombosis at 4 months.

sion. Those who underwent planned sacrifice of the involved sinus during surgery were excluded. Three patients who were enrolled did not undergo preoperative MRV and were excluded from the study.

Imaging

All patients underwent preoperative MRV or diagnostic angiography to evaluate baseline sinus patency. All patients underwent postoperative MRV to evaluate for sinus thrombosis within the same hospital admission.

The MRV studies were performed either after contrast administration or without intravenous contrast administration using the 2D or 3D time-of-flight technique. Specifically, the sites analyzed for thrombosis were the superior sagittal sinus, the inferior sagittal sinus, the transverse sinuses, the sigmoid sinuses, the internal jugular veins, and the deep venous system. The sidedness of transverse sigmoid junction dominance was also noted using either MRV or the magnetization-prepared rapid gradient-echo sequence on MRI.

Treatment

The decision to treat a thrombosis was made by the attending surgeon based on the results of postoperative imaging as well as the patient's clinical status. All patients received standard subcutaneous heparin (5000 U 3 times daily) or Lovenox (40 mg daily) for deep venous thrombosis prophylaxis as per the standard of care at our institution. Treatment for sinus thrombosis included either observation or hyperhydration with intravenous fluids. Patients who were treated with intravenous fluids received normal saline (0.9%) at 100 ml/hr or 125 ml/hr for 48 to 72 hours. Clinical outcomes, response to treatment, and complications were assessed for each patient.

Statistical Analyses

Statistical analyses were performed using IBM SPSS (version 23, IBM Corp.). Continuous variables were analyzed using the Student 2-tailed t-test. Categorical variables were tested using Pearson's chi-square or Fisher exact test, where appropriate, to determine association with sinus thrombosis. Values of $p < 0.05$ were considered statistically significant.

TABLE 1. Distribution of surgical approaches used

Approach	No. of Patients (%)
Retrosigmoid approach	26 (35.1)
Translabyrinthine approach	22 (29.7)
Supratentorial craniotomy	24 (32.4)
Middle fossa approach	2 (2.7)

Results

Patient Demographics

Twenty-five males and 49 females ($n = 74$) qualified for the study. The female/male ratio was 2:1. Ages ranged from 27 to 78 years, with a mean age of 51 years. All patients were found to have normal platelet count and coagulation both pre- and postoperatively. One patient had a known hypercoagulable history of protein C deficiency. The average BMI was 27.2 (range 17.4–44). Twenty-six patients (35.1%) underwent a retrosigmoid approach, 22 (29.7%) underwent a translabyrinthine approach, 24 (32.4%) underwent supratentorial craniotomies, and 2 (2.7%) underwent a middle fossa approach (Table 1).

Risk Factors for Postoperative Sinus Thrombosis

Twenty-four (32.4%) of the 74 patients had postoperative MRV studies confirming a sinus thrombosis. Of these 24 patients, 16 were male and 8 were female. The mean age and BMI in the thrombosis group were 49.4 ± 12 years and 26.2 ± 6.8 , respectively. The mean length of surgery was 284.79 ± 109 minutes, and the mean intraoperative fluid balance was 854.17 ± 750 cm³, with mannitol being used in 9 of the 24 cases. Twelve patients (50%) in the thrombosis group underwent surgery for vestibular schwannoma, 9 (37.5%) for meningioma, 2 (9%) for metastatic lesion, and 1 (4.5%) for an arachnoid cyst. Six patients (27.2%) in the thrombosis group underwent surgery through an infratentorial approach (6 [27.2%] retrosigmoid and 10 [41.6%] translabyrinthine) and 8 patients (33%) underwent supratentorial craniotomies. All of the thromboses occurred in the sinuses adjacent to the lesion such that in all posterior fossa approaches, the thromboses occurred on the ipsilateral side. Only 5 patients (20.8%) in the thrombosis group demonstrated invasion of the associated sinus on preoperative MRV. Gross-total resections were obtained in 16 (66%) of the 24 patients with thromboses. When comparing the thrombosis group with the nonthrombosis group, there were no statistically significant differences in any of the aforementioned variables. Data and significance values are summarized in Table 2.

Subgroup analysis of cases involving the skull base only, excluding cases of parasagittal/falcine tumors, resulted in a similar incidence of postoperative sinus thrombosis (32%) without any statistically significant risk factors. These data are summarized in Table 3.

