Investigation of a Valve-Agnostic Cranial Implant for Adult Hydrocephalus Patients Requiring Ventriculoperitoneal Shunting

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Introduction: Currently, the most effective treatment strategy for adults with hydrocephalus involves cerebrospinal fluid diversion by means of a shunt system, most commonly ventriculoperitoneal shunts (VPS). Ventriculoperitoneal shunting is associated with high complication and/or revision rates, in part due to the high-profile programmable valve designs. Thus, the valve-agnostic cranial implant (VACI) was designed and investigated as a safe and effective method of reducing the valve's high profile and is currently undergoing clinical trials. As such, the objective of this study was to collate preliminary, multi-institutional data of early outcomes using a VACI approach for patients requiring VPS by way of an Institutional Review Board approved registry.

Methods: A total of 25 adult patients across 4 institutions and 6 surgeons underwent VACI placement for VPS based on preoperative evaluation and perceived benefit. Patient demographics, operative details, and preliminary outcomes are presented here.

Results: Valve-agnostic cranial implant placement via a limited size craniectomy at time of shunt revision was performed with no adverse events. Over an average follow-up period of 1 year (394 ± 178 days), 92% of patients experienced no major shunt-related or scalp-related complications. There were 2 cases with a major complication requiring reoperation: 1 shunt tubing extrusion and 1 case of meningitis. The most frequent postsurgical intervention seen in this study was related to adjustment of drainage: a non-invasively performed valve reprogramming after initial shunt placement when proper flow rate is being established. Of the 8 cases of drainage adjustment, all but 1 (88%) were receiving a VPS for the first time, with the exception undergoing a fourth shunt revision. All instances of improper flow were treated non-surgically and remediated effectively via shunt reprogramming in clinic. Removal of the VACI was not indicated in any treatment course. In this way, all complications as they relate to the shunt valve were minor and required nonsurgical intervention, and no complications reported were directly or indirectly caused by using the VACI.

Conclusion: Preliminary findings from this multicenter trial suggest promising outcomes with a low complication rate for patients with hydrocephalus undergoing VACI placement during VPS. Ongoing research will continue to provide a more robust clinical picture of VACI in hydrocephalus management as more data becomes available.

Key Words: Cranial, cranioplasty, deformity, hydrocephalus, implant, shunt, shunt, valve

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Clinically defined as the abnormal dilation of the cerebral ventricles with pathologic accumulation of cerebrospinal fluid (CSF), hydrocephalus affects over one million Americans, with an estimated global prevalence of 85/100,000.[1] The etiologies include congenital, acquired, and idiopathic forms, and disease severity encompass a wide range of symptoms. Left untreated, hydrocephalus can result in progressive neurological damage and death, making it a major contributor to worldwide morbidity and mortality.[2,3] Despite its severity and prevalence, relatively small advances and improvement in clinical practice or treatment have been made in the past fifty years, and there remains no known cure.[4] Presently, the mainstay of hydrocephalus management in adults remains CSF diversion with shunting, most commonly ventriculoperitoneal shunts (VPS) with high-profile valve designs and programmable functions. Thus, VPS has become one of the most commonly performed neurosurgical procedures across the entire specialty.

Ventriculoperitoneal shunts placement and methodology have remained largely unevolved since development over 60 years ago, and continue to have high rates of complications and revisions.[5–8] The Hydrocephalus Association reports that up to 70% of all 40,000 hydrocephalus-related surgeries performed in the United States annually are "revision-type" surgeries, and shunt malfunction most often begin within the first year following insertion (~50% of cases).[9] Shunt failures occur due to a multitude of factors – predominantly infection, occlusion, extrusion, or migration (dislodging/ disconnecting) of the shunt.[7] As such, they are often classified as either "catheter-related" (clogging or valve dysfunction) or "scalp-related" (scalp breakdown, extrusion, or infection). These factors are further complicated by an increased number of revisions, as repeated surgical exposure contribute to scalp-related issues such as risk for incisional wound dehiscence or ulceration over the valve.

