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POINT COUNTERPOINT: SHOULD MAGNETIC RESONANCE VENOGRAPHY (MRV) BE PERFORMED ROUTINELY IN ALL PATIENTS UNDERGOING EVALUATION FOR IIH?

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Abstract

Patients with idiopathic intracranial hypertension (IIH) frequently present to the neuro-ophthalmologist prior to obtaining any neuroimaging studies. Although magnetic resonance (MR) imaging of the brain with and without contrast is the recommended diagnostic imaging modality for IIH, some authors advocate routine inclusion of MR venography (MRV), both to screen for venous sinus thrombosis as well as transverse sinus stenosis. Two experts debate whether MRV should be routinely included in the diagnostic work up of patients with suspected IIH.

MRI-based venous assessment should be performed in all patients who present with presumed IIH: Marc Dinkin, MD, Weill Cornell Medical College, New York, NY

OPENING STATEMENT

The majority of women of child-bearing age with an elevated body mass index (BMI) who present with papilledema and negative brain MRI will be diagnosed with idiopathic intracranial hypertension (IIH). The diagnostic criteria for IIH have evolved over the years, beginning with the Dandy criteria (initially requiring CT head and lumbar puncture) and evolving to the modified Dandy criteria which included the addition of MR imaging to more definitively rule out mass lesions and other etiologies responsible for the elevation in intracranial pressure (ICP). Whether or not specific MRV imaging should be included in the routine evaluation of patients suspected of IIH has remained controversial, but an analysis of its respective costs and benefits supports its use.

MRV offers an enhanced ability to detect and quantify the venous sinus stenosis that may be associated with IIH or may result from tumor compression but the primary reason to obtain an MRV in patients who present with an IIH-like syndrome is to rule out a cerebral venous sinus thrombosis (CVST).

CVST is a rare condition of obstruction of the venous sinuses due to thrombotic occlusion, with an annual incidence of 3–4 per million¹ population and up to 7 per 100,000 hospital patients per year². Its primary manifestations include venous infarct and hemorrhage with

secondary seizure and neurological deficits, and symptoms and signs of elevated ICP including abducens palsies and papilledema. While 80% of patients recover with no permanent neurological sequelae, the remainder may be left with permanent disability, and an estimated 16–28% die from associated cerebral edema and trans-tentorial herniation.^{3,4} In an estimated 37% of patients, the only manifestation is an elevation in ICP, mimicking precisely the clinical presentation of IIH.⁵

Some have argued that IIH-like CVST can be distinguished from IIH clinically based on the abrupt nature of presentation,⁶ but in a review of 624 adults with CVST, the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVST) found a subacute presentation in 55% and chronic in 7.2%. Thus, the acuteness of the clinical presentation cannot reliably be used to distinguish IIH-like CVST from actual IIH. And since up to 75% of CVST patients are women (likely attributable to an increased risk of CVST with oral contraceptives use⁷ and during pregnancy⁸), and since the median age of CVST is much younger than that of arterial stroke (median age 37 in the ISCVST), these demographic features do not offer a useful means of differentiation either.

In 2006, Lin and colleagues reviewed the charts of 106 patients with papilledema who underwent MRI and MRV where no mass lesion or meningitis was identified.⁹ Ten of these patients (9.4%) were found to have CVST and four of these patients were obese females of child-bearing age, displaying the typical demographic profile of a patient with IIH. From this we can conclude that a strategy of only searching for CVST in patients who do *not* fit the typical IIH phenotype would potentially lead to 4/106 (3.7%) patients left with undiagnosed CVST. Of note, only 1 patient in this series was diagnosed with MRI alone, while the remainder were diagnosed with MRI in conjunction with MRV.

