Effects of Cranioplasty on Cerebral Blood Flow Following Decompressive Craniectomy: A Systematic Review of the Literature

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BACKGROUND: Cranioplasty after decompressive craniectomy (DC) is routinely performed for reconstructive purposes and has been recently linked to improved cerebral blood flow (CBF) and neurological function.

OBJECTIVE: To systematically review all available literature to evaluate the effect of cranioplasty on CBF and neurocognitive recovery.

METHODS: A PubMed, Google Scholar, and MEDLINE search adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines included studies reporting patients who underwent DC and subsequent cranioplasty in whom cerebral hemodynamics were measured before and after cranioplasty.

RESULTS: The search yielded 21 articles with a total of 205 patients (range 3–76 years) who underwent DC and subsequent cranioplasty. Two studies enrolled 29 control subjects for a total of 234 subjects. Studies used different imaging modalities, including CT perfusion (n = 10), Xenon-CT (n = 3), single-photon emission CT (n = 2), transcranial Doppler (n = 6), MR perfusion (n = 1), and positron emission tomography (n = 2). Precranioplasty CBF evaluation ranged from 2 days to 6 months; postcranioplasty CBF evaluation ranged from 7 days to 6 months. All studies demonstrated an increase in CBF ipsilateral to the side of the cranioplasty. Nine of 21 studies also reported an increase in CBF on the contralateral side. Neurological function improved in an overwhelming majority of patients after cranioplasty.

CONCLUSION: This systematic review suggests that cranioplasty improves CBF following DC with a concurrent improvement in neurological function. The causative impact of CBF on neurological function, however, requires further study.

KEY WORDS: CBF, Cerebral blood flow, Cranioplasty, Sinking skin flap syndrome, Syndrome of the trephined, Systematic review

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Decompressive craniectomy (DC) is often used as a surgical treatment option for medically intractable intracranial hypertension. This procedure involves maximal bony decompression and an expansile duraplasty to accommodate edematous brain tissue and prevent compressive hypoperfusion, venous hypertension, and irreparable neurological injury.[1,2] After craniectomy, patients are potentially at risk for further neurotrauma due to the absence of a protective skull flap. Patients may develop additional complications including ex vacuo hydrocephalus, subdural hygroma, hemorrhage, infection, CSF leakage, and seizures.[3-5] Cranioplasty is performed to reconstruct the skull and potentially correct and prevent some of these complications. It has been long observed that cranioplasty often facilitates neurological recovery after trauma by restoring intracranial pressure dynamics and allowing for increased rehabilitation activities.

ABBREVIATIONS: CBF, cerebral blood flow; **CTP,** CT perfusion; **DC,** decompressive craniectomy; **MCA,** middle cerebral artery; **PET,** positron emission tomography; **PRISMA,** Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **SSFS,** sinking skin flap syndrome; **SPECT,** single-photon emission computed tomography; **ST,** syndrome of the trephined; **TCD,** transcranial Doppler; **Xe-CT,** Xenon-CT

The syndrome of the trephined (ST) is a unique phenomenon observed after DC. Originally described by Grant and Norcross[6] in 1939, patients developed headache, vertigo, memory disturbances, mood changes, and contralateral motor paresis weeks to months after DC. Approximately 50% of patients in this series developed symptoms of ST after DC. Importantly, these symptoms appeared to be reversible after cranioplasty in 25% of cases. More recently, Yamaura and Makino[7] coined the term sinking skin flap syndrome (SSFS), in which they observed similar symptoms and associated them with the concavity of the skin flap. Similarly, symptoms developed in a delayed fashion after DC, and these symptoms resolved after replacement of the patient's bone flap in 30% of patients. From a clinical perspective, many practitioners consider ST and SSFS the same clinical syndrome.[8,9] Although the exact pathophysiology remains to be elucidated, impairments of cerebral blood flow (CBF), CSF hydrodynamics, and cerebral metabolism after craniectomy have been suggested as possible mechanisms.[10,11] Recent studies have shown that cranioplasty may reverse these derangements, which correlates with neurological and functional recovery.[3,12-15]

Published reports describing the effects of cranioplasty on CBF are mostly in the form of case reports and small series. The goal of this systematic review is to evaluate the reported effects of cranioplasty on CBF dynamics and associated changes in neurological function.

METHODS

Study Selection

A PubMed search adherent to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was performed for all articles containing the terms "cranioplasty" and "cerebral blood flow," "cerebral perfusion," "hemodynamics," "hemodynamic," or "haemodynamic." A search was also conducted on Google Scholar and MEDLINE using the same criteria. Articles were limited to English and studies with human subjects. Qualifying articles were limited to clinical articles (case reports, case series, cohort studies, randomized control trials, systematic reviews, and meta-analyses) that were available in the full text. Duplicate articles, editorials, commentaries, and general reviews were excluded. Two authors (JC and SH) reviewed the articles with differences resolved by discussion with co-authors. Individual study bias was mitigated by reviewing and confirming the appropriate sources indicated. The bibliographies of relevant studies were searched to identify any additional studies.

