Cranioplasty Infection and Resorption Are Associated with the Presence of a Ventriculoperitoneal Shunt: A Systematic Review and Meta-Analysis

Christian M. Mustroph, James G. Malcolm, Rima S. Rindler, Jason K. Chu, Jonathan A. Grossberg, Gustavo Pradilla, Faiz U. Ahmad

Key words
- Craniectomy
- Cranioplasty
- Infection
- Resorption
- Ventriculoperitoneal shunt

Abbreviations and Acronyms
CI: confidence interval
CSF: cerebrospinal fluid
OR: odds ratio
VPS: ventriculoperitoneal shunt

Department of Neurological Surgery, Emory University, Atlanta, Georgia, USA

To whom correspondence should be addressed: Faiz U. Ahmad, M.D., M.Ch. [E-mail: faiz.ahmad@emory.edu]

C.M.M. and J.G.M. are co–first authors.

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BACKGROUND: **Following decompressive craniectomy, hydrocephalus is a common complication often necessitating placement of a ventriculoperitoneal shunt (VPS). Complications in the presence of a VPS have been reported, but a clear association has not been established.**

METHODS: **PRISMA guidelines were used to perform a literature search using PubMed to identify articles that published the complication rates associated with staged or simultaneous cranioplasty and VPS placement. From these event rates, odds ratios (ORs) with 95% confidence intervals (CIs) of complications were calculated. Data were pooled using the Mantel–Haenszel method. The Oxford Center for Evidence-Based Medicine guidelines were used to assess the quality of individual articles and studies. The Newcastle–Ottawa Scale was used to assess the risk of bias in studies.**

RESULTS: **Of the 30 papers reviewed for complications in the presence and absence of a VPS, 7 studies, with a total of 1635 patients, were eligible for meta-analysis. Overall rates of complications (n = 1635; OR, 9.75; 95% CI, 4.8–20.1), infection (OR, 4.9; 95% CI, 2.2–10.7), and bone resorption (OR, 10.6; 95% CI, 4.9–23.0) were increased when a VPS was placed at the time of cranioplasty. Simultaneous procedures were associated with increased complication rates (n = 283; OR, 4.3; 95% CI, 2.3–8.2) compared with staged procedures.**

CONCLUSIONS: **Cranioplasty in the presence of a VPS is associated with a higher rate of overall complications, including infection and bone resorption. Performing cranioplasty and VPS placement in the same operation is associated with an increased rate of complications compared with staged procedures. Surgeons should consider staging these procedures when possible and counsel patients about these risks.**

INTRODUCTION

Decompressive craniectomy decreases elevated intracranial pressure caused by traumatic brain injury,[1,2] ischemic or hemorrhagic stroke,[3-5] aneurysmal subarachnoid hemorrhage,[6] and various other conditions. Following decompressive craniectomy, hydrocephalus is a known complication that in some cases necessitates placement of a ventriculoperitoneal shunt (VPS).[7,8] Cranioplasty is performed after decompressive craniectomy to improve craniofacial cosmesis, provide cerebral protection, and potentially improve intracranial hemodynamics and physiological function.[9,10] Cranioplasty outcomes have been studied with regard to the timing of craniectomy,[11,12] type of material,[13,14] and indications for initial craniectomy,[15] and the perioperative risks and complications of cranioplasty, including infection and bone resorption, have been well documented.[14,16,17] Reported rates of infection and bone resorption range from 4.5% to 18.4%[18,19] and from 2% to 5.9%,[20,21] respectively. A limited number of studies have examined the rates of complications in the context of VPS and have yielded varying results. No clear association between the 2 procedures has been identified in previous retrospective studies.

Owing to the large variance in reported outcomes, the purpose of this study was to determine the rates of complications, bone resorption, and infection in the presence and absence of a VPS at the time of cranioplasty via a systematic review and meta-analysis. An increased understanding of these complications in the presence and absence of a VPS at the time of cranioplasty may improve outcomes and better identify risks and the necessary interventions in selected patients.

