Syndrome of the Trephined: A Systematic Review

Kimberly Ashayeri, BA*
Eric M. Jackson, MD‡
Judy Huang, MD‡
Henry Brem, MD‡
Chad R. Gordon, DO, FACS‡§

*Albert Einstein College of Medicine, New York, New York; ‡Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland; §Department of Plastic and Reconstructive Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

Correspondence:
Chad Gordon, DO, FACS,
Multidisciplinary Adult Cranioplasty Center,
Department of Plastic Surgery and Neurosurgery,
Johns Hopkins School of Medicine,
601 N. Caroline St, 8th Floor,
Baltimore, MD 21287.
E-mail: cgordon@jhmi.edu

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BACKGROUND: Syndrome of the trephined (SoT) is a rare, important complication of a craniectomy characterized by neurological dysfunction that improves with cranioplasty. Its varied symptoms include motor, cognitive, and language deficits. Its exact characterization appears suboptimal, with differing approaches of evaluation. Accordingly, this topic is in great need of further investigation.

OBJECTIVE: To accurately describe SoT and explore methods of an objective diagnosis/evaluation.

METHODS: Electronic searches of PubMed, MEDLINE, Web of Knowledge, and PsycINFO databases used the key words "syndrome of the trephined" and "sinking skin flap." Non–English-language and duplicate articles were eliminated. Title and abstract reviews were selected for relevance. Full-text reviews were selected for articles providing individual characteristics of SoT patients.

RESULTS: This review identified that SoT most often occurs in male patients (60%) at 5.1 ± 10.8 months after craniectomy for neurotrauma (38%). The average reported craniectomy is 88.3 ± 34.4 cm^2 and usually exists with a "sunken skin flap" (93%). Symptoms most commonly include motor, cognitive, and language deficits (57%, 41%, 28%, respectively), with improvement after cranioplasty within 3.8 ± 3.9 days. Functional independence with activities of daily living is achieved by 54.9% of patients after 2.9 ± 3.4 months of rehabilitation. However, evaluation of SoT is inconsistent, with only 53% of reports documenting objective studies.

DISCUSSION: SoT is a variable phenomenon associated with a prolonged time to cranioplasty. Due to current weaknesses in objectivity, we hypothesize that SoT is often underdiagnosed and recommend a multifaceted approach for consistent evaluation.

CONCLUSION: SoT is a serious complication that lacks exact characterization and deserves future investigation. Improved understanding and recognition have important implications for early intervention and patient outcomes.

KEY WORDS: Craniofacial reconstruction, Cranioplasty, Decompressive craniectomy, Neurosurgery, Rehabilitation, Syndrome of the trephined, Systematic review

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Syndrome of the trephined (SoT) is a poorly understood complication of craniectomy, characterized most commonly by unexplained neurological dysfunction in patients with acquired skull defects and subsequent improvement after secondary cranial reconstruction (ie, cranioplasty). SoT was first described in 1939 by Grant and Norcross[1] as an aggregate of symptoms including severe headache, dizziness, pain/discomfort at the craniectomy site, apprehension, and/or mental depression. Since then, based on the majority of reported cases, an overlapping constellation of symptoms has been identified, including 3 main components: (1) long-term neurological deficits usually beginning weeks to months after craniectomy, (2) occurrence independent of the location of the lesion, and (3) clinical improvement after cranioplasty.[1-10]

Although this common symptomatology exists in craniectomy patients, in the past century,

ABBREVIATIONS: ADLs, activities of daily living; **CBF,** cerebral blood flow; **SoT,** syndrome of the trephined; **VP,** ventriculoperitoneal

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a wide spectrum of patient subtypes with a broad array of symptoms has been described. Furthermore, reports associating SoT with a long interval between craniectomy and cranioplasty and with larger craniectomy size show unreliable consistency in relation to symptom onset and resolution.[11-13] To date, the characterization of patients with suspected SoT has been inconsistent—either underreported or not reported at all. Thus, the multifarious nature of this syndrome, combined with the rarity of reports, makes it difficult to identify a clear picture and served as the main impetus for this study.[5]

With this in mind, we performed a systematic review of the literature in an effort to concretely describe the syndrome, identify positive predictors of the patient population at greater risk of the development of SoT, explore existing objective and evaluative methods for SoT, and review all theories related to the underlying pathophysiology and subsequent causation.