Title and abstract review was performed once the initial list of studies was generated (Figure). The reviewers met prior to commencing study selection to ensure consistency in the application of the inclusion criteria. Studies were selected if they met the following 3 inclusion criteria: (1) reports that contained 1 or more patients who underwent DC and cranioplasty; (2) reports that contained documented neurological examination for patient(s) before and after cranioplasty; and (3) measurement of CBF before and after cranioplasty utilizing transcranial Doppler (TCD), CT, positron emission tomography (PET), or MRI techniques. A full-text review was performed on all remaining studies following the title and abstract review. Additional studies that did not meet inclusion criteria were excluded.

For non-randomized cohort and case–control studies, the Newcastle-Ottawa Scale was used to assess quality and risk of bias.[16] This is a 9-point scale assessing cohort selection, comparability, and outcome, with a higher score indicating higher quality. Case reports and case series could not be assessed for bias and are included only for descriptive purposes. Standard levels of evidence was applied for each study. The last search was performed on April 23, 2016.

Data Abstraction

The following data, if reported, were abstracted for qualifying articles: age, reason for DC, neurological examination before and after cranioplasty and at last follow-up visit, time from DC to cranioplasty, technique for CBF estimation, CBF measurements before and after cranioplasty, location of CBF measurements, and timing of CBF measurements before and after cranioplasty.

Not all studies provided data or information on each subset of patients; therefore, comparative analysis is limited by the nature of the source data. Data for all patients was included when reported in the literature. Statistical analysis was not conducted for this review because comparative analyses could not be performed.

RESULTS

Study Selection

The initial PubMed, Google Scholar, and MEDLINE search returned a total of 49 articles. There was 1 duplicate article removed, leaving 48 articles available for screening. Abstracts for the remaining 48 articles were reviewed and a total of 21 studies met inclusion criteria. Among these, 13 were retrospective studies[1,5,10,15,17-25] and 8 were prospective studies.[26-33] The PRISMA flow chart of the screening process is illustrated in Figure. The studies are summarized in Table.

Two-hundred and five patients underwent DC and subsequent cranioplasty. Of these patients, 2 did not undergo CBF evaluation; therefore, data from a total of 203 patients were available for review. Two studies also enrolled 29 control subjects for CBF measurements (n = 5, n = 24).[18,33]

Patient Demographics

Of the total of 203 patients who underwent both DC and cranioplasty with subsequent CBF measurements, age ranged from 3 to 76 years. When reported, there were 95 males and 41 females. When reported, the reason for DC was trauma (n = 155), ischemic stroke (n = 11), hemorrhagic stroke (n = 20), infection (n = 3), and other (n = 1, hemorrhage from preoperative embolization for a meningioma[30]). Neurological examinations pre- and postcranioplasty were reported in all studies. Time to cranioplasty was reported in 16 studies and ranged from 4 weeks to 18 years. All studies reported improvement in postcranioplasty neurological examination compared to precranioplasty. Time to follow-up was reported in all studies and ranged from 1 week to 6 months postcranioplasty.

