Endovascular Treatment for Venous Sinus Stenosis in Idiopathic Intracranial Hypertension: An Observational Study of Clinical Indications, Surgical Technique, and Long-Term Outcomes

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BACKGROUND: **Idiopathic intracranial hypertension (IIH) is characterized by increased intracranial pressure. IIH causes significant morbidity marked by incapacitating headaches and visual disturbances. This study investigated the long-term outcomes of venous sinus stenting in a large group of patients with IIH.**

METHODS: **We retrospectively reviewed all patients at our institution who underwent venous sinus stenting for IIH over 6 years (July 1, 2012—June 30, 2018). A particular focus was dedicated to collecting demographic, clinical, radiologic, and outcomes data. All patients had failed medical management.**

RESULTS: **Of the 110 patients evaluated for IIH, 42 underwent venous sinus stenting, with a mean follow-up of 25.6 months (range, 8.7—60.7 months). The mean age was 32 years (range, 15—52 years), 38 (90%) were women, and the mean body mass index was 35.6 kg/m^2 (range, 18.6—47.5 kg/m^2). Prior to the stenting procedure, all patients had headaches, visual disturbances, and papilledema. Of the 39 patients who had an ophthalmologic evaluation post-stenting, 29 (74%) had resolution of their papilledema. Eighteen patients (43%) had complete resolution of their headaches after the stenting procedure, whereas 22 patients (52%) remained under a neurologist's care for chronic migraine and other types of headaches. Two patients underwent a restenting procedure for disease progression, and 1 patient experienced an in-stent thrombosis.**

CONCLUSIONS: **A multidisciplinary approach involving neurosurgeons, ophthalmologists, radiologists, and neurologists is integral in the management of patients with IIH to prevent the complications of papilledema. Venous sinus stenting offers a safe and effective means of treating IIH.**

INTRODUCTION

Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri and benign intracranial hypertension, is a condition of unknown etiology.[1,2] This disorder primarily affects obese women of childbearing age and is marked by chronically elevated intracranial pressure without ventriculomegaly, which may present clinically with headaches, visual loss, diplopia, and pulsatile tinnitus.[3] Papilledema is the most concerning neurologic sign that may lead to progressive optic atrophy, visual impairment, and blindness. Friedman et al. proposed the revised diagnostic criteria for IIH: papilledema; normal neurologic examination except for sixth cranial paresis/palsy; normal brain imaging, without evidence of hydrocephalus or structural mass, or meningeal abnormalities; normal cerebrospinal fluid (CSF); and elevated lumbar puncture opening CSF pressure (250 mm H_2O or higher in adults).[4]

There are no widely accepted standardized guidelines to treat IIH. The primary goals of treatment include decreasing intracranial pressure to improve headaches and to preserve vision. Weight loss, treatment with the carbonic anhydrase inhibitor acetazolamide, serial lumbar punctures, optic nerve sheath fenestration,

Key words
- Endovascular
- Idiopathic intracranial hypertension
- Neurosurgery
- Pseudotumor cerebri
- Stent
- Venous sinus stenosis

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
IIH: Idiopathic intracranial hypertension
MRI: Magnetic resonance imaging
MRV: Magnetic resonance venography

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CSF shunting, and cerebral transverse venous sinus stenting have been proposed as beneficial therapeutic options.[1,3,5]

In our multidisciplinary study, we present the characteristics and long-term outcomes of patients who underwent a cerebral venogram, a pressure gradient measurement across the sinus stenosis, and a transverse-sigmoid stenting procedure for IIH at our institution. A unique aspect of this study is the overlap and common features shared between patients with IIH and chronic migraines and other types of headaches.

METHODS

Under an institutional review board–approved protocol, we retrospectively reviewed all patients at our institution who underwent venous sinus stenting for IIH over 6 years (July 1, 2012–June 30, 2018). We documented demographics, subjective symptoms such as headaches, visual disturbances, and tinnitus, body mass index, presence of papilledema as documented by an ophthalmologist, and previous treatment for IIH. The criteria for performing a cerebral angiogram with venous sinus manometry across the stenotic site included worsening papilledema, visual symptoms, severe headaches, high CSF opening pressure on lumbar puncture, and severe stenosis in the dominant transverse-sigmoid sinus junction on cranial magnetic resonance venography (MRV). Data consisted of opening CSF pressure, magnetic resonance imaging (MRI) and MRV findings, pressure gradient across the stenosis, side of the stenosis, procedural complications, and long-term outcomes. After the stenting procedure, the outcomes with respect to headaches were present or resolved, and the outcomes regarding papilledema were present or absent. Visual outcome was based on ophthalmology examination follow-up after stent placement.