MRV vs. MRI Alone

MRI alone may detect CVST, especially when there is associated intraparenchymal hemorrhage, but MRV obtained alongside MRI is the most widely accepted technique for diagnosing CVST and has been shown to correlate well with the results of conventional catheter based contrast angiography.¹⁰ There are three primary types of MRV: 1) a 2-dimensional time of flight (2D-TOF) with saturation of arterial flow; 2) phase contrast (PC) MRV; and 3) gadolinium-enhanced 3-dimensional MRV (Gd-MRV). 2D-TOF MRV benefits from a short acquisition time (5–8 minutes) and its spatial resolution. Absence of normal signal in the sinus suggests CVST, as do the indirect signs of collateral veins and visualization of emissary veins. Its major disadvantage is a low sensitivity to blood flowing within the acquisition plane (coronal for MRV), potentially causing drop out that can mimic stenosis or thrombosis. PC MRV utilizes the fact that protons flowing through a magnetic field will demonstrate a phase shift which is proportional to the velocity of flow. Thus direction and speed of flow can be determined. PC MRV there has the advantage of a greater ability to differentiate slow flow from true thrombosis. Gd-MRV demonstrates a flow-independent 3D image of the venous lumen, and therefore removes the in-plane drop out problem of 2D-TOF imaging. In order to maximize the flow of contrast during acquisition time, an auto-triggered elliptic centric ordered (ATECO) system may be utilized, which begins acquisition after 8 second delay. This method has been shown to provide greater

visibility of the venous structures (complete in 92% of patients).¹¹ Finally, time-resolved contrast 3D MRV (also known as “contrast-enhanced 4D venography”) create subtracted images of the contrast bolus in the venous system similar to digital subtraction venography.

The false positive rate of MRV alone, based on misinterpretation of a congenital absent anterior superior sagittal sinus (SSS), prominent arachnoid granulations or blood flow in the direction of the imaging plane as CVST, can be reduced with the concomitant analysis of the conventional MR images. The same can be said for the false negative rate of MRV alone, which may be due to misinterpretation of the high signal of a subacute thrombus as normal flow. Modern MR imaging has become increasingly sensitive at visualizing intra-arterial or intravenous thrombus.

Indeed, a hyperintense thrombus may be noted on SE T1-weighted MRI in CVST, and for that reason alone, a concomitant MRI is always useful in conjunction with MRV for the diagnosis of CVST. More recently, T2*SW (susceptibility-weighted) MRI has been shown to be more sensitive for the detection of CVST than T1, T2 and FLAIR imaging, as well as for the intraparenchymal and subarachnoid blood which may accompany CVST.^{12,13} However, T2 spin echo sequences may produce *false negative* results as the thrombus may appear hypointense in the acute period, mimicking normal flow, while contrast MRI may produce a false negative when contrast at the edge of a thrombus simulates a patent sinus. The addition of MRV to MRI helps to address these pitfalls.

The various modalities were compared in a retrospective study of 39 patients with CVST, in which a neuroradiologist, masked to the patients’ clinical condition reviewed MRIs and MRVs.¹⁴ The sensitivity of MRV at onset was 95% vs. only 84% for T1 spin echo imaging. Of note, a magnetic susceptibility effect (MSE) was seen on T2*SW imaging in 90% of patients at presentation. One study compared time-resolved contrast 3D MRV to TOF MRV and conventional MRI and found a significantly higher sensitivity (90%) and specificity (100%) for CVST as compared to TOF MRV (83% and 79%), T2W MRI (75% and 97%) and gradient echo imaging (55% and 95%).¹⁵

In short, inclusion of TOF and contrast-enhanced MRV, as well as susceptibility-weighted imaging MR scans will improve the sensitivity for CVST when compared to conventional MRI alone, by up to 15%. Furthermore, in the real world, where radiologists are not always made aware of the clinical context, it is likely that the inclusion of MRV will further improve sensitivity for CVST simply by alerting the interpreting radiologist to the clinicians’ suspicions for the condition.

MRV should NOT be performed routinely in all patients undergoing evaluation for IIH: Heather E. Moss, MD, Ph.D., University of Illinois at Chicago

Opening Statement

MRV has two potential applications in the evaluation of patients with suspected IIH. First, it is the gold standard test to exclude cerebral venous sinus thrombosis (CVST), which is

another condition that causes elevated intracranial pressure, and therefore is an important consideration in the differential diagnosis of some patients with suspected IIH. However, while this is a serious diagnosis that requires directed management, it is not common in typical IIH patients and therefore does not need to be excluded in all suspected IIH patients. One prospective series of 22 typical IIH patients who had MRV found venous sinus thrombosis in none¹⁶. Second, it may be important for identifying patients with primary or secondary venous sinus stenosis, directed treatment of which is an emerging therapeutic option for IIH in select patients. However, this is only a consideration when non-medical treatment options are being considered, which is not the case in most patients and therefore does not need to be evaluated in all patients.