METHODS

Search Strategy

Following PRISMA guidelines, we performed a systematic literature search using PubMed. Articles reporting complications related to cranioplasty after decompressive craniectomy were recorded if they stratified the cranioplasties in the absence or presence of a VPS. PubMed was searched using the terms "cranioplasty" as

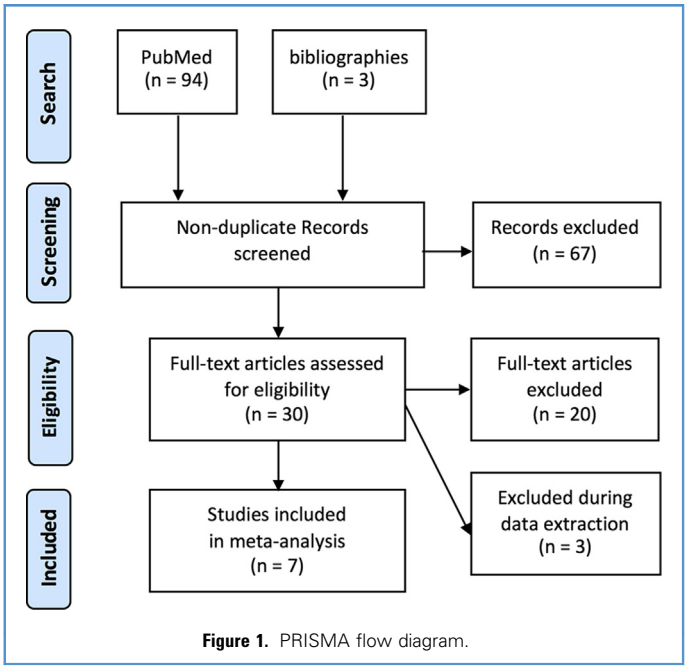

Figure 1. PRISMA flow diagram.

well as "shunt," "ventriculoperitoneal," or "VPS" in all fields. Journal articles indexed in the database before March 2017 were included, and a bibliographic search was performed to identify qualifying articles and relevant medical journals for inclusion.

Study Selection

Articles describing the complications related to the presence or absence of VPS at time of cranioplasty in adults were included in the analyses. Cohort studies and case series that compared infection, resorption, and reoperation rates in more than 20 adults were included. Operative notes and case reports were excluded. No meta-analyses or reviews were found. Studies of pediatric populations[22-24] and non-English articles[25,26] were excluded, and attempts were made to contact the authors of 3 articles that reported the presence or absence of a VPS but did not differentiate among complications. The search results were screened independently by 2 authors (J.G.M. and C.M.M.), and disagreements were resolved by consensus.

Data Extraction

Data on the number of patients, indications for decompressive craniectomy, anatomic locations of the procedure, and cranioplasty-associated complications were compiled from each article. Complications were grouped into the following categories: total overall complications; infection requiring treatment (with antibiotics, drainage, or reoperation), bone resorption (by clinical examination or imaging), and reoperation. Cranioplasties also were stratified by the timing of VPS placement as either simultaneous or staged (before and after).

The Oxford Center for Evidence-Based Medicine guidelines were used to assess the quality of individual articles and studies.[27] The risk of bias was evaluated using the Newcastle—Ottawa Scale, a 3-category, 9-point scale for assessing cohort selection, comparability, and outcome.[28] A higher score indicates higher quality.

Data Analysis

Data were analyzed using RevMan 5.3.5 (The Cochrane Collaboration, London, United Kingdom). If overall complications were not reported in a study, then individual complications were summed. For articles reporting event rates, odds ratios (ORs) with 95% confidence intervals (CIs) of infection, resorption, and reoperation were calculated. Data were pooled via the Mantel—Haenszel method using a fixed- or random-effects model, depending on the heterogeneity of data. For articles only reporting ORs and 95% CIs (and not event counts), these were used to calculate standard error and incorporated manually into the Mantel—Haenszel calculations. The I^2 metric was reported to quantify heterogeneity (0%, no heterogeneity; 100%, maximal heterogeneity).[29] A P value of <0.05 was considered statistically significant.

