The promise and challenges of CSF-venous fistula treatment

Peter George Kranz, Timothy J Amrhein

In their *JNIS* paper, Brinjikji *et al* report on the treatment outcomes of transvenous embolization for patients with spontaneous intracranial hypotension (SIH) caused by cerebrospinal fluid-venous fistulas (CVFs).[1] This retrospective observational cohort study describes the rates of improvement in the symptoms and the imaging for 40 patients with CVF treated with transvenous embolization. Outcomes were measured with validated headache measures (Headache Impact Test—HIT-6, a severity scale ranging from 36 to 78) and patient satisfaction scores (Patient Global Impression of Change—PGIC) at 3 months after the intervention. Brain imaging was also obtained before intervention and at 1–4 months after treatment.

The results obtained are encouraging. Mean headache severity, as measured by HIT-6, improved from an average score of 67 (the most severe impact category) to 42 (the least severe category). Patient-reported perception of global improvement in symptoms was also promising, with 83% reporting much or very much improvement on the PGIC. These symptomatic improvements were accompanied by improvements in brain imaging as well, with decreases in brain MRI changes of SIH in all but two patients.

The authors also report good technical success, with acceptable minor complication rates and no severe complications. Optimal technical results (delivery of embolic agent proximal to the site of the fistula) were achieved in 36 of 40 subjects. Two patients required re-treatment for persistence of the fistula after embolization; one of those patients remained symptomatic after re-treatment. No permanent complications or spinal injury was seen in this cohort. Temporary pain at the embolization site was reported in 30%, and asymptomatic embolization of liquid embolic agent to the lungs was seen in three patients.

Together, these results help establish transvenous embolization as a serious contender among treatment strategies for CVFs. The fact that the authors were able to accumulate sufficient data for publication of this cohort in less than a year after publication of the initial technical description indicates the frequency with which CVFs are now being diagnosed, and the lack of consensus on a dominant treatment strategy.

The authors also should be commended for their incorporation of several very important methodological details that have historically been absent from most outcome studies on SIH. Specifically, these include a clear description of how the diagnosis of SIH was established (ie, International Classification of Headache Disorders, third edition (ICHD-3) criteria), the use of validated outcome measures (ie, HIT-6, PGIC), clear reporting on the timing of outcome measure collection, and how complications were assessed.

Since their first description as a cause of SIH in 2014, CVFs have been the subject of intense investigation into optimal methods for diagnosis and treatment.[2–4] This is in part due to the fact that the discovery of CVFs helped to shed light on a longstanding and highly vexing problem related to SIH, namely, that some patients showed clear imaging evidence of CSF volume depletion on brain imaging despite the fact that no leak of fluid into the epidural space could be found on spinal imaging. It has become increasingly clear that many, if not all, of these cases of SIH without extradural fluid are caused by CVFs that were unrecognizable using older imaging techniques. The development of newer imaging myelographic methods performed with decubitus positioning, either using digital subtraction fluoroscopy or CT imaging, has led to much higher rates of CVF detection and spurred a sea change in the treatment algorithms for SIH.[3 5] Still, detection of CVFs remains very challenging in some cases, and further innovation in diagnostic modalities is needed.

Regarding treatment of CVFs, there is still much that is not yet established. Early literature suggested that epidural patching of CVFs was not highly effective, resulting in frequent relapses. In one series of patients with CVFs, only 14% were treated successfully with epidural patching alone.[6] A subsequent investigation found that only 2.5% of patients treated with epidural patching had good long-term outcomes requiring no further treatment.[7] Surgical intervention in the form of ligation of the nerve root from which the CVF was found to arise proved to be a much more effective intervention. One investigation found surgery to be highly effective in 83% of cases, with all patients reporting partial improvement after surgery.[8] Another investigation reported that surgical treatment of CVFs resulted in a 50% improvement in symptoms in 75% of patients.[7]

As effective as surgical intervention has proven to be, however, it is not without its own limitations. Some CVFs may be found at spinal levels where the nerve root is functional, precluding ligation of the root. Additionally, some treatment failures have been observed in patients undergoing surgery, including recurrence of fistulas at the treated level or the de novo development of new CVFs at other spinal levels after treatment.[9] Such treatment failures could also become apparent with longer follow-up times after embolization. Surgical intervention is also invasive, requiring inpatient hospitalization and postoperative recovery time. Transvenous embolization has the potential to circumvent these limitations.

Enthusiasm for this new procedure must be tempered by the fact that experience with and follow-up after embolization is currently still in its nascent stage, and it remains to be seen whether long-term outcomes for embolization remain favorable. In particular, a question yet to be answered is whether CVFs may recruit new drainage pathways and become symptomatic again if embolization is insufficiently proximal to the actual site of the fistula. When treatment fails, defining what salvage therapies (either surgical or percutaneous) are feasible will also be important. Finally, repeat imaging evaluations of post-treatment CVFs are difficult due to the marked attenuation of X-rays caused by the embolic agent, and this fact poses challenges for follow-up of patients with residual or recurrent symptoms.

Answering the question of which therapy for CVFs is best will require multiple well designed prospective observational cohort studies or, ideally, randomized trials of percutaneous, surgical, and endovascular techniques. A recent publication has reported good outcomes with percutaneous injection of fibrin glue for CVFs, potentially re-awakening the discussion about this treatment for CVFs as well.[10] Designing and executing such head-to-head trials will not be a trivial undertaking. As this investigation

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by Brinjikji *et al* shows, currently available clinical outcome measures lack the nuance to distinguish headache associated with SIH from headache associated with rebound intracranial hypertension, an expected post-treatment outcome after treatment of SIH, which may confound outcome assessment.[1] Further, existing headache scores will not be able to assess outcomes among patients who present without headache; two such patients were seen in this study. Outcomes measures specifically designed and validated for SIH would be optimal for future prospective studies. Longer-term follow-up should also be a component of future trials, and a multicenter approach would also likely help to provide more broadly generalizable conclusions. Progress toward the goal of better and more effective care for patients with SIH requires a series of many steps, and this manuscript represents an important one in that direction.

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