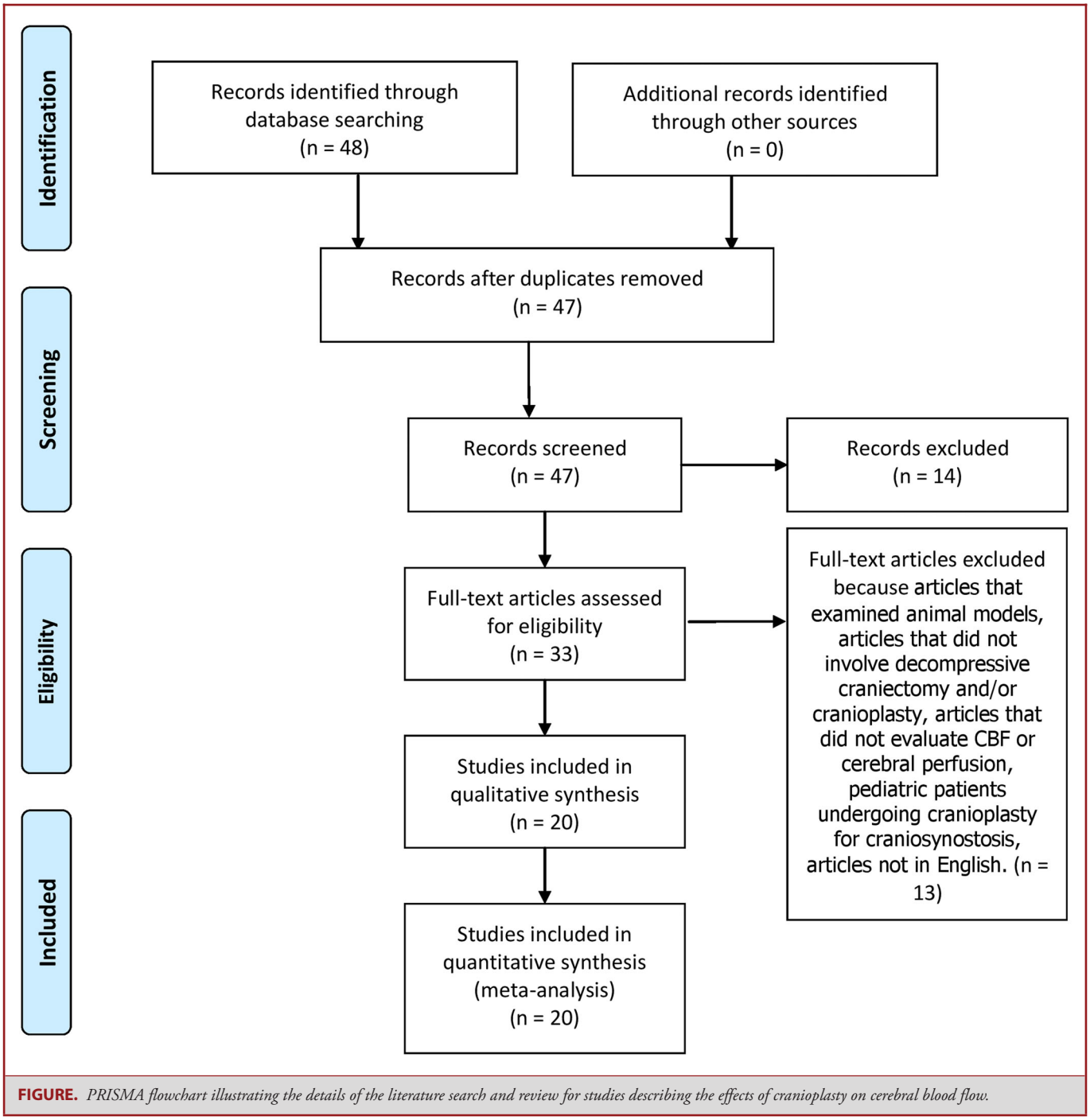

FIGURE. *PRISMA flowchart illustrating the details of the literature search and review for studies describing the effects of cranioplasty on cerebral blood flow.*

Study Quality and Risk of Bias

All case reports and case series were designated level of evidence 4, whereas the 2 matched cohort studies were level of evidence 3. Erdogan et al[18] used an age- and sex-matched cohort that did not undergo cranioplasty to estimate the distribution of normal perfusion against which to compare pre- and postcranioplasty patients (Newcastle-Ottawa Scale 8). Song et al[33] analyzed the timing of delayed cranioplasty on the change in CBF using 2 age-sex-matched cohorts: cranioplasty within 12 weeks and beyond 12 weeks (Newcastle-Ottawa Scale 9). A third study, Yoshida et al,[10] was primarily a case series but mentioned a control group without characterizing its patients; this was not

TABLE. Summary of All Included Studies of Patients Who Underwent Cranioplasty After Decompressive Craniectomy, Listed Chronologically and Grouped by Imaging Modality Used to Measure Cerebral Hemodynamics

Author, year	Study design	Level of evidence	NOS	CBF modality	Patients	Mean age (yr)	Time to CP	Results	Conclusions
Tabaddor and LaMorgese, 1976[24]	Case report	4	NA	CTP	1	41	NR	Hemiparesis and impaired proprioception associated with a sunken flap improved after CP. There was a unilateral increase in CBF pre-CP, but became equal in both hemispheres 1 mo post-CP.	The gradient between the atmospheric pressure and intracranial pressure causes inward displacement over cranial defect and may contribute to neurological deficits. This may be improved by CP.
Suzuki et al, 1993[25]	Case series	4	NA	CTP	6	42.5 ± 10.7	3.6 ± 2.4 mo	Most patients (5/6) had improved consciousness, motor weakness, and aphasia after CP. There was an average increase of 2% and 20% in blood flow volume on the ipsilateral and contralateral side, respectively, post-CP; statistically significant 15% increase in peak blood flow volume compared to pre-CP.	CP may normalize CSF compliance and may influence the cerebrovascular resistance and the autoregulatory function of CBF in both hemispheres.
Sakamoto et al, 2006[17]	Case report	4	NA	CTP	1	57	4 yr	SSFS improved after CP; there were "no neurological deficits" at 2-wk follow-up. CBF increased bilaterally after CP.	CTP may be useful for determining the prognosis of SSFS.
Decaminada et al, 2008[27]	Case series	4	NA	CTP	8	40 (range 20-58)	4-5 mo (range 1-13)	There were improvements in hemiparesis and urinary incontinence 1 mo post-CP. Incidence of comatose or bedrest patients decreased from 40% to 20% and 20% to 10%, respectively. Significant increase in CBF seen 15 d after CP was preserved at 3 and 6 mo. Patients undergoing unilateral CP (n = 4) had significant increase in contralateral CBF.	CBF after unilateral DC showed statistically significant improvement bilaterally after CP, which was associated with clinical and functional improvements.