RESULTS

Our literature review results are depicted in a PRISMA flow diagram in **Figure 1**. Ninety-seven nonduplicate articles were screened, including 94 articles from the database search and 3 articles from bibliographic searches.[30,31] Twenty articles were excluded after a full-text review for reasons including lack of data on the presence and absence of VPS data,[2,16,32-36] insufficient data (i.e., authors unreachable or unable to provide),[37] and nonreporting of cranioplasty complications.

Seven studies, with a total of 1635 patients and 180 shunts, met our inclusion criteria (**Table 1**).[30-32,38-41] All 7 studies had an Oxford Center for Evidence-Based Medicine level 4 as nonmatched cohort studies. Indications for initial craniectomy included traumatic brain injury, subarachnoid hemorrhage, intracerebral hemorrhage, intraventricular hemorrhage, ischemic stroke, ruptured aneurysm, extra-axial hematoma, infection, aseptic bone necrosis, cerebrovascular disease, cerebral infarction, arteriovenous malformation, and tumor. Cranial procedure locations, when specified, included unilateral, bilateral, frontotemporal, temporal, frontal, and occipital. To further investigate staged versus simultaneous VPS and cranioplasty, we included 3 additional studies from the PRISMA search that did not meet our inclusion criteria because they provided only event counts of complications for simultaneous and staged procedures. In addition, 2 studies that met the PRISMA search criteria and provided complication rates for simultaneous versus staged procedures were included in this analysis (**Table 2**).[2,32,34,36,42]

Study quality ranged from 6 to 7 out of a possible 9 on the Newcastle—Ottawa

Table 1. Characteristics of Included Studies Reporting Complications Related to Cranioplasty in the Presence or Absence of VPS

Reference	Indication for Decompressive Craniotomy	Location	Number of Patients		Complications
			VPS	None	
Mracek et al., 2015[38]	Stroke, TBI, SAH, ICH	Unilateral	22	127	Complication, postoperative length of stay, removal
Piedra et al., 2014[30]	TBI		18	157	Complication, hematoma, hydrocephalus, infection, resorption
Schuss et al., 2013[31]	ICH, ischemic stroke, ruptured aneurysm, TBI, other	Bifrontal, unilateral	61	254	Abscess, CSF, fistula, EDH/SDH, hygroma, wound healing disturbance
Schwarz et al., 2016[39]	SAH, ischemic stroke, tumor, ICH, extra-axial hematoma, infection, aseptic bone necrosis, other	Bilateral, unilateral	21	482	Bone flap necrosis
Tsang et al., 2015[40]	Cerebrovascular disease, infection, TBI, tumor		21	141	Flap depression, infection
Yang et al., 2013[32]	ICH, ischemic stroke, SAH, TBI, tumor		21	109	Infection, resorption
Zhang et al., 2017[41]	TBI, SAH, ICH, tumor, arteriovenous malformation	Frontotemporal, temporal, frontal, occipital	16	185	Resorption
Totals			180	1455	
			1635		

VPS, ventriculoperitoneal shunt; TBI, traumatic brain injury; SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; CSF, cerebrospinal fluid; EDH, epidural hemorrhage; SDH, subdural hemorrhage.

Scale. None of the studies included matched cohorts, which significantly increases the risk of selection bias. All studies had adequate follow-up time, with low patient loss.

Overall Complications

All 7 studies reported complications in the presence and absence of a VPS (Table 3).[30-32,38-41] The pooled rate of overall complications in these studies reporting event rates was 7.0% (52 of 746), with rates for individual studies ranging from 3.2% to 11.1%.[30,37] The overall rate of complications was significantly higher in the presence of a VPS compared with the absence of a VPS (18.5% [22 of 119] vs. 5.1% [30 of 589]; OR, 9.75; 95% CI, 4.8–20.1; $P < 0.01$) using a random-effects model ($I^2 = 87\%$; $P < 0.01$).