Surgical Technique of Cerebral Angiogram and Venous Sinus Manometry

Cerebral angiogram and venous sinus manometry were performed with the patients either under general anesthesia (n = 38) or monitored anesthesia care (n = 4). A 5-French femoral sheath was placed in the femoral artery and an 8-French sheath was inserted in the femoral vein. The patients were given 80 U/kg intravenous heparin. The 5-French diagnostic catheter was passed through the arterial sheath, and cervical and cerebral angiography were performed.

Pressure manometry using a microcatheter with an internal diameter of 0.053 cm was performed proximal and distal to the sinus stenosis. Under roadmap guidance, the microcatheter was tracked over a 0.104 cm diameter microwire to access the superior sagittal sinus. The microcatheter was then attached to a pressure transducer. A Perceptor DT Disposable Transducer (Navilyst Medical, Marlborough, Massachusetts, USA) was attached to the anesthesia console. The microcatheter was slowly pulled back, allowing for real-time measurement of the sinus pressures in millimeters of mercury.

Angioplasty and stenting were considered if there was a significant pressure gradient across the dominant transverse-sigmoid sinus junction. A stent was placed when the pressure gradient across the transverse-sigmoid junction was 5 mm Hg or greater. A Zilver biliary self-expanding stent (Cook Medical, Los Angeles, California, USA) was delivered across the stenotic sinus segment. In rare cases where there was significant residual stenosis, balloon angioplasty was performed. Each patient was treated with a loading dose of aspirin 325 mg followed by 81 mg daily indefinitely and a loading dose of clopidogrel 600 mg and then 75 mg daily for 3 months. Both the aspirin and the clopidogrel were administered 1–2 weeks before the procedure. In rare cases where the procedure was done emergently, the medication loading was performed immediately prior to the procedure.

Statistical Analysis

The proportion of cases in which papilledema resolved after stent placement was estimated with a 95% confidence interval.

RESULTS

Cerebral Venogram and Manometry with Transverse Sinus Stenting

A total of 110 patients were referred to our neurosurgical practice for evaluation of IIH. Of the 64 patients who underwent venography and manometry, a total of 42 patients (65.6%) demonstrated a significant pressure gradient across the transverse-sigmoid venous sinus to warrant stent placement (**Figure 1**). **Tables 1** and **2** display the features of patients who underwent venography, manometry, and stent insertion. Cerebral angiography was performed with attention to the venous phase to confirm the location and extent of venous sinus stenosis. This also served as a partial roadmap to help us navigate the guide catheter and the microcatheter into the proper location in the venous sinuses. All patients in our study exhibited transverse venous sinus stenosis on a preoperative brain MRV scan, whereas 4 had an empty sella. Two patients had undergone previous treatment for IIH, specifically, bilateral optic nerve fenestration. Thirty-six patients (86%) required a stent despite a trial of acetazolamide and continued papilledema and visual symptoms. Only the dominant transverse-sigmoid junction was stented. In cases where there was a codominant venous sinus system, only one side was stented. **Figure 1** exemplified bilateral transverse-sigmoid venous sinus stenosis, and only one side was stented. Of the 4 patients treated with monitored anesthesia care and 38 patients treated with general anesthesia, the average pressure measurements were 14.5 and 11.2, respectively.

The mean duration of follow-up was 25.6 months (range, 8.7–60.7 months). Eighteen patients (43%) had complete resolution of their headaches after the stenting procedure. Of the 39 patients who had an ophthalmologic evaluation poststenting, 29 (74%) had resolution of their papilledema. Therefore, the success rate was 74% with a confidence interval of 57.5%–86.4%. Of the 10 patients (24%) who did not have resolution of their papilledema after the stenting procedure, 7 patients remained under the care of a neurologist for chronic migraines (n = 6) and seasonal headaches (n = 1) and 2 patients did not undergo further treatment because their headaches had resolved. One patient underwent a ventriculoperitoneal shunt insertion exactly 3 months after the stent. Clopidogrel had already been discontinued, and the patient remained on aspirin.