Our team previously described concerns regarding the current high-profile design and stiff materials used for shunt valve fabrication, and the pressure-induced ischemia in the overlying scalp, analogous to the pathophysiological mechanism of sacral pressures ulcer commonly encountered by plastic surgeons.[10] Compounded by a lack of advancement in treatment, technology, and research, the rate of shunt complications has facilitated a normalcy of tens to hundreds of surgical revisions in the lifespan of a patient with hydrocephalus. In fact, VPS placement has one of the highest failure rates of any surgical treatment.[11] This is especially relevant given current healthcare economic challenges, and governmental policies now in place to both support "above-average performance" and to penalize "below-average performance".[12] Equally relevant is legislature preventing hospital reimbursement for perioperative readmissions directly related to surgical complications.[13,14]

Recognizing this high revision rate and demand for advances to mitigate the known causes of shunt-related complications, our team was the first to report the perceived benefits of incorporating a novel cranial implant design as a valve-agnostic, low-profile intercranial device (LID) platform, now known as the InvisiShunt (Longeviti Neuro Solutions, Hunt Valley, MD).[15] This valve agnostic cranial implant (VACI) was developed to improve safety and minimize complication risk by

1. removing excessive scalp stretch and pressure,
2. preventing deformity of the head/skull,
3. restoring/maintaining cranial contour to that of one's "preoperative appearance," and
4. providing neurosurgeons a prefabricated, customized shunt valve cavity for deep inset, thereby utilizing ones skull space as a limited-size cranioplasty (approximately 7 cm in length).

Since initial conception, this unique cranioplasty platform has been utilized to lower the predesigned, high-profile nature of all programmable shunt valves, while supporting its location and orientation. As such, we sought to assess the safety and efficacy of the VACI at mitigating the commonly reported, shunt-related complications via an Institutional Review Board (IRB) approved, multi-institutional, retrospective review of a prospectively collected database. Preliminary data from this ongoing, active multicenter study is reported here.

METHODS AND MATERIALS

A retrospective analysis of a prospectively collected database was performed to evaluate clinical outcomes for the first 25 patients undergoing VACI reconstruction over a 2-year period (January 2018–March 2020). Appropriate informed patient consent was obtained according to IRB guidelines, and in accordance with human trials standards set forth in the Declaration of Helsinki. Inclusion criteria were defined as all adult patients (at least 18 years of age) presenting with insertion or revision of a VPS. No exclusion criteria were exercised. All cranioplasty reconstructions and shunt-valve insertions were performed by a neurosurgeon, with or without an accompanying neuroplastic surgeon.

Briefly, the justification for utilizing a VACI was determined by the attending neurosurgeon, and informed patient consent was obtained. All VACI surgeries were performed according to the US Federal Drug Administration (FDA) approved indications. Reasons cited for use included restoration of cranial contour and/or prevention of shunt valve extrusion, shunt migration, and compromised scalp (ie, excessive scarring present) with increased risk for breakdown over the valve. Surgeries were performed either concurrently with placement of a new shunt or modification of an existing shunt. The type of shunt valve was determined by the neurosurgeon, and the VACI was customized and prefabricated to fit the valve being utilized. Approach for VACI placement has been standardized between all 4 institutions, involving a scalp incision away from the device (ie, avoiding an incision directly over the implant), and the placement of a burr hole at Kocher point (11 cm posterior to glabella, 3 cm lateral to midline). An accompanying cutting guide (included with the VACI) is used to design the presized craniectomy to ensure a precise VACI fit. After the VACI is placed in the craniectomy space, the valve is inlaid in the mirroring trough and secured in place using either suture or titanium plate(s). The VACI is made from high-density polyethylene (which has a long, safe history in craniofacial reconstruction)[17] and measures 7 cm in length, with a depth of 7 mm to accommodate a valve up to 8 mm in height (Fig. 1). For instance, in the case of an 8-millimeter-tall programmable shunt valve, there is reduction of 7 mms equating to a 1 mm net difference between the VACI trough and the valve. In turn, this allows for a slight palpability, allowing clinical detection when shunt drainage adjustments are needed. The scalp is closed in multiple layers, ensuring meticulous galeal closure. A subcutaneous closed suction drain may or may not be placed, depending on surgeon judgement/preference. If a drain is placed it is removed within 1 to 2 days postoperatively.[18]