Infection

Three studies reported infectious complications that necessitated antibiotic treatment with or without reoperation for abscess drainage or implant removal (Table 4).[30,31,38] The studies used a wide range of definitions of infection, including osteomyelitis of the bone flap and surgical site infections, as demonstrated by fever, erythema, drainage, or cellulitis[30,32,40]; elevated white blood cell count or evidence of infection on computed tomography scan[30]; epidural and subdural empyema[32]; and others.[32] Three studies did not report the rate of infection in the presence and absence of a VPS.[31,38,39]

The pooled rate of infection for those reporting event rates was 9.0% (25 of 292), with rates for individual studies ranging from 8.0% to 9.2%.[30,31] The presence of a VPS at cranioplasty was associated with a significantly increased rate of infection compared with the absence of a VPS (26.2% [11 of 42] vs. 5.6% [14 of 250]; OR, 4.9; 95% CI, 2.2–10.7; $P < 0.01$) using a random-effects model ($I^2 = 89\%$; $P < 0.001$).

Bone Resorption

Six studies reported bone graft resorption, as determined by clinical examination or imaging (Table 5).[30,31,38-41] The pooled rate of bone resorption for those reporting events rates was 3.98% (27 of 678), with rates for individual studies ranging from 3.09% to 5.9%.[30,37] The presence of a VPS at the time of cranioplasty was associated with a significantly increased rate of resorption necessitating reoperation compared with the absence of a VPS (11.2% [11 of 98] vs. 2.76% [16 of 580]; OR, 10.6; 95% CI, 4.86–22.97; $P < 0.01$) using a random-effects model ($I^2 = 62\%$; $P < 0.01$).

Simultaneous and Staged VPS

Five studies reported complications that could be stratified into simultaneous or staged VPS (Figure 2). Complications included infections, resorption, reoperation, intracerebral hemorrhage, epidural hemorrhage, subdural hemorrhage, and hydrocephalus. The pooled rate of all complications in simultaneous and staged VPS was 23.0% (65 of 283), with rates in individual studies ranging from 9.2% to 45.8%.[2,38] Simultaneous VPS and cranioplasty was associated with a higher rate of complications compared with staged surgeries (45.7% [43 of 94] vs. 11.6%

Table 2. Characteristics of Included Studies Reporting Complications Related to Cranioplasty with Staged or Simultaneous VPS

Reference	Indication for Decompressive Craniotomy	Location	Number of Patients		Complications
			Simultaneous	Staged	
Heo et al., 2014[34]	Trauma, SAH, ICH, cerebral infarction, brain tumor, IVH		32	19	Subdural fluid collection, SDH, infection, ICH, EDH
Jung et al., 2015[2]	TBI, aneurysm, ICH, infarction	Unilateral, bilateral	14	10	Infection, SDH, resorption, shunt malfunction
Schuss et al., 2015[42]	TBI, SAH, ICH	Unilateral	17	24	Bleeding, infection/wound healing disturbance, hygroma, other
Von der Brelie et al., 2015[36]	TBI, ischemic stroke, hemorrhagic stroke		27	10	Aseptic necrosis, empyema, explantation of bone flap
Yang et al., 2013[32]			21	109	Infection, resorption
Totals			111	172	
			283		

SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; SDH, subdural hemorrhage; EDH, epidural hemorrhage; TBI, traumatic brain injury.

[22 of 189]; OR, 4.31; 95% CI, 2.25–8.23; $P < 0.0001$) using a fixed-effects model ($I^2 = 0\%$; $P = 0.65$).

DISCUSSION

In this systematic review of reports on the complications associated with the presence and absence of a VPS at the time of cranioplasty, we found that VPS placement at the time of cranioplasty is associated with a greater overall risk of complications and an increased risk of infection and bone resorption. In addition, staging of the VPS and cranioplasty procedures was associated with lower complication rates compared with performing these procedures simultaneously. In patients needing cranioplasty and a VPS, it may be prudent to stage these procedures whenever clinically possible. Furthermore, in susceptible patients, surgeons should consider using nonresorptive synthetic implants and an extended course of perioperative antibiotics. The effects of lumbar drains or external ventricular drains for the sole purpose of delaying VPS have not been well reported in the literature.