Six patients underwent additional surgical treatment after stent placement, including a bilateral optic nerve fenestration in 1 patient,

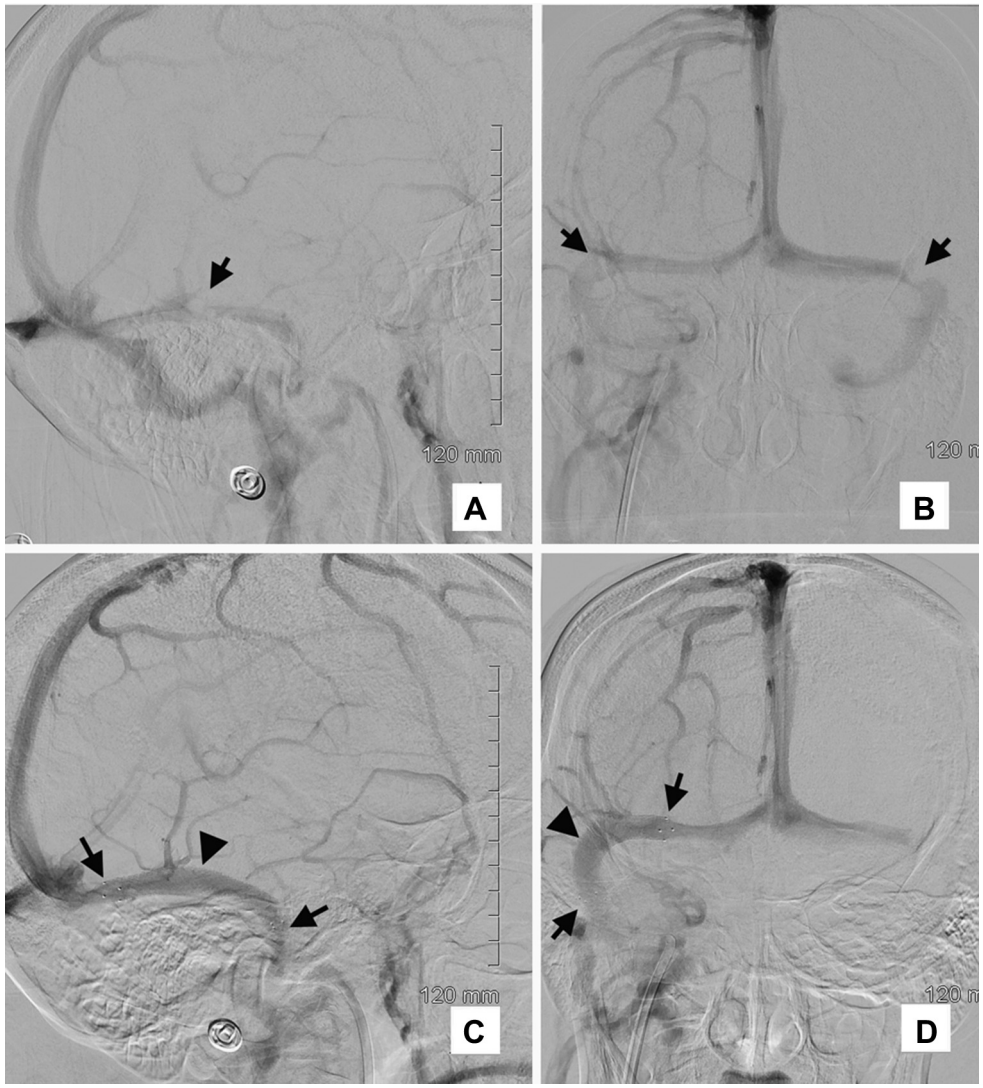

Figure 1. (**A**) Lateral and (**B**) AP preoperative subtraction venogram images showing a high-grade stenosis of both transverse-sigmoid sinus junctions (*arrows*). Only the right side was stented. (**C**) Lateral and (**D**) anteroposterior postoperative venogram demonstrating resolution of the transverse-sigmoid sinus stenosis (*arrowheads*). *Arrows* identify the proximal and distal ends of the stent.

a second stent placement in 2 patients, and a ventriculoperitoneal shunt placement in 3 patients. Twenty-two patients (52.4%) remained under a neurologist's care for chronic headaches and were treated with standard of care regimens for treating chronic headache, such as botulinum toxin injections and/or one or more of the following medications: topiramate, gabapentin, sumatriptan, gabapentin, and rizatriptan. All patients who underwent stent placement underwent a computed tomography venogram 6 months postoperatively. The stent was patent in all cases.

Complications of Transverse Sinus Stenting. One patient experienced an in-stent thrombosis 1 month postoperatively. This was thought to be secondary to suboptimal placement of the original stent with residual stenosis proximal to the stent. The patient subsequently underwent successful mechanical thrombectomy and repeat stent placement and balloon angioplasty. The patient had resolution of the IIH symptoms.