All outcomes related to patient pathology and comorbidities, neurosurgical/craniofacial surgical history, shunt history (VPS and external ventricular drains), surgeon rationale for use, operative variables (shunt valve type/implant model, surgical blood loss, implant/cranioplasty location, complications, etc), postoperative length of stay, postoperative complications (major and minor) with associated interventions, and total length of follow-up were reviewed. Complications were defined as "major" if they required additional surgical intervention and/or hospital readmission within 30 days. All other complications, whether "self-limiting" or requiring intervention occurring in an outpatient clinic, were defined as "minor." Total length of follow-up was defined as time elapsed between date of VACI placement and most recent postoperative visit.

RESULTS

Twenty-five (25) consecutive adult patients with hydrocephalus underwent VACI placement at 4 institutions by 6 attending

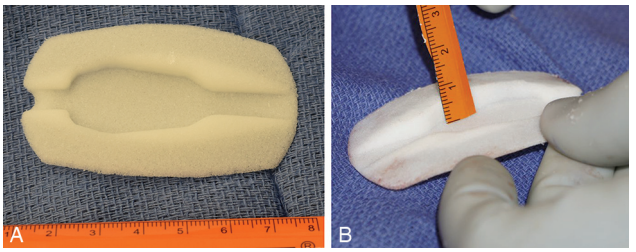

FIGURE 1. Representative photographs of the valve-agnostic cranial implant, demonstrating the length of 7 cm (A) and the depth up to 7 mm (B).

surgeons. Demographic features of the study participants are detailed in Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B564. The average age was 59 years, ranging from 22 to 84 years. There was a slight female predominance, with 56% (n = 14) females. The majority of patients (88%) had acquired (secondary) onset hydrocephalus. History of generalized neurocranial surgery was indicated in 20% of cases (including Chiari decompression, aneurysm clipping, tumor resection, and traumatic brain injury cranioplasty reconstruction), and history of shunting surgery was indicated in 58% of cases (36% of patients having had an external ventricular drain placed; 24% of patients having had previous VPS surgery).

The most common diagnoses for patients undergoing VACI placement were normal pressure hydrocephalus and subarachnoid hemorrhage with acquired hydrocephalus, accounting for 64% of cases (Fig. 2; Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B564). Of the 25 patients, hydrocephalus developed predominantly in adulthood (acquired onset: 85.7%). In all cases, no intraoperative complications were reported. Review of hospital documentation shows an average blood loss of 79 cc and postoperative length of stay of 5.6 days (±4.4 days). Following discharge, 1 patient left the hospital system and was lost to follow up despite all best efforts by surgeons and investigators. Additionally, during the follow up period 2 patients died of causes unrelated to VACI placement (one from a subarachnoid hemorrhage while incarcerated, another from a pulmonary emboli). These patients were nevertheless included in the study and in this report, to fully represent all patients who underwent VACI placement during the study period.

During a mean follow-up of 394 days (12.9 months ± 5.8 months, range 41–782 days), 92% of patients (n = 23) experienced no major scalp or shunt-related complications. There were no major complications directly attributed to the VACI. In particular, in all 24 patients with follow up, the VACI procedure did not directly correlate with any scalp-related complication such as exposure, bleeding, cerebrospinal (CSF) fluid leaking, and/or incisional dehiscence/wound breakdown. However, there were 2 major complications noted within the study with relevance and are thus noted here (Fig. 3).