Clinical Course and Treatment of Sinus Thrombosis

Treatments decisions were made at the discretion of the attending surgeon based on analysis of the extent of thrombosis on imaging as well as the patient's clinical status. All 24 patients were asymptomatic from their throm-

TABLE 2. Characteristics of the thrombosis and no thrombosis groups

	No Thrombosis	Thrombosis	p Value
Sex			0.955
Male	17	8	
Female	33	16	
Mean age, yrs	49.49	52.4	0.352
Mean BMI	26.21	27.31	0.454
Mean length of surgery, mins	284.79	291.64	0.785
Mean fluid balance, ml	854.17	835.76	0.943
Mannitol			0.136
Yes	28	9	
No	22	15	
Tumor type			
Vestibular schwannoma	20	12	0.46
Other	30	12	
Meningioma	26	9	0.321
Other	24	15	
Surgical approach/location			0.909
Infratentorial*	34	16	
Supratentorial	16	8	
Extent of resection			0.253
Gross total	40	16	
Other	10	8	
CSF leak			0.012
Yes	2	6	
No	48	18	

Values are presented as the number of patients unless stated otherwise. Boldface type indicates statistical significance.

There was no statistically significant difference in sex, age, BMI, length of surgery, fluid balance, use of mannitol, tumor type, surgical approach/location, or extent of resection. There was a statistically significant difference in the number of patients with and without CSF leakage between the thrombosis and no thrombosis groups.

* Includes retrosigmoid and translabrynthine.

bosis. Of the 24 patients who developed a postoperative thrombosis, 23 were left untreated and were simply observed. The remaining patient was treated with hydration using intravenous fluids at 125 ml/hr for 48 hours. Within the skull base subgroup, 6 of 16 patients (37.5%) who had a postoperative sinus thrombosis developed a CSF leak. This was statistically significant when compared with the leakage rate of the nonthrombosis group ($p = 0.01$). Of these 6 cases of CSF leakage in the thrombosis group, 4 required lumbar drainage, 1 was oversewn at the bedside, and 1 was operatively repaired. None of these patients required permanent shunting. There were no instances of venous infarction or hemorrhage.

Discussion

While the incidence, risk factors, clinical course, and outcomes for spontaneous CVST are relatively well understood, those for postoperative CVST are less clear. There are several retrospective studies that have evaluated postoperative sinus thrombosis in the setting of skull base surgery and have reported a 5%–12% incidence of postoperative CVST.^{2,10,14} Furthermore, these studies demonstrated

TABLE 3. Subgroup analysis of cases involving the skull base only

	No Thrombosis	Thrombosis	p Value
Sex			0.514
Male	9	6	
Female	25	10	
Mean age, yrs	53.47	46.31	0.074
Mean BMI	27.69	25.43	0.244
Mean length of surgery, mins	316.38	303.19	0.637
Mean fluid balance, ml	805.53	761.06	0.877
Mannitol			0.225
Yes	18	5	
No	16	11	
Tumor type			
Vestibular schwannoma	19	12	0.228
Other	15	4	
Meningioma	13	2	0.099
Other	21	14	
Extent of resection			0.163
Gross total	28	10	
Other	6	6	
CSF leak			0.009
Yes	2	6	
No	32	10	

Values are presented as the number of patients unless stated otherwise.

Boldface type indicates statistical significance.

Within this subgroup, there was no statistically significant difference in sex, age, BMI, length of surgery, fluid balance, use of mannitol, tumor type, or extent of resection between the thrombosis and no thrombosis groups. There was a statistically significant difference in the the number of patients with and without CSF leakage.

that treatment with anticoagulation in the postoperative setting can increase the risk of complications.^{2,10,14} This study is the first of its kind to evaluate, in a prospective fashion, the incidence, risk factors, and clinical course of patients with postoperative CVST after surgery surrounding the major dural venous sinuses in a single institutional series of 74 patients. We demonstrate that the incidence of postoperative CVST is considerably higher than that documented in the literature, which is limited to retrospective case series. We did not identify patient-specific or surgery-related risk factors that affected the thrombosis risk in a statistically significant manner. We conclude that asymptomatic postoperative CVST has a relatively benign clinical course and patients can have good outcomes with conservative management while avoiding the increased risks associated with full-dose anticoagulation in the postoperative setting.