There is little debate that MRV is an essential part of the evaluation for IIH in some patients. This group consists of patients that are more likely to have CVST as a cause of headache and papilledema based on history of present illness or past medical history. Historical features such as acute presentation of headache, particularly with crescendo symptoms are concerning for possible CVST¹⁷. Patients with risk factors for CVST or hypercoagulability such as dehydration, pregnancy, infection, recent head trauma, history of cancer or history of clotting disorder are also more likely to have CVST^{1,18}. Finally, MRV is also essential for evaluation of patients who are less likely to have IIH based on their demographic, for example, males, prepubertal girls, older women and non-obese women.

There are also patients in whom there is little debate that MRV need not be performed due to a very low probability that they have CVST. For example, a patient with stable papilledema and headache for six months who had normal brain MR imaging during this period is unlikely to have CVST. In a patient such as this where the benefit of MRV is low, the risks may outweigh the benefits. Risks include those associated with gadolinium contrast, which can cause allergic reactions and serious conditions such as nephrogenic sclerosing dermopathy, particularly in individuals with renal failure. Many patients find the duration and configuration of the MR scanner to be uncomfortable and some require sedation, which carries with it inherent risks. Another consideration is cost, both to the medical system and to the patient. MRV brain and MRI brain are two separate tests. Thus, completing both doubles the duration of testing time (from 30–60 minutes to 60–90 minutes) and doubles the testing cost (from ~\$4000 to ~\$8000). Patient charges vary based on insurance and authorization and can be in the \$300–\$550 for MRV without gadolinium for a patient who has coinsurance and has not met their deductible (this range includes self pay, commercial and Medicare/Medicaid). There can be an additional \$150–\$450 charge to the patient (depending on insurance provider) if MRV is performed both with and without contrast. These charges to the patient are in addition to those for MRI brain.

Perhaps the most important consideration in deciding to not perform brain MRV in suspected IIH patients who have a low likelihood of CVST is the risk of false diagnosis, which can lead to unnecessary therapy, with associated risks, and/or additional, possibly invasive, testing, which also has associated risks. This possibility of false positive studies is not trivial. There are various MRV protocols, which vary in sensitivity, specificity and inter-rater reliability for detection of venous sinus thrombosis. Contrast enhanced 3D MRV has greater diagnostic sensitivity and is less subject to artifact than 2D time of flight, non-

contrast enhanced MRI¹⁹. In my experience, some facilities do not use the most sensitive or specific protocols. Furthermore, expertise in MRV and CVST is necessary for a radiologist to accurately interpret the study²⁰. This is because transverse sinus thrombosis, which is the kind most likely to present with isolated headache similar to IIH¹⁷ is the most difficult to detect on MRV due to the high prevalence of anatomic variants and artifacts in normal individuals^{21–23}, and distinct, non-thrombotic venous abnormalities in IIH patients²⁴.

The challenge is to determine criteria for which patients do not need an MRV to be performed. Chronicity of symptoms is likely the most important consideration. In a series of 1876 patients referred to a headache clinic who were symptomatic for more than 4 weeks at time of evaluation and had at least 3 months of follow up, 4 had papilledema, 3 of which were diagnosed with IIH and 1 was diagnosed with malignant glioma²⁵. None were diagnosed with CVST. Another perspective is provided by the International Study on Cerebral Vein and Dural Sinus Thrombosis, in which over 600 patients with CVST were studied^{26,27}. Time from symptom onset to diagnosis was positively skewed with the median (7 days) being much less than the mean of 14.5 days. 75% of CVT were diagnosed less than 16 days after symptom onset in this cohort. Together these studies suggest that the likelihood of CVST diagnosis decreases with increasing duration of stable symptoms.