Firstly, there was a single major complication involving a case of cerebral meningitis which required VP shunt explantation in concordance with standard protocol to remove any and all indwelling shunt tubing at the time of a meningitis diagnosis; however, the VACI itself was not removed. Upon further review, the source of CSF infection was later determined by the surgical team to be a lumbar puncture source and not related to the VACI, the shunt valve, or the surgical site incision (Fig. 4).

In addition, there was a second case reported during the trial categorized as "removed hardware." This patient had a history of total calvarial radiation and multiple prior cranial surgeries, resulting in compromised scalp tissue. This resulted in scalp breakdown over titanium plates at sites distant to the VACI, with the exposed hardware removed during a subsequent surgery being performed for

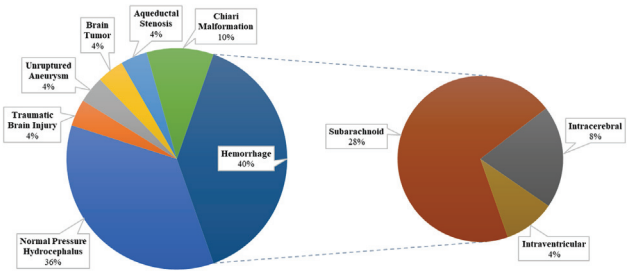

FIGURE 2. Clinical diagnoses represented in our initial patient cohort receiving valve-agnostic cranial implant cranioplasty in combination with ventriculoperitoneal shunting (n = 25).

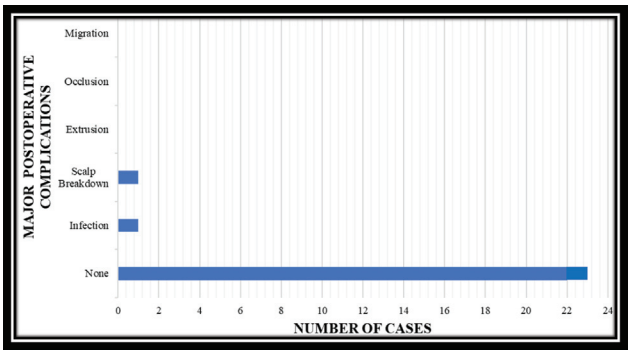

FIGURE 3. Summary of postoperative complications identified in our preliminary patient cohort (n = 25) undergoing VACI cranioplasty. One patient was lost to follow is excluded from this calculation. There were no major complications in 23 of the cases. One patient had scalp breakdown over titanium hardware at a site distant to the VACI, which was removed concurrently in a surgery to resect a glioblastoma. The VACI was not removed during this surgery. A separate patient had a cerebrospinal fluid infection/meningitis corresponding to lumbar-puncture related inoculation; the shunt tubing was explanted according to clinical guidelines however the VACI was not removed. VACI, valve-agnostic cranial implant.

a brain tumor (subsequently diagnosed with glioblastoma). The VACI was not removed during this operation, however the patient subsequently developed another scalp wound infection near the site of the proximal shunt catheter, and shunt externalization was performed. Although the VACI was not directly involved, it was