TABLE ***Continued.***

Author, year	Study design	Level of evidence	NOS	CBF modality	Patients	Mean age (yr)	Time to CP	Results	Conclusions
Stiver, 2009[5]	Case series	4	NA	CTP	2	NR	NR	There was focal decrease in CBF in areas of injury after TBI; following CP, CTP at 48 h and 5 d demonstrated improvements in ipsilateral CBF, CBV, and MTT. Improvements were coincident with rapid improvement in contralateral motor deficits.	Improvements in CBF may predict improvements in contralateral motor strength following CP.
Sarubbo et al, 2014[31]	Case series	4	NA	CTP	6	45.7 ± 18.9	158.0 ± 30.6 d (range 97-177)	MRS remained unchanged prior to 7 d, and 3 mo after CP. Ipsilateral CBF and CBV increased from pre-CP to 7 d post-CP; 3 mo post-CP decreased to below pre-CP levels. Ipsilateral MTT increased between 7 d and 3 mo post-CP.	Decline in CBF at 3 mo is likely due to restoration of flow to meet decreased metabolic demand rather than impaired perfusion.
Wen et al, 2015[32]	Case series	4	NA	CTP	9	41.6 (range 19-62)	2-8 mo	Over half (5/9) of patients had improved mRS scores following CP. CBF increased significantly in bilateral parietal lobes, ipsilateral occipital lobe, and basal ganglia.	CP may increase CBF and benefit recovery in patients with DC for TBI.
Mah and Kass, 2016[28]	Case series	4	NA	CTP	22	32.7 (range 19-55)	67.3 ± 66.3 d	MMSE and FAB clinical measures significantly improved after CP, whereas GOS remained unchanged. CBF increased at both ipsilateral and contralateral sites 6 wk post-CP.	CBF increases in bilateral hemispheres, after CP, but does not correlate with overall outcome.
Kemmling et al, 2010[19]	Case report	4	NA	MRP	1	42	4 mo	The patient's left upper extremity weakness and dysesthesia resolved within 4 wk of CP. There was a focal perfusion deficit under skin flap on MRP. CBF increased post-CP.	Impaired brain perfusion may play a role in SSFS. CP improves CBF and neurological deficits.

TABLE ***Continued.***

Author, year	Study design	Level of evidence	NOS	CBF modality	Patients	Mean age (yr)	Time to CP	Results	Conclusions
Voss et al, 2011[22]	Case report	4	NA	PET, fMRI	1	19	NR	A patient emerged from minimally conscious state after bilateral CP (CRS-R = 20). After second right CP, PET showed increased metabolism in left mesial frontal regions, upper brainstem, and thalamus.	CP significantly increases global and regional cerebral metabolism concurrent with neurological recovery.
Matsumura al, 1996[20]	Case report	4	NA	SPECT	1	3	3 and 5 yr	A child underwent CP at age 3 yr and a second CP at 5 yr. There was decreased CBF on SPECT at site of the bone defect before the first CP, which improved after each CP.	Localized CBF improved after CP.
Maeshima et al, 2005[21]	Case report	4	NA	SPECT	1	76	1 mo	Cognitive function in a patient with SSFS improved within 10 d of CP. There was bilateral increase in CBF on SPECT after CP.	CP improves symptoms in this patient with SSFS. CBF increased bilaterally after CP.
Winkler, 2000[30]	Case series	4	NA	TCD, PET	13	50.8 ± 14.7 (range 25-69)	25 ± 66.6 mo(range 1.5-234 mo)	There was overall improvement in functional and cognitive status after CP. Resting MCA velocity significantly improved post-CP. Cerebrovascular reserve capacity and 18-FDP uptake significantly improved in both hemispheres after CP.	DC impairs blood flow and cerebrovascular reserve capacity in the ipsilateral hemisphere; CP reverses these abnormalities.
Erdogan et al, 2003[18]	Prospe-ctive cohort	3	8	TCD	18; 24 controls	NR	12 mo (range 9-22)	Patients experienced neurological (14/18) and motor (5/18) improvement after CP. TCD values were restored to normal values in both hemispheres after CP.	CP restores TCD values to near normal and correlates with neurological improvement.
Kuo et al, 2004[26]	Case series	4	NA	TCD	13	48.3 ± 13.6 (range 21-72)	119.4 ± 104.4 d (range 32-367)	CP significantly improved GCS, arm muscle power, and Barthel index in all patients. TCD velocity increased after CP, which was significant in the contralateral MCA only.	CP improved both neurological status and global TCD velocities. Longer intervals between DC and CP may negatively affect neurological improvement.