It is important to remember that not performing MRV does not imply lack of evaluation for CVST. This is because brain MRI has limited sensitivity for CVT, which, in a population with low CVST prevalence, can translate to substantial negative predictive value. One study found the multiple non-MRV sequences to have sensitivities between 33 and 67% for CVT detection²⁸. While these may seem inadequate, in the authors' population of patients with MRVs performed for clinical indications, the negative predictive value exceeded 95% for all non-MRV sequences studied. It is therefore appropriate that recent guidelines for diagnosis of IIH advise performing brain MRI in all patients and brain MRV only in select patients²⁹.

REBUTTAL- Dr. Dinkin

Dr. Moss makes several excellent points regarding the assessment of patients with IIH-like presentations with MRV. As she makes clear, the incidence of CVST among patients with classic demographic features of IIH is low. The prevalence of CVST in the study quoted may offer false reassurance however, given the small size (n=22) of that study. Based on the 3.7% prevalence in Lin et al's study of 106 patients⁹, less than one patient with presumed IIH and typical features would be expected to have CVST among a group of 22. So the question is whether it's worthwhile to obtain an MRV if it only would benefit 3.7% of the patients. While that is a low number, the decision to test for an entity should not only be based on a pretest probability of a positive result, but on the consequences of missing the diagnosis. In this case, severe vision loss, neurologic disability and death could result from missing the diagnosis, justifying acquisition of MRV despite the low possibility of a thrombosis.

I agree with Dr. Moss that an MRV really is not essential in patients who have symptoms of elevated ICP and stable papilledema for 6 months or have optic atrophy at presentation. But this is no more the standard IIH presentation than a thin male with papilledema. The recommendation to obtain an MRV really should apply to patients who

present with acute or subacute symptoms, where there is a real possibility of acute CVST. Furthermore, although none of the 1876 patients in the Sempere et al study²⁵ (which included only patients with greater than 4 weeks of symptoms) were found to have CVST, only 4 of the patients had papilledema, so little can be concluded about the rate of CVST among patients with headache *and* papilledema from this study.

MRV Risks

Dr. Moss is also correct in identifying potential inconveniences and even risk resulting from obtaining an MRV. These include a) extra time spent in the scanner b) risk of false positive results, c) risk of contrast reaction and d) expense, ranging from \$500–600 per MRV.

Time in the scanner—Regarding time in the scanner, it is difficult to quantify the harm of these extra minutes spent in the scanner, but for the average non-claustrophobic patient, it is incomparable with the risk of permanent neurological defects from missing a CVST, especially since they all will ostensibly be in the scanner anyway for an MRI with and without contrast. The time of a standard MRI with and without contrast is already 40 minutes, while an MRV (without MRA) adds only an additional 10–15 minutes (potentially even shorter: total imaging time of ATECO contrast MRV has been reported to be 2 minutes and 24 seconds³⁰ so it does not double the time in the scanner. Furthermore, those patients with severe claustrophobia will need sedation or an open MRI facility anyway for the MRI brain.

Contrast Reaction—Regarding contrast reactions, a standard TOF MRV does not require contrast. And while contrast-enhanced MRVs may offer greater accuracy, patients with presumed IIH should undergo contrast enhanced MRI anyway, so there is no increased risk with the addition of contrast MRV.

False Positive Results—The risk of false positive results is real, but as stated above, it is reduced with concomitant MRI. For example, absence of the anterior portion of the superior sagittal sinus on MRV might mimic CVST, but if one looks at the coronal spin echo images, one would see that the sinus is not occluded but is instead small³¹. Furthermore, while loss of signal may occur when the direction of blood flow is within the imaging plane on TOF MRV, this artifact too can be avoided by reviewing contrast enhanced MRV. There is no question that MRV should only be acquired when the neuroradiologist is equipped to interpret the study and understands the pitfalls and how they may be countered. In the end, the best balance of sensitivity and specificity will occur when MRV and MRI (preferably with T2* SWI imaging) are both acquired and analyzed together.