METHODS AND MATERIALS

Literature Search Strategy and Data Sources

All popular databases were searched for primary studies performed through July 2015, including PubMed, MEDLINE, PsycINFO, and Web of Science. The search used key words and no language restrictions. Search term combinations are shown in Table 1. Bibliographies from selected papers were also hand-searched.

Eligibility Criteria

Study Selection

Search results were compiled and summarized for the purpose of this article. Duplicate citations were deleted. Non-English articles were discarded from the study cohort. Data collection was limited to full-text articles only. Once collated, all remaining titles and abstracts were assessed for relevance to SoT. All qualifying articles were then fully examined and reviewed in depth. Study inclusion was decided in unblinded fashion (Figure 1).

Study Design

The majority of the existing studies, classified as case reports and/or case series, were objectively summarized for the purpose of this systematic review (see Table, **Supplemental Digital Content 1,** http://links.lww.com/NEU/A891).[2,3,6,7,9-11,14-35,36-57] Individual studies are not at risk of significant bias when evaluated by the Cochrane Handbook recommended criteria.[58]

Population

The target population consisted of adults (defined as older than 18 years of age) with the following inclusion criteria: (1) history of large-sized craniectomy, (2) neurological symptoms during the interval between craniectomy and cranioplasty, and (3) retrospective assessment of clinical improvement after cranioplasty reconstruction. Studies were then further reviewed to identify pertinent patient-specific data as detailed here.

TABLE 1. Search Term Combinations

Syndrome of the trephined
Sinking skin flap
Sunken skin flap
Postcraniectomy deficit

Data Extraction and Data Items

Data were obtained from eligible sources using a prespecified electronic data collection form. Collected data included (1) age, (2) sex, (3) indication for craniectomy, (4) craniectomy to symptom development time interval, (5) craniectomy to cranioplasty time interval, (6) exact symptoms experienced during interval between craniectomy and cranioplasty, (7) size of skull defect, (8) degree of sunken skin flap, (9) placement of shunt and/or lumbar drain, (10) paradoxical herniation, (11) time interval from craniectomy to symptom improvement, (12) extent/degree of improvement, and (13) methods of patient evaluation.

Synthesis of Results

Statistical averages and relative percentages of all patient characteristics were combined, when and if appropriate.

RESULTS

Patient Characteristics

Age/Sex

The average age ± SD of the symptomatic patients (n = 54) with SoT was 49.3 ± 16.4 years (range, 19-79 years). Of the group, 60% of patients were male.

Indication for Craniectomy

SoT symptoms developed most commonly in craniectomy patients with history of neurocranial trauma (40.7%, n = 22). This was followed by aneurysm (16.7%, n = 9) and meningioma (14.8%, n = 8). Less common causes were hemorrhage (13.0%, n = 7), infarct (11.1%, n = 6), and infection (3.7%, n = 2) (Table 2).

Presenting Symptoms

Presenting symptoms varied and were classified according to underlying features. The most common was motor weakness (61.1%) followed by cognitive deficits (44.4%), language deficits (29.6%), altered level of consciousness (27.8%), headache (20.4%), psychosomatic disturbances (18.5%), seizures or electroencephalographic changes (11.1%), and cranial nerve deficits (5.6%) (Table 3). Of the 24 patients with cognitive deficits, the most commonly reported specific cognitive symptoms were decreased attention (n = 9, 37.5%), memory impairment (n = 9, 37.5%), and executive function difficulties (n = 6, 25.0%).