TABLE ***Continued.***

Author, year	Study design	Level of evidence	NOS	CBF modality	Patients	Mean age (yr)	Time to CP	Results	Conclusions
Coelho et al, 2014[1]	Case report	4	NA	TCD, CTP	1	44	8 mo	The patient's symptoms resolved within 6 mo of CP, with improvement in memory, language, executive function, and ADLs. TCD values increased in ipsilateral MCA. There was increased CBF bilaterally.	CP may improve neurophysiological impairments as well as cranial CBF.
Song et al, 2014[33]	Prospe-ctive cohort	3	9	TCD	43 Early:25 Late: 18	41.8 ± 16	Early: 52.8 ± 13.58 d Late: 176.9 ± 43.91 d	There were significant increases in ipsilateral MCA, ICA, and contralateral MCA velocities after early CP (<12 wk). There was significant increase in the ipsilateral MCA after late cranioplasty (>12 wk). There was a higher change in ipsilateral MCA velocity after CP in the early group.	CP performed within 12 wk had greater CBF improvements than if performed after 12 wk.
Paredes, 2016[29]	Case series	4	NA	TCD, CTP	49	41.7 ± 15.5	309 ± 237 d	CP resulted in clinical improvement in 40% of the patients and increased post-CP CBF.	Positional changes in Lindegaard index may predict clinical improvement.
Yoshida et al, 1996[10]	Case series	4	NA	Xe-CT	7	Range 45-65	NR	All patients were neurologically intact before and after CP. There were global increases in CBF after CP, most significantly in bilateral thalami. Cerebral metabolism according to MRS significantly increased in bilateral hemispheres post-CP.	DC may result in decreased cerebral blood flow and cerebral metabolism. Perform CP when intracranial hypertension resolves.
Agner et al, 2002[15]	Case report	4	NA	Xe-CT	1	34	NR	There was a 126% increase in CBF in a left frontal cranial defect 3 wk post-CP. There was an associated 48% and 33% improvement in Cognistat and EXIT interview scores, respectively, after CP.	Changes in CBF may be associated with neurocognitive changes after CP.

TABLE ***Continued.***

Author, year	Study design	Level of evidence	NOS	CBF modality	Patients	Mean age (yr)	Time to CP	Results	Conclusions
Isago et al, 2004[23]	Case report	4	NA	Xe-CT	1	28	Left side: 8 mo Right side: 12 mo	Pre-CP, the patient was bedridden, aphasic, paretic, and fed parenterally. Postbilateral CP, the patient was ambulatory with wheel chair, experienced improved aphasia, concentration, and memory. One week post-left CP, CBF increased in right hemisphere compared to pre-CP; 3 mo post-CP, CBF in the left hemisphere increased 2-fold and 1.5-fold in the right compared to pre-CP.	Bilateral CP improves symptoms of SSFS and CBF after bilateral DC.

ACA, anterior cerebral artery; CBF, cerebral blood flow; CBV, cerebral blood volume; CP, cranioplasty; CRS-R, Coma Recovery Scale Revised; CTP, CT perfusion; DC, decompressive craniectomy; FAB, frontal battery assessment; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; ICA, internal carotid artery; MCA, middle cerebral artery; MMSE, mini-mental state examination; MRP, magnetic resonance perfusion; mRS, modified Rankin scale; MTT, mean transit time; NA, not applicable; NOS, Newcastle-Ottawa Scale; NR, not reported; PCA, posterior cerebral artery; PET, positron emission tomography; SSFS, sinking skin flap syndrome; TBI, traumatic brain injury; TCD, transcranial Doppler; TTP, time to peak (time between arterial inflow and venous outflow); Xe-CT, Xenon-CT.

counted as a cohort study. These studies, although prospective, are level 3 evidence and therefore have accompanying risk of biases, including observer bias (these were not blinded studies) and selection bias (both groups matched patients by age and sex; however, severity of injury, size of cranioplasty, and other variables were not considered). Apart from these cohort studies, the case reports and series were unable to be objectively assessed for bias and are included for descriptive purposes. In case reports and series, the results are biased on the authors' experience or opinions, with no control for confounding factors, and must therefore be considered in our review.[34]

CBF Studies

All studies reported CBF measurements. CT-based evaluation of CBF (CT perfusion [CTP, including dynamic CT], n = 10; Xenon-CT [Xe-CT], n = 3) was used in 13 studies, TCD in 6 studies, and nuclear isotope-based evaluation in 4 studies (single-photon emission computed tomography [SPECT], n = 2; PET scanning, n = 2). MR perfusion was used in 1 study. There were 3 studies that used multiple modalities for evaluating CBF (CTP and TCD,[1,29] TCD and PET[30]). Exact timing of CBF evaluation precranioplasty was reported in 7 studies and ranged from 2 days to 6 months. All other studies stated CBF evaluation was done "prior to cranioplasty" without mention of a specific time frame. Timing of postcranioplasty CBF evaluation was reported in all studies and ranged from 3 days to 6 weeks. Two studies reported multiple postcranioplasty CBF evaluations: one at 7 days and 3 months[31], and a second at 15 days, 3 months, and 6 months.[27]

Where reported, CBF values pre- and postcranioplasty are shown in Table. All studies utilizing Xe-CT (n = 3) demonstrated decreased CBF ipsilateral or bilateral to the craniectomy site, which increased after cranioplasty. Similar trends were found in studies utilizing CTP (n = 10). Nine studies also reported increased CBF contralateral to the site of cranioplasty.