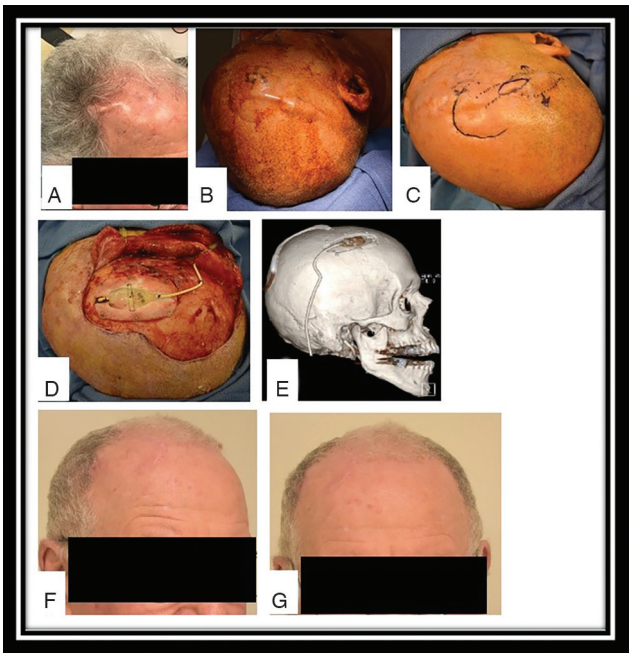

FIGURE 4. Serial images of a patient referred for VACI with normal pressure hydrocephalus (NPH) and standard, right frontal, high-profile, programmable hydrocephalus shunt valve in place. Note the easily visible and palpable acquired head deformity from the valve, and more importantly, the threatened soft tissue envelope with ischemic color change (A). Intraoperative photographs again show the high-profile subcutaneous valve contour (B), with the surgical markings outlining the valve and the scar from the previous surgery (C). The VACI was placed with intraoperative shunt mobilization, with no valve or shunt exchange necessary. Nylon stay sutures were placed to further secure the valve in place (D). Lateral view of postoperative 3D CT scan shows contour of the VACI (also seen is the temporary closed suction drain that was utilized in this case, (E). Postoperative photograph demonstrating a much-improved cranial contour with the same valve embedded within a VACI. Note the concerning skin changes above previously are no longer present (F-G). VACI, valve-agnostic cranial implant.

removed during this procedure because there was no longer an indwelling shunt valve. This patient ultimately died from pulmonary complications related to his comorbidities.

The most frequent postsurgical intervention seen in this study was related to adjustment of drainage: a noninvasively performed valve reprogramming after initial shunt placement when proper flow rate is being established. Of the 8 cases of drainage adjustment, all but 1 (88%) were receiving a VPS for the first time, with the exception undergoing a fourth shunt revision. All instances of improper flow were treated nonsurgically and remediated effectively via shunt reprogramming in clinic. One minor complication involved a very small, localized wound dehiscence near the VP shunt burr hole site. This patient had a history of greater than 250 shunt revisions, presenting with significant scalp erosion and thinning before VACI implantation. Wound healing was accomplished non-surgically using calcium alginate wound dressing. Removal of the VACI was not indicated in any treatment course. In this way, all complications as they relate to the shunt valve were minor and required nonsurgical intervention, and no complications reported were directly or indirectly caused by using the VACI.

DISCUSSION

Based on experience, the cranial bone space – ranging from 4 to 5 millimeters in thickness – is a newfound weapon against neurosurgical-induced deformities, postoperative complications and suboptimal surgical outcomes.[20] Not only can life-altering, implantable neurotechnologies be safely embedded within customized cranial implants,[10,15] but the transformational evolution of "basic" cranial implants into "smart" cranial implants—with integrated biosensors such as wireless intracranial pressure monitors, able to provide realtime feedback for clinical-decision making—is now a futuristic reality.[16] Furthermore, as shuntologists continue to innovate newfound technologies to diagnose shunt catheter flow (flow meters) and abnormal intracranial pressure changes, this VACI provides the field newfound real-estate for nearby implantation and prefabrication.

One area of immediate impact is that of adult-onset hydrocephalus. The current standard of practice management algorithm for this patient population is challenged by the need for programmable hardware with valuable functions and an enlarged housing unit thereby requiring a high-profile design (ie, additional space within). Therefore, the lifelong risk for revision surgery, scalp breakdown, chronic pain, social stigma, daily apprehension of head/shunt valve bumping, and repeated surgery are all major concerns for the adult hydrocephalus patient.[1] Based on current reports, being diagnosed with hydrocephalus almost certainly entails a lifelong journey of repeat VPS surgeries with chronic sequalae and frequent neurosurgical revisions, yet its treatment remains largely unaltered since original conception.[9,19] For these adults, commonly-reported complications warranting "revision" include hardware infection (most often secondary to scalp breakdown and exposure), internal occlusion, external extrusion, and/or device migration (dislodging/disconnecting), many of which increase in occurrence in direct correlation to number of surgical revisions.[10,19,20]