Given the association between VPS placement at the time of cranioplasty and simultaneous/staged procedures and an increased risk of complications, it may be inferred that VPS placement after cranioplasty may be recommended over VPS placement before cranioplasty. Similarly, Oh et al.[33] showed that in large concave flaccid cranial defects complicated by hydrocephalus, neurologic outcomes (as measured by the Glasgow Outcome Scale), dysphagia, and visual acuity tended toward improvement in patients undergoing VPS placement after cranioplasty compared with those undergoing VPS placement before cranioplasty. In addition, compared with a combined group of patients with VPS placement before and during cranioplasty, patients with staged VPS placement after cranioplasty had a lower rate of complications as measured by subdural hygroma, subdural hematoma, epidural fluid collection, and reoperation.[35] It may be that until the cranioplasty is in place, the cerebrospinal fluid (CSF) dynamics are in flux, possibly resulting in further shunt revisions and other complications.

Table 3. Event Rates and Odds Ratios of Overall Complications for Individual Studies and Pooled Results

Reference	Totals		Complications		OR (95% CI)
	VPS	None	VPS	None	
Piedra et al., 2014[30]	18	139			0.68 (0.15–3.01)
Mracek et al., 2015[38]	22	127			35.6 (9.96–127)
Schwarz et al., 2016[39]	21	482			1.73 (1.02–2.92)
Tsang et al., 2015[40]	21	141	9	9	11.0 (1.81–74.1)
Yang et al., 2013[32]	21	109	5	7	4.55 (3.29–5.81)
Schuss et al., 2013[31]	61	254	4	6	2.90 (1.60–4.20)
Zhang et al., 2017[41]	16	185	4	8	7.38 (0.68–1.94)
Pooled*					9.75 (4.79–20.1)

VPS, ventriculoperitoneal shunt; OR, odds ratio; CI, confidence interval.
*Mantel-Haenszel method using a random-effects model with heterogeneity; $I^2 = 87\%$, $P < 0.01$.

Comparison with Previous Reviews

No previous reports have addressed this question, despite the fact that VPS is often necessary after decompressive craniectomy and before cranioplasty. In a meta-analysis investigating the timing of cranioplasty and subsequent complications, early cranioplasty (within 90 days)

Table 4. Event Rates and Odds Ratios of Infections for Individual Studies and Pooled Results

	Totals		Infections		
Reference	VPS	None	VPS	None	OR (95% CI)
Yang et al., 2013[32]	21	109	5	7	4.55 (1.29–16.10)
Piedra et al., 2014[30]	18	157			1.94 (0.52–7.18)
Tsang et al., 2015[40]	21	141	6	7	7.66 (2.27–25.78)
Pooled*					4.85 (2.21–10.65)

VPS, ventriculoperitoneal shunt; OR, odds ratio; CI, confidence interval.
*Mantel–Haenszel method using a random-effects model and heterogeneity; $I^2 = 89\%$, $P < 0.001$.

was associated with an increased risk of developing hydrocephalus.[12] With this in mind, it is important to investigate the optimal timing for shunt placement and associated complications.

The present review includes studies spanning the last decade, highlighting the continued interest in minimizing complications associated with routine cranioplasty. Despite this interest, however, no prospective studies have yet addressed the topic of complications associated with cranioplasties in relation to VPS placement.

Overall Complications

The overall rate of complications rate in the included studies varied widely, from 3.17% to 11.1%.[31,37] A recent large systematic review reported a 6.4% rate of cranioplasty complications.[43] The difference in overall complication rates may be the result of widely varying definitions of complications and might be resolved with more clearly defined complications or a narrower list. The relatively high rate of complications related to cranioplasty demonstrates the need to further investigate outcomes and find improved interventions for these patients. We believe that reporting specific complication rates instead of overall complication rates will be more informative in future studies.