Analysis of Morbidity, Mortality and Cost

The expense of obtaining an MRV in all patients presenting with possible IIH does add up as one contemplates all the additional MRVs performed in patients with papilledema who fit the criteria for an IIH patient. The cost of MRV can vary considerably from state to state and between radiological suppliers but I found an asking price of \$1300 in a New York City Park Avenue practice with a maximum payment by Medicare of \$520. Many insurance companies model their payment scales after Medicare, but let's assume a higher actual

payment of \$800. Assuming an incidence rate of IIH of 2 per 100,000³², and a population of 320 million in the United States, an estimated 6400 patients are diagnosed with IIH in the US per year. Assuming that we would all perform MRV on the male patients with new onset papilledema since they are not typical IIH patients, and a female: male ratio of 8:1 (REF), incorporating MRV in the work up of “typical” IIH patients would lead to an additional $8/9 * 6400 = 5688$ MRVs per year, yielding an additional cost of $5688 * \$800 = \4.5 million per year in the United States alone. However, when we compare this expense to the expense related to the morbidity that could result from missing CVST (forgetting about patient suffering for a moment), it is easily eclipsed.

Assuming that 3.7% of the patients who present with an IIH-like picture actually harbor CVST (see above), there would be an estimated $6400 * 3.7\% = 236$ patients annually in the US who present with an IIH-like case of CVST. Assuming an increased sensitivity of 15% by including MRV and T2* imaging specifically aimed at ruling out CVST (see above), an estimated $236 * 15\% = 35$ more patients would be correctly diagnosed per year.

The benefits of treatment of CVST are difficult to quantify as a large randomized trial vs. placebo would be unethical at this point since it has become the standard of care. However, in one small, patient-blinded, randomized controlled trial, 60% of the patients in the control arm were left with neurological deficits and 20% died, while only 20% in the treatment group were left with “slight” neurological deficits and none died³³. Assuming therefore that treatment could reduce the risk of neurological disability by 40%, then, this would mean: 35 patients diagnosed with CVST due to the inclusion of MRV and susceptibility-weighted MRI * 40% reduction in the rate disability from treatment = 14 patients per year spared lifetime disability. Assuming loss of employment due to disability with median US annual income currently \$52000, and an expected 30 years of working (retirement age 67 - mean age of CVST 37 = 30), that’s \$1,560,000 of lost income per patient * 14 patients = \$21,840,000, a much higher value than the \$4.5 million cost of the 5688 additional MRVs per year. Now if you include the direct medical costs of caring for these 14 patients, basing it on the annual cost of medical care of patients following ischemic and hemorrhagic strokes³⁴, which was estimated in Finland in 2007 (likely underestimating 2015 US costs) to be \$32,900 (averaging ischemic and hemorrhagic stroke since CVST can cause both) multiplied by an estimated 30 years of medical care until retirement age (assuming conservatively that healthcare costs after retirement would be high anyway), that adds an additional \$987,000 per patient, or \$13,818,000. Thus the total cost in terms of lost employment and added healthcare costs to the US society of missing 35 cases of CVST by failing to obtain an MRV and MRI T2* is estimated at \$21,840,000 (employment) + \$13,818,000 (healthcare costs) = \$35,658,000. This analysis, which focused only on the financial cost of additional disability, and did not even address the “cost” of additional deaths, and suggests that including an MRV in the work up of routine IIH would be cost effective in the long-run.

It is therefore apparent that inclusion of modalities to rule out CVST in the typical IIH patient will save lives, prevent disability, and when accounting for the financial burden of the morbidity and mortality prevented by finding the diagnosis in the rare patients who are positive, is even cost-effective in the long term.

Assessment of venous sinus stenosis

Over the last 14 years it has become evident that a majority of patients with IIH demonstrate stenosis at the junction of the transverse and sigmoid sinuses either unilaterally or bilaterally, leading to the hypothesis that this stenosis played a role in the pathophysiology of the elevated intracranial pressure. Specifically, such stenosis was observed in 90% of IIH patients vs. only 6.7% of controls using ATECO MRV³⁵. Beginning with the first stent placement by Higgins in 2002³⁶, and culminating in a large retrospective review of 52 patients treated with stents in 2011³⁷, an increasing body of evidence has grown to support a role for venous stenting as an option for IIH patients who are refractory to medications and in which a significant trans-stenotic gradient exists across the stenosis. In the patient who is suspected to have IIH, but in whom the results of funduscopy are equivocal (papilledema vs. drusen for example) and lumbar puncture is borderline (e.g., opening pressure of 22 cm of water), the identification of venous sinus stenosis can help support a diagnosis of IIH, along with other clinical and radiological features. Despite the positive retrospective data supporting venous stenting as safe and effective, it remains an experimental procedure with little prospective or controlled data, and is best reserved for patients with vision-threatening, medically-refractory IIH. Dr. Moss is correct in stating that the majority of patients will not require such a procedure, but in practice, I find it helpful to know early on if a patient might be a candidate for stenting should they become refractory to medications, so that if they become refractory, the decision to move on to stenting is not delayed by having first to acquire an outpatient MRV (which can take days) and only then moving on to venography.