Incidence

There are certain pathologies, such as meningiomas, whose attachments are to the dural folds and subsequently often invade and partially or fully obstruct the sinuses. In order to evaluate the ability to obtain a gross-total resection of such a meningioma, dedicated imaging must be performed. This can be in the form of CTV, MRV, or diagnostic angiography. Additionally, those involved si-

nuses would likely be closely evaluated on postoperative imaging as well. However, there are many other tumors that require a posterior fossa approach, such as vestibular schwannomas, hemangioblastomas, and other skull base pathologies where pre- and postoperative imaging to evaluate the patency of the venous sinuses would not be necessary. Therefore, we concluded that the literature grossly underestimates the actual incidence of postoperative venous sinus thrombosis. The prospective nature of our study allowed us to control this variable by obtaining pre- and postoperative images to evaluate sinus patency in all patients ($n = 74$). An incidence of 32.4% is significantly higher than that previously reported by Apra et al.² (6.7% incidence in a retrospective study that included 180 patients), Keiper et al.¹⁰ (4.7% incidence in a retrospective study that included 107 cases), and Moore et al.¹⁴ (11.6% incidence in a retrospective study that included 43 cases). This strikingly high incidence in asymptomatic patients renders postoperative sinus thrombosis an important phenomenon to study further in order to determine the natural history, the clinical course, and the risk factors associated with it. Ultimately, this may allow surgeons to better stratify their patients with regard to this potentially devastating complication.

Patient-Specific Risk Factors

Patient-specific factors that have been documented in the literature to contribute to the formation of spontaneous and postoperative CVST include dehydration, use of oral contraceptives,^{5,12} and presence of hematological conditions such as factor V Leiden.¹¹ Within our series, only 1 patient had a history of a hypercoagulable state within the thrombosis group, which did not reach statistical significance. We also did not note any statistically significant difference between the thrombosis and no thrombosis group in terms of age ($p = 0.352$) or sex ($p = 0.995$). Obesity has been associated with elevated intracranial pressure.^{19,20} It can be speculated that patients who are obese and already have an elevated baseline intracranial pressure are less likely to tolerate a venous sinus thrombosis and more likely to become symptomatic. This could be attributed to venous hypertension caused by the thrombosis, leading to altered CSF dynamics, similar to the phenomenon of postoperative pseudotumor cerebri that is described in the literature.^{9,10} While it seems intuitive that elevated BMI could be a risk factor for postoperative CVST, we did not note this trend in our series. In fact, both groups had elevated BMIs and the difference between BMI in the thrombosis and no thrombosis groups was not statistically significant ($p = 0.454$). It is possible that a larger sample size is needed for a statistically significant relationship between BMI and CVST.

Surgery-Related Risk Factors

Aside from patient-specific factors that can contribute to the formation of postoperative CVST, there are also intraoperative and surgery-related factors that are thought to contribute to CVST formation. Most theories suggest that surgical techniques such as intraoperative manipulation or retraction of the sinus, mechanical injury from drilling,

excessive bone wax use and propagation, or extended exposure to air contribute to CVST formation. These factors are difficult to quantify and were accounted for by the fact that the same 5 attending surgeons (3 neurosurgeons and 2 neurotologists) performed all surgeries in this study.

One surgery-related factor that surprisingly did not affect the risk of postoperative CVST in a significant manner was intraoperative fluid balance ($p = 0.934$) and mannitol use ($p = 0.136$). As a general principle, when resecting tumors where there is significant edema on preoperative imaging, most surgeons request that the anesthesia team limit intravenous fluids so as to maintain a net-negative fluid balance. If there is concern about brain swelling on opening the dura, surgeons will frequently ask that mannitol be administered to achieve diuresis. While diuresis and a net-negative fluid balance can assist with safely performing the operation, it can lead to a relative hypovolemic state. Similar to dehydration, this can then affect the rheology of the blood and thus put patients at a theoretical risk for thrombus formation. Given that we did not see a statistically significant difference for either net fluid balance or mannitol use, one can conclude that the benefits of both outweigh any theoretical risk, which we demonstrate is negligible.

Another interesting association noted in other cohorts is the increased risk of thrombosis based on tumor type. One theory is that meningiomas are more likely to develop CVST due to their adherent nature to the dural lining of the cerebral sinuses. Additionally, parasagittal meningiomas often grow into the sinus, resulting in stenosis and perhaps requiring some degree of sinus manipulation or repair. Obtaining a gross-total resection, which was accomplished in all patients who developed CVST after meningioma resection, requires significant manipulation of the dura in order to remove the tumor's dural attachment. Therefore, one would expect a higher risk of CVST in patients undergoing meningioma resection as opposed to other tumors. However, we did not find this to be true. There was no statistically significant difference between the 2 groups when the pathology was broken down into meningioma versus other ($p = 0.321$) and vestibular schwannoma versus other ($p = 0.46$). Again, given the limited sample size, this may have been underpowered to reach statistical significance.