Infection

The pooled infection rate of infection of 9.0% identified in our analysis is comparable to previously reported combined infections rates of 4.5%–18.4.[18,19] The infection rates in patients undergoing cranioplasty are reportedly affected by length of hospital stay, interval between craniectomy and cranioplasty, presence of systemic infection, low hemoglobin, poor neurologic status, additional operations, and stroke.[12,15,42]

Table 5. Event Rates and Odds Ratios of Resorption for Individual Studies and Pooled Results

	Totals		Resorption		
Reference	VPS	None	VPS	None	OR (95% CI)
Schuss et al., 2013[31]	61	254	4	6	2.90 (0.79–10.6)
Piedra et al., 2014[30]	18	157			0.68 (0.15–3.01)
Mracek et al., 2015[38]	22	127			35.6 (9.96–127)
Schwarz et al., 2016[39]	21	482			1.73 (1.02–2.92)
Tsang et al., 2015[40]	21	141	3	2	11.6 (1.81–74.1)
Zhang et al., 2017[41]	16	185	4	8	7.38 (0.68–1.94)
Pooled*					10.57 (4.86–22.97)

VPS, ventriculoperitoneal shunt; OR, odds ratio; CI, confidence interval.
*Mantel–Haenszel method using a random-effects model with heterogeneity; $I^2 = 62\%$, $P < 0.01$.

Resorption

The pooled rate of bone resorption of 3.98% is comparable to rates of 3.09% and 4.18% reported previously.[30,31] Bone resorption rates as high as 16% have been reported in adult patients, and rates of 14%–42% have been reported in pediatric populations.[43] It may be prudent to further investigate bone resorption in the presence of a VPS in this population. Zhang et al.[41] postulated that the changes in fluid mechanics and intracranial pressure associated with a VPS lead to fine motion causing increased bone resorption at the edges of a bone flap. The increased rate of resorption may make the use of artificial bone flaps more favorable in patients needing cranioplasty and VPS placement.

Simultaneous and Staged VPS

The pooled rate of all complications was 23.3% (66 of 283), with individual rates ranging from 9.2% to 45.8%. This pooled rate was driven primarily by Heo et al.,[34] who reported a complication rate of 43.2% (22 of 51). Of the 22 complications reported by Heo et al., 17 consisted of infections and subdural fluid collection, 2 of the most common complications associated with cranioplasty. The high rate of subdural fluid collection may be explained by the difficulty in adjusting the VPS for changing intracranial pressure. Heo et al. postulated that increased or decreased pressure in the subdural space after cranioplasty alters intracranial pressure, and that this change, combined with altered cerebral vasculature and cerebral perfusion pressure, causes fluctuations in intracranial pressure. Furthermore, the weight of this study in the meta-analysis (27.4%, calculated directly from its standard error) is comparable to that of Jung et al.[2] (27.2%) and Yang et al.[32] (20.1%) and, therefore, does not appear to significantly skew the results.

In light of these studies, we believe that when a patient requires both operations simultaneously, especially with a bulging brain preoperatively, CSF drainage via lumbar or ventricular puncture should be considered to control the intracranial pressure and avoid complications. VPS

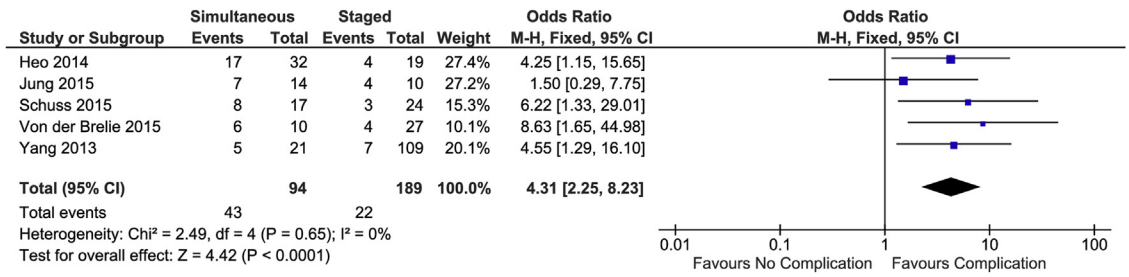

Figure 2. Forest plot of studies reporting complications of cranioplasty with staged or simultaneous VPS. The *blue square data markers* indicate odds ratio (ORs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The *horizontal lines* indicate 95% confidence interval (CI). The *diamond data markers* represent the subtotal and overall OR and 95% CI. The *vertical solid line* indicates the line of no effect (OR 1). Results indicate decreased overall complications with staged cranioplasty and VPS procedures.