In summary, I recommend a careful assessment of the venous system, preferably with a combination of contrast-enhanced MRV along with a contrast MRI that includes T2* susceptibility weighted imaging, in all patients who present with the symptoms and signs of presumed IIH, in order to increase the sensitivity for the rare possibility of IIH-like CVST, and help lessen the morbidity and mortality of that disease. The associated risks and costs of such an assessment are low when compared to the risk and long-term costs of missing the diagnosis in even one of our patients. An added benefit to careful venous assessment is the identification of venous sinus stenosis which can help support the diagnosis of IIH in questionable cases, and could have implications for therapy with venous sinus stenting in medically-refractory cases.

Rebuttal- Dr. Moss

I agree wholeheartedly with Dr. Dinkin that the presentation of CVST can overlap with IIH, that MRV is the gold standard for diagnosing it, and that directed therapy is necessary for CVST to mitigate risk of substantial morbidity or mortality. For these reasons it is imperative that every physician who is evaluating a patient with papilledema must consider CVST as a “can’t miss diagnosis” in the same way that they consider tumor as a “can’t miss diagnosis”. It is also imperative that physicians consider immediate and downstream risks of all diagnostic tests that they order. Diagnostic testing is a complement to, not a replacement for careful clinical evaluation and judgment. In the case of papilledema and possible CVST, clinical evaluation and prior diagnostic testing determine pre-test probability of CVST. If this is low, as it is for patients with documented longstanding papilledema, chronic headaches, and normal MRI brain, the potential benefit of add on MRV to make a diagnosis

of CVST is low, and the risks of MRV, including complications, false diagnosis, inadequate study and cost become relevant and worthy of consideration. When the risks exceed the benefit for a particular patient, MRV need not be performed in that patient.

Conclusions

The sensitivity and resolution of MRV has increased over the past decade and further advances in neuroimaging should continue to improve the technical aspects of this modality. The authors have presented compelling arguments both for and against the routine inclusion of MRV in the work up of IIH. All neuro-ophthalmologists should have a low threshold for ordering MRV in patients who have a high risk of CVST. The decision to include MRV in the majority of suspected IIH patients should include factors such as the technical quality of the test at the specific facility, the skill of the interpreting neuroradiologist, the time and cost of the testing, and the degree to which the presence or absence of transverse sinus stenosis influences diagnosis and management.