Similar results were seen in the TCD (n = 6) studies. Four studies reported increased CBF, with 3 of these reporting increases in the ipsilateral MCA.[1,30,33] Another study utilizing TCD compared TCD values in cranioplasty patients vs control subjects, and noted a decrease in TCD velocities (anterior cerebral artery, middle cerebral artery [MCA], and posterior cerebral artery) both ipsilateral and contralateral to the DC site.[18] TCD velocities increased bilaterally postcranioplasty and were comparable to those seen in control subjects.

The study using MR perfusion found increased ipsilateral CBF postcranioplasty.[19]

Both studies that utilized PET scans showed global increases in metabolism postcranioplasty, with greater increases noted on the ipsilateral side.[22,30]

DISCUSSION

DC has been widely used to treat malignant intracranial hypertension. Originally believed to be solely a cosmetic procedure, recent evidence suggests that cranioplasty may also serve an important functional role. In fact, it has been well documented that cranioplasty resolves symptoms of SSFS[19,21,33] Several studies have reported significant improvement in CBF and glucose metabolism among other proxy measures for cerebral perfusion.[5,26,30,35] This systematic review of the literature confirms that CBF is abnormally low in patients after decompressive hemicraniectomy and is restored after cranioplasty.

Effect of DC and Cranioplasty on CBF

The results from this review confirm 2 findings: first, there is a reduction in CBF ipsilateral to the cranial defect that occurs after DC, and second, there is restoration of CBF ipsilateral to the side of cranioplasty irrespective of the modality used to measure CBF. The exact physiology underlying this change remains unknown; however, it is thought that the brain becomes vulnerable to the effects of atmospheric pressure after bone flap removal. Once the effects of intracranial hypertension resolve, this pressure gradient causes compressive effects on the brain parenchyma, resulting in a concave or "sunken" skin flap, which may lead to impairments of CBF and tissue hypoperfusion as well as the development of the delayed neurological symptoms seen in SSFS.[7,36] Replacement of the bone flap shields the brain from this atmospheric gradient, enabling restoration of normal CBF and resolution of neurological symptoms. This is supported by Richaud et al,[37] who suggested a 15% to 30% increase in CBF in the cortex ipsilateral to the cranioplasty.

Whereas all of the studies in this review consistently demonstrated that impaired CBF is restored ipsilaterally after cranioplasty, several authors also observed CBF increases in the contralateral hemisphere.[1,10,17,18,21,25,27,30,32,33] Interestingly, there is discrepancy about the presence of decreased contralateral CBF prior to cranioplasty. This heterogeneity may be partially due to author variability in selecting ROIs and to the differences in techniques used to study CBF. For example, not all studies measured contralateral CBF and used the same method of CBF estimation. Nevertheless, these data suggest that the effect of atmospheric pressure on the cranial defect may impair global CBF in addition to local effects underneath the skull defect. The normal atmospheric pressure is 760 mm Hg at sea level, and it therefore seems probable that such a large pressure gradient across a cranial defect could be transmitted through the entire cerebrum, especially given that this is an order of magnitude greater than normal intracranial pressure. While the biomechanics of atmospheric pressure on the brain are beyond the scope of this review, we speculate that external compression is resisted by the combined tissue compliance properties of the scalp, brain parenchyma, CSF, and vasculature. For example, Carmelo et al[38] suggested that the venous system typically acts as a compensatory "buffer" mechanism, as loss of superior sagittal sinus pulsations after DC were restored after cranioplasty. It is interesting to consider that the amount of external force transmitted to the cerebral vasculature may be great enough to cause reduced CBF

but not cause complete arterial or capillary collapse, as delayed cerebral infarction is typically not observed after DC or in SSFS.

In our review, there were only a few studies that examined the temporal evolution of CBF after cranioplasty and included multiple estimates of CBF over time. Decaminada et al[27] reported an increase in ipsilateral CBF after cranioplasty that was preserved at 2 weeks, 3 months, and 6 months after cranioplasty. Conversely, Sarubbo et al[31] noted an increase in ipsilateral CBF 1 week after cranioplasty but observed a progressive decline in CBF in the ipsilateral hemisphere at 3 months postcranioplasty. The latter authors suggest that the reduction in CBF over time was due to homeostatic mechanisms that tailored CBF to meet the metabolic demands of the tissue. Similarly, Wen et al[32] found a similar decrease in CBF in 4 of their 9 patients at 3 months after cranioplasty. Interestingly, all of these studies utilized CTP as the modality to study CBF, and the discrepancy between these two results may be partially due to differences in the CTP protocols and ROI studied. Regardless, there remains a consensus that there is at least a short-term increase in CBF after cranioplasty, and future investigations need to address the temporal course of CBF changes after cranioplasty.