In their report of postoperative CVST, Moore et al. discussed potential risk factors to surgery in the cerebellopontine angle.¹⁴ They noted that there was no statistically significant difference between the thrombosis and no thrombosis group in terms length of operation. This was an interesting finding in that length of surgery can be a surrogate marker for time during which the sinus could be exposed to effects of desiccation and surgical manipulation, both of which have been reported to increase the risk for CVST. However, our results confirm their finding that the difference is not statistically significant, with the thrombosis group averaging a surgical time of 284.79 minutes versus 291.64 minutes for the non-CVST group ($p = 0.785$).

Clinical Course of Postoperative CVST

Although there was a significant number of patients with sinus thromboses, none of them became symptomatic.

atic, even though 6 (25%) of 24 patients had thromboses in their dominant sinuses. This is likely because there was robust collateral venous drainage, thus making the thromboses well tolerated. The fact that 18 (75%) of 24 patients had thromboses in their nondominant sinus also makes sense physiologically, with the nondominant sinuses having smaller calibers and slower flow, thus making these patients more at risk for thromboses. These findings highlight the importance of performing preoperative MRV that can aid with operative planning to avoid injury to major draining veins that may provide collateral drainage in the setting of dominant sinus thrombosis. Furthermore, while all patients with postoperative CVST were clinically asymptomatic, there was a relatively high incidence of CSF leakage (28.5%) in patients with CVST, and this was statistically significant ($p = 0.012$). This may imply that the CSF leaks are a function of elevated pressure within the sinuses secondary to the thrombus leading to altered CSF dynamics and resorption. An alternative explanation for this could be surgical techniques such as the extent of mastoid drilling, the use of bone wax, and the use of a fat graft. These questions must be answered in a separate study.

Management of CVST

The decision to treat was made by the attending surgeon. This decision was based on interpretation of the imaging studies (including collateral venous drainage) and the patient's clinical status (including volume status). Only 1 patient was treated with intravenous hydration, as per the surgeon's preference. The rationale behind intravenous fluids was to prevent dehydration, which is a known risk factor for sinus thrombosis even in the setting of spontaneous CVST. All other patients were asymptomatic, and therefore the decision was made to observe only. There were no complications associated with either treatment strategy, hydration or observation. This suggests a much safer management strategy for asymptomatic patients and avoids the increased risks of postoperative complications documented in previous studies.

Limitations

One limitation of this study is the sample size, which may have led some of the subgroups to be underpowered and therefore could explain the lack of statistical significance. Another limitation of this study is that the management strategy was not randomized or standardized but rather was up to the discretion of the attending surgeon. Finally, this study evaluated only the patency of the sinuses immediately after surgery and did not include long-term clinical or imaging follow-up, which limits any conclusions regarding the natural history of postoperative CVST in the long term.

Conclusions

The incidence of postoperative CVST is much higher than that documented in the literature previously. MRV is a noninvasive method to evaluate the caliber and patency of dural venous sinuses in pre- and postcraniotomy patients. We did not identify any patient-specific or surgery-related risk factors for postoperative CVST. There was a correla-

tion between CVST and CSF leakage, which warrants further investigation. All patients remained asymptomatic and had favorable outcomes with conservative treatment approaches, which is safer than anticoagulation or antiplatelet therapy in the postoperative setting.

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Disclosures

The authors report no conflict of interest concerning the materi-

als or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Pacione, Benjamin. Acquisition of data: Pacione, Benjamin, R Sen. Analysis and interpretation of data: Pacione, Benjamin, R Sen. Drafting the article: Pacione, Benjamin, R Sen. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Pacione. Statistical analysis: Pacione, Benjamin, R Sen. Administrative/technical/material support: Pacione, Benjamin. Study supervision: Pacione, Golfinos, C Sen, Roland, McMenomey.

Supplemental Information

Previous Presentations

Portions of this work were presented in an oral presentation at the 27th Annual Meeting of the North American Skull Base Society, in New Orleans, Louisiana, March 4, 2017.

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