DISCUSSION

The pathophysiology of raised intracranial pressure in IIH remains uncertain; however, proposed mechanisms include increased brain water content, excess CSF production, reduced CSF absorption, and increased cerebral venous pressure.[1,6] Because of the high percentage of obese females with IIH, it is speculated that obesity increases intra-abdominal pressure and cardiac filling

Table 1. Demographic Features of Patients Diagnosed with Idiopathic Intracranial Hypertension Who Underwent a Venogram, Manometry, and Stent Placement (N = 42)

Feature	Category	Value
Age (years)		32.5 (15–52)
Sex	Female	38 (90.5)
	Male	4 (9.5)
Previous surgery for IIH prior to venogram	Yes	2 (4.8)
	No	0 (0)
BMI (kg/m^2)		35.6 (18.6–47.5)
	<25	2 (4.8)
	25–30	5 (11.9)
	30–35	15 (35.7)
	35–40	6 (14.3)
	>40	14 (33.3)
Smokes	Yes	8 (19)
	No	34 (81)
Acetazolamide	Yes	36 (86)
	No	6 (14)
Headaches	Yes	42 (100)
	No	0 (0)
Visual abnormalities	Yes	42 (100)
	No	0 (0)
Tinnitus	Yes	23 (55)
	No	19 (45)
Papilledema	Yes	42 (100)
	No	0 (0)
Opening CSF pressure of LP	Pressure known	35 (83.3) (mean, 38.0)
	Pressure >20 mm H_2O	7 (16.7)

Values are mean (range) or number (%).
IIH, idiopathic intracranial hypertension; BMI, body mass index; CSF, cerebrospinal fluid; LP, lumbar puncture.

Table 2. Venography, Manometry, and Venous Sinus Stenting and Follow-Up Course in Patients with Idiopathic Intracranial Hypertension (N = 42)

Feature After Stent Placement	Category	Value
Pressure gradient across stenosis		23.6 (4–33)
Duration of follow-up (months)		25.6 (8.7–60.7)
Ophthalmology appointment	Yes	39 (93)
	No	1 (2)
	Lost to follow-up	2 (5)
Papilledema resolved	Yes	29 (69)
	No	10 (24)
	No ophthalmology appointment	1 (2)
	Lost to follow-up	2 (5)
Headaches resolved	Yes	18 (43)
	No	24 (57)
Additional surgical treatment	Yes	6 (14.6)
	No	0 (0)
	Lost to follow-up	1 (2)

Values are mean (range) or number (%).

pressures.[7] These rises in pressures impede venous return from the brain, leading to an elevation in intracranial venous pressure. Hormonal and metabolic alterations may also play a role.[1] Weight loss is a crucial aspect in decreasing the morbidity associated with IIH.

After a lumbar puncture to confirm an elevated opening pressure, a brain MRI with and without gadolinium contrast and venous imaging (MRV or computed tomography venography) may suggest IIH.[8,9] Although these findings are not confirmatory of IIH, their presence in conjunction with papilledema or other symptoms of IIH warrants further investigation. It has been reported in the literature that brain MRI scans demonstrate classic findings of IIH, including empty sella, cerebellar tonsillar herniation, meningoceles, CSF leaks, and transverse venous sinus stenosis.[4,8] All patients in our study exhibited transverse venous sinus stenosis, whereas 4 had an empty sella.

Stenting of the transverse venous sinus stenosis has emerged as an effective means of improving the signs and symptoms of IIH by decreasing the venous pressure gradient, which is thought to improve CSF absorption and lower intracranial pressure.[1,10-13] Several complications have been observed after this procedure, including venous sinus perforation, stent migration, in-stent thrombosis, subdural hemorrhage, and development of recurrent stenosis immediately proximal or distal to the stent.[14]

Initially described by Higgins et al.,[12] several studies in the literature have addressed venous sinus stenting for IIH (**Table 3**).[10,12,15-24] Our study closely reflects the characteristics of patients who have undergone venous sinus stenting for IIH (**Table 3**). The resolution of headaches after this procedure varies widely among studies, ranging from 17% to 100% of patients. A total of 43% of patients who underwent stent placement in our study had resolution of their headaches. Twenty-two patients (52.4%) remained under a neurologist's care for chronic migraines or other types of headaches. Interestingly, it has been reported that migrainous features (nausea or photophobia-phonophobia) are present in 71.5% of patients with IIH.[25] The overlap between the headaches associated with IIH and chronic migraines may account for the high number of patients who continue to experience headaches after receiving a stent. It is possible that the headaches after stent placement were related to elevated intracranial pressure; however, they were not associated with transverse sinus stenosis. This finding was confirmed by the computed tomography venogram performed 6 months