One question we had difficulty addressing was how the size of DC would affect decreases in CBF. Difficulty arose mainly due to lack of reported craniectomy size in the reports used in our review. One would assume that a larger size would expose more of the cerebrum to atmospheric pressure and a greater reduction in CBF. However, Matsumura et al[20] reported a significant decrease in CBF in a 3-year-old with only a 30 × 20 mm skull defect. It is clear that more information is required to determine if there is a correlation between the 2.

Imaging of CBF

Each method of CBF estimation has their respective strengths and weaknesses, with PET considered the gold standard for quantitative assessment of cerebral hemodynamics.[39] For example, CTP requires contrast administration and high radiation dose, and there is no ability to evaluate cell viability or functionality, as is possible with diffusion-weighted MR.[40] Additionally, the relative cost of MR perfusion and PET imaging is high in comparison to CTP and TCD, and the cost–benefit ratio is unlikely to be favorable for clinically tracking patient progress. TCD is user dependent, and interuser reproducibility is a common problem, limiting its widespread use for accurate CBF estimations.

In clinical studies, Xe-CT and SPECT have fallen out of favor and are most commonly replaced with TCD and CTP, as these are more likely to be readily available at most institutions. Although TCD is used to measure cerebral blood velocity and identify vasospasm, one cannot safely assume that it is an accurate representation of CBF. Brauer et al[41] demonstrated that intracranial pathology creates variability in correlation of mean velocity and CBF, and therefore TCD may not be an accurate measure of CBF. PET has recently evolved to be considered the gold standard for measurement for studying cerebral hemodynamics. However, PET imaging involves the injection of radioactive tracers, which limits its repeatability, and is not cost effective when alternative, potentially equally accurate, imaging modalities are available.[42] Our review found PET to be used in only 2 studies, and in both instances it was used in conjunction with other modalities.

Neurological Recovery After Cranioplasty

It was not surprising that the majority of the included studies in this review reported an improvement in neurological status after cranioplasty. Moreover, these studies were able to correlate this improvement with objective improvements in CBF regardless of the modality utilized. Reported neurological recovery occurred in the realm of headaches, motor strength (improvements in paresis, dysphagia, gait disturbances, etc), sensory changes (resolution of paresthesias, spatial neglect, auditory, etc), and cognition (improvements of level of consciousness, aphasia, memory and concentration, confusion, anxiety, etc). Improvements in motor function and cognitive areas were the most common forms of neurological recovery encountered.

Interestingly, Voss et al[22] explored changes in resting-state cortical networks and cerebral metabolism in a patient prior to and after cranioplasty. Utilizing fMRI, these authors noted improved connectivity in the default mode, dorsal attention, sensory-motor and auditory-phonological neuronal networks after cranioplasty. The largest improvements after cranioplasty were seen in the sensory-motor, default mode, and auditory-phonological networks. More importantly, this increase in neuronal network activity not only correlated with improvements of CBF by PET scanning, but also with the patient's clinical emergence from a minimally conscious state after cranioplasty. Although this is a case study of a single patient, this study is highlighted because it provides objective evidence linking improved cerebral metabolism, increased activity in resting-state neuronal networks, and neurological recovery after cranioplasty.

The level of reported recovery varied amongst studies and ranged from minor improvements to complete neurological recovery. One important consideration when tracking neurological recovery after cranioplasty is the initial reason for DC. Our review identified trauma as the most frequent clinical indication (n = 155), followed by stroke (total, n = 33; hemorrhagic, n = 20; and ischemic, n = 11) and infection (n = 3). The severity of the initial insult as well as the presence of permanent precranioplasty deficits may influence the degree of CBF improvement after cranioplasty and the patient's subsequent neurological recovery. For example, patients who underwent DC for stroke may not have the same potential for recovery as trauma or infection patients. Unfortunately, the heterogeneity of the reported data in our review did not allow us to tease out details for subgroup analysis. To better address these questions, future studies should incorporate this information to better identify and to help stratify patients that may receive maximal benefit after cranioplasty.