References

1. Stam J. Thrombosis of the Cerebral Veins and Sinuses. *N Engl J Med*. 2005; 352:1791–8. [PubMed: 15858188]
2. Daif A1, Awada A, al-Rajeh S, Abduljabbar M, al Tahan AR, Obeid T, Malibary T. Cerebral venous thrombosis in adults. A study of 40 cases from Saudi Arabia. *Stroke*. 1995 Jul; 26(7):1193–5. [PubMed: 7604412]
3. Patil VC, Choraria K, Desai N, Agrawal S. Clinical profile and outcome of cerebral venous sinus thrombosis at tertiary care center. *J Neurosci Rural Pract*. 2014 Jul; 5(3):218–24. [PubMed: 25002759]
4. Coutinho JM, Zuurbier SM, Stam J. Declining mortality in cerebral venous thrombosis: a systematic review. *Stroke*. 2014 May; 45(5):1338–41. [PubMed: 24699058]
5. Biousse V, Ameri A, Bousser MG. Isolated intracranial hypertension as the only sign of cerebral venous thrombosis. *Neurology*. 1999; 53:1537–42. [PubMed: 10534264]
6. Purvin VA, Trobe JD, Kosmorsky G. Neuro-ophthalmic features of cerebral venous obstruction. *Arch Neurol*. 1995 Sep; 52(9):880–5. [PubMed: 7661725]
7. Martinelli I, Sacchi E, Landi G, Duca F, et al. High risk of cerebral vein thrombosis in carriers of a prothrombin gene mutation and in users of oral contraceptives. *N Engl J Med*. 1998; 338:1793–1797. [PubMed: 9632445]
8. Cantu C, Barinagarrementeria F. Cerebral venous thrombosis associated with pregnancy and puerperium: review of 67 cases. *Stroke*. 1993; 24:1880–4. [PubMed: 8248971]
9. Lin A, Foroozan R, Danesh-Meyer HV, De Salvo G, Savino PJ, Sergott RC. Occurrence of cerebral venous sinus thrombosis in patients with presumed idiopathic intracranial hypertension. *Ophthalmology*. 2006; 113:2281–2284. [PubMed: 17157135]
10. Mattle HP, Wentz KU, Edelman RR, et al. Cerebral venography with MR. *Radiology*. 1991; 178:453–458. [PubMed: 1987608]
11. Farb RI, Scott JN, Willinsky RA, Montanera WJ, Wright GA, terBrugge KG. Intracranial venous system: gadolinium-enhanced three-dimensional MR venography with auto-triggered elliptic centric-ordered sequence—initial experience. *Radiology*. 2003 Jan; 226(1):203–9. [PubMed: 12511691]
12. Boukobza M, Crassard I, Bousser MG, Chabriat H. MR imaging features of isolated cortical vein thrombosis: diagnosis and follow-up. *AJNR Am J Neuroradiol*. 2009 Feb; 30(2):344–8. [PubMed: 19095790]
13. Selim M, Fink J, Linfante I, Kumar S, Schlaug G, Caplan LR. Diagnosis of cerebral venous thrombosis with echo-planar T2*-weighted magnetic resonance imaging. *Arch Neurol*. 2002 Jun; 59(6):1021–6. [PubMed: 12056941]