placement could be done at a later date to decrease the risk of complications. In addition, when planning very early cranioplasty, patients with a high external ventricular drain output (>150 mL/day) may require simultaneous shunt placement.[44] The therapeutic benefits of these procedures must be weighed against the increased risks, including infection, neurologic sequelae, and bone resorption. The rate of postdural puncture meningitis has been reported as 1.3/10,000, whereas the rate of neurologic deterioration after lumbar puncture in patients with elevated intracranial pressures has been reported to be between 12% and 13%.[45-47] The risks of these procedures in the setting of cranioplasty has not yet been examined, and further investigation is needed to better clarify the role of these procedures in helping stage cranioplasty and VPS placement.

The mean interval between initial craniectomy and cranioplasty in the 7 studies varied from 46 days to 370 days.[38,39] The time between VPS and cranioplasty was not specified in the 7 studies that we evaluated, and this information may help elucidate an optimal window between the 2 procedures to minimize complications. Cranioplasty performed within 90 days of VPS placement is associated with an increased risk of developing hydrocephalus, suggesting that an interval of >90 days may be preferred for patients susceptible to hydrocephalus.[12]

Study Strengths and Limitations

This report is the sole systematic review and meta-analysis published to date exploring the effect of VPS placement at the time of cranioplasty on complication rates. It builds on previous studies that have addressed the question of complications associated with the presence of a VPS during cranioplasty and the timing of the 2 procedures in relation to one another. Through communication with the authors of those studies, we have added new data to more completely address this question.

Limitations of this study include the heterogeneity of the study populations, which included multiple indications for decompressive craniectomy and varying anatomic locations. Five of the 7 studies included in this analysis incorporated a mix of indications.[30,37,40,41,48] Although the majority of craniectomies were performed for decompressive indications, we were unable to quantify their proportion in our meta-analysis. Complication type and frequency have been shown to differ by indication for craniectomy; thus, it may be prudent to further stratify craniectomies in terms of their indication to better understand the possible influence of VPS.[43]

The presence of a VPS and its association with increased complications may be confounded by patients with a more severe presentation manifesting in increased complications. The patient populations in the evaluated studies varied in terms of demographics, size of craniectomy defect, indications for craniectomy, type of craniectomy, and severity of hydrocephalus; however, the total population size and strength of associations still suggest that the presence of the shunt itself may be an issue. We recommend that any randomized trial control for these variables as markers of severity or include these variables as covariates in a propensity score analysis.

Three of the 7 studies specified the location of decompressive craniectomy, either unilateral or bifrontal, whereas the remaining 4 did not.[37,40,41] Complication rates have been shown to differ between these 2 surgical approaches, owing to inherent differences in underlying anatomy cerebral blood flow, CSF flow dynamics, and bone flap and surface area size.[45,49] The presence of a VPS shunt may help reduce complications especially in cases of CSF flow disruption, and thus subgroup analysis may help further clarify the effect of VPS placement depending on the type of cranioplasty.

Definitions of complications varied widely among the evaluated studies, relying on imaging, laboratory test, and clinical examination findings. Owing to the heterogenous definitions of complications, the severity of complications, clinical implications, and outcomes are difficult to assess and cannot be readily stratified based on severity.

CONCLUSION

In this systematic literature review and meta-analysis, we investigated the complication rates associated with cranioplasty in the presence and absence of a VPS. Our findings suggest that VPS placement at the time of cranioplasty is associated with an increased overall rate of complications, particularly infection and resorption, compared with staged cranioplasty and VPS placement. Future studies should address these findings in specific patient populations and focus on the

prevention of resorption and infection in the setting of simultaneous cranioplasty and VPS placement.

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