Timing of Cranioplasty

The timing of cranioplasty after DC is a point of great debate. It is suggested that following craniectomy, there is a period of increased perfusion possibly due to inflammatory factors, but as this resolves, there begins a period of hypoperfusion responsible for neurological decline. It has been further shown that cranioplasty may restore normal hemodynamics.[35]

Kuo et al[26] reported a series of 13 patients undergoing cranioplasty and correlated TCD values to objective scales of neurological and functional status (Glasgow Coma Scale, motor strength, and Barthel index). Although they noted a significant increase in CBF after cranioplasty, they also found that early cranioplasty may favor neurological recovery. A delay in cranioplasty was also seen in Winkler et al,[30] where 2 patients underwent cranioplasty at 3 and 18 years after their DC. Not surprisingly, these patients had little to no improvement in their preoperative symptoms after surgery. Song et al[33] examined the association between timing of cranioplasty and TCD-measured CBF in early (<12 weeks) and late (≥12 weeks) groups. TCD values showed significant increases in both groups following cranioplasty; however, patients in the early group demonstrated a significantly higher change in both ipsilateral and contralateral MCA velocity, while the late group only in the ipsilateral MCA. The authors concluded that early cranioplasty has potential benefits for cerebral perfusion. Overall, these data would suggest that early cranioplasty improves CBF and has the potential to improve neurological function more so than if cranioplasty is delayed. Further studies evaluating the true impact of cranioplasty on cerebral metabolism are needed to determine its effect on timing of the procedure and on the incidence of postcraniectomy-related complications.

Limitations

While informative, this systematic review has important limitations. The majority of our reports were small case reports and series, and therefore we are limited to descriptions of the types of perfusion studies conducted, general findings relative to cranioplasty, and range of clinical outcomes that often accompany these measurements. Such case reports and series are inherently subject to both reporting and selection bias. Of the 2 cohort studies, our risk analysis showed that the control groups were sufficient in addressing the particular questions posed.

Although the current body of literature suggests that cranioplasty increases CBF and these changes are likely related to neurological recovery, causation cannot be assumed. Some authors have suggested that the neurological improvements after cranioplasty may be multifactorial in nature.[9] Meta-analysis could not be performed due to the variability of reported data in the included studies. This resulted in a qualitative assessment of the literature, rather than a quantitative one. Finally, as part of our inclusion criteria, we had limited articles to the English language, and there is a possibility that we may have excluded reports with higher levels of evidence. However, in our experience, restricting articles to English assists with accessibility of full-text articles and prevents a "lost-in-translation" scenario, in which information could be misinterpreted by faulty translation to English.

CONCLUSION

This systematic review confirms that CBF was decreased after craniectomy and cranioplasty improved CBF. Although there is a general belief that cranioplasty improves functional outcome, predicting which patients will benefit most from cranioplasty remains difficult. Randomized controlled trials and other prospective cohort studies that use a single imaging modality and take into account timing of cranioplasty and other unified outcome predictors are needed to better explore the relationship between cranioplasty, CBF, and clinical outcomes.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

This meta-analysis on the impact that cranioplasty has on cerebral blood flow (CBF) after decompressive craniectomy provides summary evidence to support what many have observed or suspected for years. That is, performing cranioplasty results in an improvement in neurological functioning and that this may in fact be mediated by an improvement in CBF. Many questions remain: Is any observed improvement in CBF responsible for the clinical improvement? Does a patient who underwent decompressive craniectomy for an ischemic stroke benefit as much in terms of increased CBF as a patient who suffered from a traumatic injury? Is there a temporal pattern to the decreased CBF after decompressive craniectomy which suggests an optimal time for cranioplasty? In any case, the authors are to be commended for this well-written review of a topic that should serve as impetus for, and useful background for designing, future studies on this topic.

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In this article, the authors systematically review and present a meta-analysis for the effects of cranioplasty on CBF and neurologic outcome in patients with previous decompressive craniectomies. A total of 203 patients collated from 21 articles were reported to have increased CBF ipsilateral to the side of the cranioplasty, though the exact influences on neurologic function remain unknown.

Time to cranioplasty has not been fully established and has been extensively reviewed along with infection risk, hydrocephalus, perioperative complications, and outcome, as a few studied metrics.[1,2,3] Notably, this review demonstrates a wide variation of time to cranioplasty of 4 weeks to 18 years and these patients all reportedly had improved post-cranioplasty neurologic function. The timing of the pre-cranioplasty neurologic exam is also key to this assessment, as an early neurologic exam may be significantly improved post-cranioplasty if done years later. This was not specifically indicated and may not have been explicitly noted in the published data, though this may be a potential reason of positive influences on neurologic improvement. The authors, however, do point out that causation cannot be inferred.

It is also important to remember that CBF is a function of cerebral perfusion pressure and cerebrovascular resistance. The ability of cerebral autoregulation in these patients with varying systemic issues and cerebral oxygen demands (effectively, cerebral metabolic rate of oxygen consumption) must be taken into account as ongoing confounders in this complex population. Therefore, the delineation between a temporal relationship vs a direct relationship yielded through cause and effect is a difficult endeavor to undertake in the clinical setting. Reported definitions of neurologic recovery in the reviewed literature are also broad. The authors elegantly discuss and address the appropriate limitations.

These results from this review are stimulating and encourage further qualitative and quantitative measurements on serial CBF after decompressive craniectomies and after cranioplasties.

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