Recognizing the frequency of shunt revision, mutilated scalps, and a preventable cause of complications, a group of neurosurgeons across 4 institutions have elected to trial and use a new platform (the VACI) in an attempt to mitigate common issues such as scalp ischemia, migration, and exposure. As with other "first-in-human" innovations previously described,[10] the VACI is designed to eliminate deformities caused by the unavoidable high-profile shunt valve, restore normal cranial contour, and support location/orientation to prevent migration. Strategic utilization of the cranial space, as opposed to standard placement above the skull, represents a newfound potential for implantable neurotechnologies.[10,16,21,22] As such, 25 patients with hydrocephalus were enrolled in this IRB approved, multi-institutional trial to further assess the safety and efficacy of the VACI.

The VACI was used exclusively on label to reconstruct the cranium following a cutting-guide fashioned, 7 cm long, limited-size craniectomy. Per preoperative reports, the surgical indications for VACI reconstruction were variable. Predominantly, surgeons cited restoration of cranial contour; however, it was also utilized for erosion and extrusion avoidance due to thin or radiated scalp, and for extensive history of shunting or neurocranial surgery. Additional expressed rationale to perform cranial reconstruction with the VACI was risk of infection secondary to scalp-related concerns regarding closure. For all respective justifications for cranioplasty, the results to date suggest that the VACI was effective in meeting expectations (n = 24). Operative reports indicated that VACI placement did not produce significant blood loss, add cause for underlying injury related to small-sized craniectomy, and displayed relatively short postoperative lengths of stay, largely contingent on the severity of the pathology and coexisting comorbidities.

Overall, no complications (revision, infection, etc) have been directly attributed to the VACI. When reviewing shunt-related complications, no instances of migration or occlusion were discovered, supporting the VACI design to maintain orientation and location of the shunt. Although one instance of both "hardware removal" and "CSF infection" were revealed in this trial, these complications were not directly related to the VACI. Furthermore, when reviewing for minor shunt-related postoperative complications, only a small wound dehiscence (n = 1) was discovered, which was corrected by local wound care.

A limitation of this study is the relatively short follow up period (average 1 year). Given that the study has been ongoing for over 2 years, we felt it important to evaluate and report results to date, such that our and other neurosurgical and neuroplastic surgery groups may utilize this data to guide surgical management of this complex patient population. Another shortcoming is the small sample size (n = 25); however, at this phase a preliminary report was warranted to discuss efficacy and safety of the device, especially given the uncertainty in outcomes and the exponential increase in expense, personnel and infrastructure that accompanies prospective, multicenter investigations. We anticipate more widespread utilization and clinical trial enrollment based on the data thus far. Thus, despite the limitations, these preliminary results represent promising indications for the VACI platform to be studied at a higher level by other neurosurgical groups.

CONCLUSION

Based on preliminary findings from this first, multicenter trial investigating the VACI, these promising results represent an important step in the evolution of modern-day treatment for adult patients with hydrocephalus. Herein, we sought to evaluate this platform in hopes of mitigating the burden of VPS placement via a limited size craniectomy/cranioplasty, as a new method to alter a high-profile shunt valve into a low-profile intercranial device. Our team's findings suggest that patients implanted with the VACI implant had reduced pressure/ischemia and stretch on their overlying scalp, which may contribute to reduced scalp pain and less risk of scalp breakdown over the shunt valve. Additionally, by supporting orientation and location, the VACI preliminarily appears to minimize migration and exposure/extrusion. While limited data exists, results to date indicate that this approach is successful in meeting its original aims, as no major or minor complications or revisions directly related to VACI were identified. Long-term, continued surveillance of these VACI patients will be conducted by our team in order to evaluate and confirm that these commonly reported, shunt-related complications remain prevented and/or reduced over time.

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