Table 3. Venous Sinus Stenting for Idiopathic Intracranial Hypertension in the Literature

Study	Number of Patients	Median Age (years)*	Female Sex (%)	BMI	Headaches (%)*	Visual Symptoms (%)*	Papilledema (%)*	Tinnitus (%)	Opening CSF Pressure	Resolution of Headache (%)
Higgins et al.,[12] 2003	12	33	100	36.9	100	100	67	NR	33.7	42
Donnet et al.,[15] 2008	10	42	80	28.7	100	80	100	90	40.2	80†
Bussiere et al.,[16] 2010	13‡	34	100	35.0	100	77	92	23	NR	100†
Ahmed et al.,[10] 2011	52	34	90	>30 (90% pts)	83	§	88	33	32.9	85
Kumpe et al.,[17] 2012	18	38	67	31.6	72	94	100	N/R	39.6	17
Radvany et al.,[18] 2013	12	39	92	32.6	100	100	100	92	39.4	58
Fields et al.,[19] 2013	15	34	100	39.0	100	100	100	93	NR	67
Ducruet et al.,[20] 2014	30	33	83	NR	100	NR	100	N/R	NR	70
Teleb et al.,[21] 2015	18	30	83	36.0	100	100	100	28	NR	56
Aguilar-Perez et al.,[22] 2017	51	40	80	31.2	74	78	50	18	35.5	84
Satti et al.,[23] 2017	43	35	91	34.8	100	88	65	NR	35.8	69†
Liu et al.,[24] 2017	10	34	90	41.5	100	100	70	50	42.5	90†
Present study, 2018	42	32	90	36.0	100	100	100	55	38.0	43
Average	25	35	96	35.8	94	92	87	54	37.5	66

BMI, body mass index; CSF, cerebrospinal fluid; NR, not recorded; pts, patients.
*Clinical manifestations prior to venous sinus stenting.
†Significant improvement or resolution of headache.
‡Ten of 13 patients underwent stent.
§Visual acuity loss: 13, visual field loss: 30, transient visual obscurations: 19, and diplopia: 6.

postoperatively that revealed a patent stent in all patients. Furthermore, the stent procedure proved successful as indicated by the resolution of papilledema in most patients.

Our study is one of the largest in the literature highlighting the long-term outcomes of patients with IIH treated with endovascular stent placement. Two patients underwent restenting which was attributed to disease progression and stenosis either proximally or distally to the first stent. These patients underwent placement of the second stent 1 and 2 years after the initial stent, respectively. Using a longer stent at the first surgery may lessen the likelihood of a second stenting procedure. In-stent thrombosis has rarely been reported in the literature.[12,26] In the Higgins et al. study[12] of 12 patients treated with venous sinus stenting, 2 patients experienced an intraluminal thrombus which resolved with thrombolytic treatment. Our only case of in-stent thrombosis was felt to be secondary to technical error in placement of the original stent.

This study is limited by its retrospective nature and lack of documentation of the poststent pressure gradients in all patients. In addition, a more thorough visual examination pre- and poststenting including visual fields testing and determination of optic atrophy and acuity would be beneficial. The large cohort of patients, detailed description of the endovascular surgical technique of cerebral angiogram, venous sinus manometry, and venous sinus stenting, and long-term outcomes of patients permit external validity and generalizability of our study results.

CONCLUSIONS

A multidisciplinary approach with primary care physicians, neurosurgeons, ophthalmologists, neurologists, and radiologists is necessary for comprehensive management of IIH to prevent the devastating sequelae of blindness. Our study demonstrates that venous sinus stenting is relatively safe and efficacious in most patients if the pressure gradient across the transverse-sigmoid junction was above 5 mm Hg. Many articles describing IIH and venous sinus stenting report a high number of patients whose headaches resolved after this procedure. However, approximately half of our patients continued to experience headaches, representing the overlap between the headaches accompanying IIH and chronic migraines. Future randomized controlled trials are necessary to confirm the long-term efficacy of venous sinus stent placement in patients with IIH. As advances in endovascular technology and our understanding of underlying mechanisms of IIH evolve, endovascular intervention will likely increase as an accepted standard treatment in carefully selected patients.

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