14. Idbah A, Boukobza M, Crassard I, Porcher R, Bousser MG, Chabriat H. MRI of clot in cerebral venous thrombosis: high diagnostic value of susceptibility-weighted images. *Stroke*. 2006 Apr; 37(4):991–5. [PubMed: 16484607]
15. Meckel S, Reisinger C, Bremerich J, Damm D, Wolbers M, Engelter S, Scheffler K, Wetzel SG. Cerebral venous thrombosis: diagnostic accuracy of combined, dynamic and static, contrast-enhanced 4D MR venography. *AJNR Am J Neuroradiol*. 2010 Mar; 31(3):527–35. [PubMed: 19892813]
16. Lee AG, Brazis PW. Magnetic resonance venography in idiopathic pseudotumor cerebri. *J Neuroophthalmol*. 2000; 20:12–13. [PubMed: 10770498]
17. Cumurciuc R, Crassard I, Sarov M, Valade D, Bousser MG. Headache as the only neurological sign of cerebral venous thrombosis: a series of 17 cases. *J Neurol Neurosurg Psychiatry*. 2005; 76:1084–1087. [PubMed: 16024884]
18. Ferro JM, Canhao P. Cerebral venous sinus thrombosis: update on diagnosis and management. *Curr Cardiol Rep*. 2014; 16:523. [PubMed: 25073867]
19. Klingebiel R, Bauknecht HC, Böhner G, Kirsch R, Berger J, Masuhr F. Comparative evaluation of 2D time-of-flight and 3D elliptic centric contrast-enhanced MR venography in patients with presumptive cerebral venous and sinus thrombosis. *Eur J Neurol*. 2007; 14:139–143. [PubMed: 17250720]
20. Leach JL, Fortuna RB, Jones BV, Gaskill-Shipley MF. Imaging of cerebral venous thrombosis: current techniques, spectrum of findings, and diagnostic pitfalls. *Radiographics*. 2006; 26(Suppl 1):S19–41. discussion S42–13. [PubMed: 17050515]
21. Alper F, Kantarci M, Dane S, Gumustekin K, Onbas O, Durur I. Importance of anatomical asymmetries of transverse sinuses: an MR venographic study. *Cerebrovasc Dis*. 2004; 18:236–239. [PubMed: 15273441]
22. Ayanzen RH, Bird CR, Keller PJ, McCully FJ, Theobald MR, Heiserman JE. Cerebral MR venography: normal anatomy and potential diagnostic pitfalls. *AJNR Am J Neuroradiol*. 2000; 21:74–78. [PubMed: 10669228]
23. Bono F, Lupo MR, Lavano A, Mangone L, Fera F, Pardatscher K, Quattrone A. Cerebral MR venography of transverse sinuses in subjects with normal CSF pressure. *Neurology*. 2003; 61:1267–1270. [PubMed: 14610135]
24. Higgins JN, Gillard JH, Owler BK, Harkness K, Pickard JD. MR venography in idiopathic intracranial hypertension: unappreciated and misunderstood. *J Neurol Neurosurg Psychiatry*. 2004; 75:621–625. [PubMed: 15026510]
25. Sempere AP, Porta-Etessam J, Medrano V, Garcia-Morales I, Concepcion L, Ramos A, Florencio I, Bermejo F, Botella C. Neuroimaging in the evaluation of patients with non-acute headache. *Cephalalgia*. 2005; 25:30–35. [PubMed: 15606567]
26. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke*. 2004; 35:664–670. [PubMed: 14976332]
27. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F, Massaro A, Ducrocq X, Kasner SE. Delay in the diagnosis of cerebral vein and dural sinus thrombosis: influence on outcome. *Stroke*. 2009; 40:3133–3138. [PubMed: 19608994]
28. Saindane AM, Mitchell BC, Kang J, Desai NK, Dehkharghani S. Performance of spin-echo and gradient-echo T1-weighted sequences for evaluation of dural venous sinus thrombosis and stenosis. *AJR Am J Roentgenol*. 2013; 201:162–169. [PubMed: 23789671]
29. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*. 2013; 81:1159–1165. [PubMed: 23966248]
30. Agid, Ronit MD.; Shelef, Ilan MD.; Scott, James N MD.; Farb, Richard I MD. Imaging of the Intracranial Venous System. *Neurologist*. 2008 Jan; 14(1):12–22. [PubMed: 18195652]
31. Wasay M, Azeemuddin M. Neuroimaging of Cerebral Venous Thrombosis. *J Neuroimaging*. 2005; 15:118–128. [PubMed: 15746223]
32. Kesler A1, Stolic N, Bluednikov Y, Shohat T. The incidence of idiopathic intracranial hypertension in Israel from 2005 to 2007: results of a nationwide survey. *Eur J Neurol*. 2014 Aug; 21(8):1055–9. [PubMed: 24698554]

33. Einhaupl KM, Villringer A, Meister W, et al. Heparin treatment in sinus venous thrombosis. *Lancet*. 1991; 338:597–600. [Erratum, *Lancet* 1991;338:958.]. [PubMed: 1679154]
34. Meretoja A1, Kaste M, Roine RO, Juntunen M, Linna M, Hillbom M, Marttila R, Erilä T, Rissanen A, Sivenius J, Häkkinen U. Direct costs of patients with stroke can be continuously monitored on a national level: performance, effectiveness, and Costs of Treatment episodes in Stroke (PERFECT Stroke) Database in Finland. *Stroke*. 2011 Jul; 42(7):2007–12. [PubMed: 21527757]
35. Farb RI, Vanek I, Scott JN, Mikulis DJ, Willinsky RA, Tomlinson G, terBrugge KG. Idiopathic intracranial hypertension: the prevalence and morphology of sinovenous stenosis. *Neurology*. 2003 May 13; 60(9):1418–24. [PubMed: 12743224]
36. Higgins JN, Owler BK, Cousins C, Pickard JD. Venous sinus stenting for refractory benign intracranial hypertension. *Lancet*. 2002 Jan 19; 359(9302):228–30. [PubMed: 11812561]
37. Ahmed RM, Wilkinson M, Parker GD, et al. Transverse sinus stenting for idiopathic intracranial hypertension: a review of 52 patients and of model predictions. *AJNR Am J Neuroradiol*. 2011 Sep; 32(8):1408–14. [PubMed: 21799038]