Average Time Interval From Craniectomy to Onset of SoT Symptoms

The time interval from craniectomy to onset of SoT symptoms was defined as either abrupt failure to continue along a path of progressive neurological rehabilitation or initial gains in rehabilitation followed by rapid deterioration. After analytical review, the

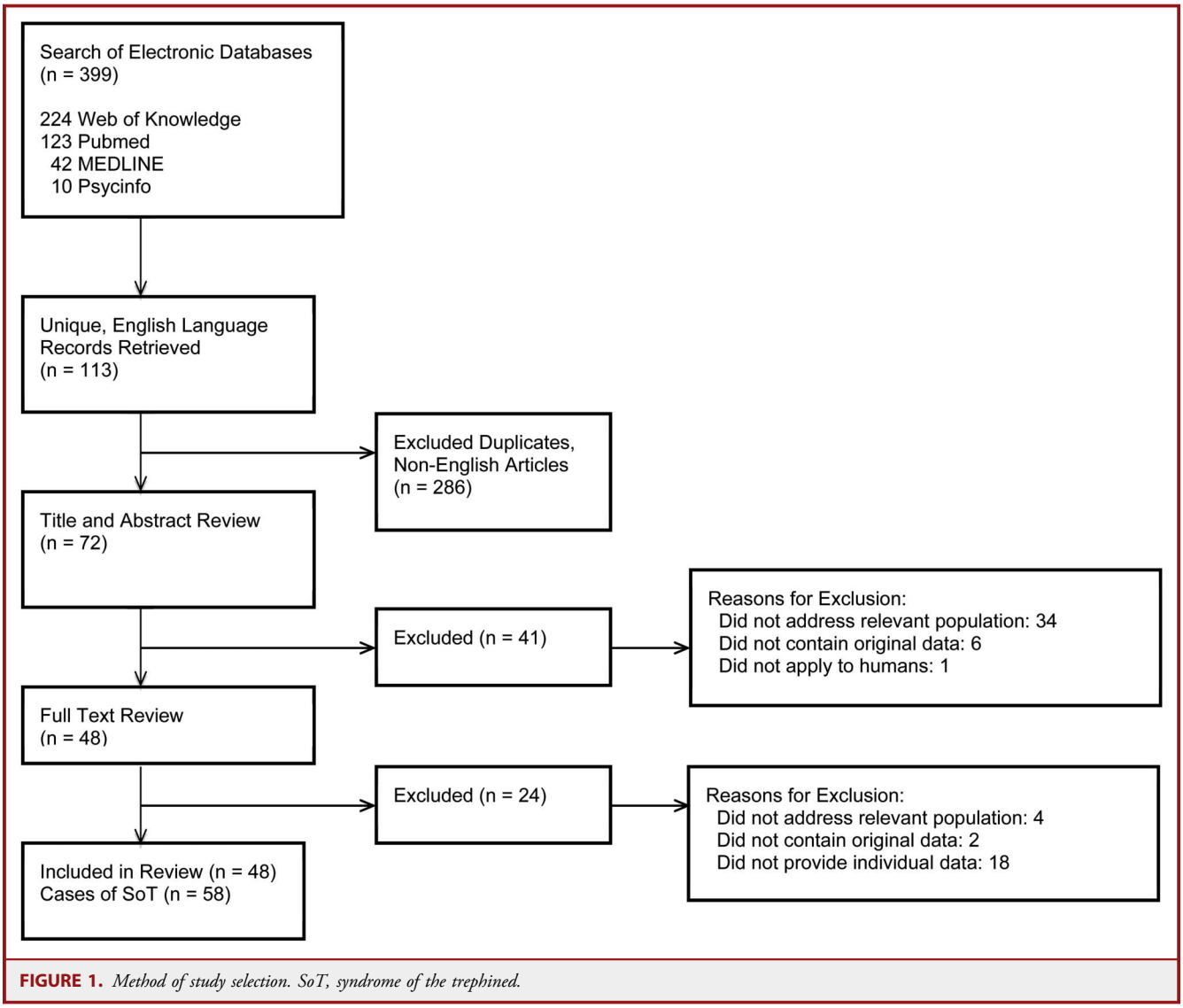

FIGURE 1. *Method of study selection. SoT, syndrome of the trephined.*

average ± SD interval identified was 5.1 ± 10.8 months, with a wide range of 3 days to 7 years.

Average Time Interval From Craniectomy to Cranioplasty

The time interval from craniectomy to cranioplasty was reported in 33 of 54 cases (61.1%). Statistical analysis demonstrated that the average ± SD elapsed time interval was 9.1 ± 14.6 months, with a wide range of 10 days to 7 years (Figure 2). Of these cases, 10 patients (30.3%) underwent cranioplasty within 3 months and 8 (24.2%) underwent cranioplasty between 3 and 6 months. In 6 cases (18.2%), infection was specifically listed as the cause of delay of cranioplasty. In an additional 5 cases in which the exact timing of cranioplasty was not given, an infection delaying cranioplasty was reported. Therefore, 11 of 54 cases (20.4%) were complicated by infection. In 10 of the 33 cases (30.3%) with given time intervals, a specific reason for delay was not stated.

Average Size of the Craniectomy Defect

The exact size of each symptomatic cranial defect was reported in only 7 cases. The average ± SD area was 88.3 ± 34.4 cm^2.

Incidence of Shunting

Eighteen reported cases described SoT symptoms after either ventriculoperitoneal (VP) shunt placement or lumbar drainage for findings consistent with increased intracranial pressures. Of these, 7 patients (39%) underwent VP shunting vs 11 (61%) undergoing lumbar puncture/lumbar drain placement. In addition, there were

TABLE 2. Indications for Craniectomy

Indication	No. (%) of Cases
Trauma	22 (37.9)
Aneurysm	9 (15.5)
Meningioma	8 (13.7)
Hemorrhage	7 (12.1)
Infarct	6 (10.3)
Infection	2 (3.4)

2 reports of patients being treated with a VP shunt or lumbar puncture for SoT symptoms who unfortunately had further worsening of their neurological conditions.

Positional Symptoms

Ten patients showed that neurological symptoms worsened when in the upright position and improved when in the horizontal position. Of these, 9 had no form of cerebrospinal fluid (CSF) drainage (90%), and only 1 had VP shunting (10%).

Sunken Skin Flap

In total, an overwhelming majority of patients (93%, n = 54) exhibited a visibly sunken skin flap consistent with scalp contraction.

Paradoxical Herniation

There have been limited reports of patients with SoT experiencing paradoxical herniation with further deterioration of their condition.[48,49] Of the cases reviewed, 2 patients were found: 1 with no previous CSF drainage and 1 with history of lumbar drainage whose condition eventually worsened until death.

Postcraniectomy Improvement

When reported, the mean ± SD time interval to achieve appreciable resolution of SoT symptomology was 3.8 ± 3.9 days after cranioplasty reconstruction. The average ± SD time interval until the greatest reported improvement was achieved was 2.9 ± 3.4 months. Of note, the majority of cases (87.9%, n = 51) described the extent of improvements after cranioplasty. Of these, 18 (34.6%) reported complete recovery from neurological symptoms consistent with SoT. In 10 patients (19.6%), functional independence with the ability to perform activities of daily living (ADLs) developed. Three reports (5.9%) indicated a return to neurological baseline compared with the pre-SoT state. Five patients (9.8%) performed some ADLs with moderate assistance. Three patients (5.9%) reported near-normal cognition after cranioplasty. In 5 patients (9.8%), improved cognition with better attention and ability to communicate were noted. Six patients (10.3%) displayed significant improvements in hemiparesis and/or motor function, but did not reach complete functional independence. One patient (1.7%) died of complications of paradoxical herniation, as mentioned previously.

TABLE 3. Presenting Symptoms of SoT, Grouped According to Unifying Features

Presenting Symptom	No. (%) of Cases
Motor weakness	33 (56.9)
Cognitive deficits	24 (41.4)
Language deficit	16 (27.6)
Altered level of consciousness	15 (25.7)
Headache	11 (19.0)
Psychosomatic	10 (17.2)
Seizure	6 (10.3)
Cranial nerve deficits	3 (5.2)

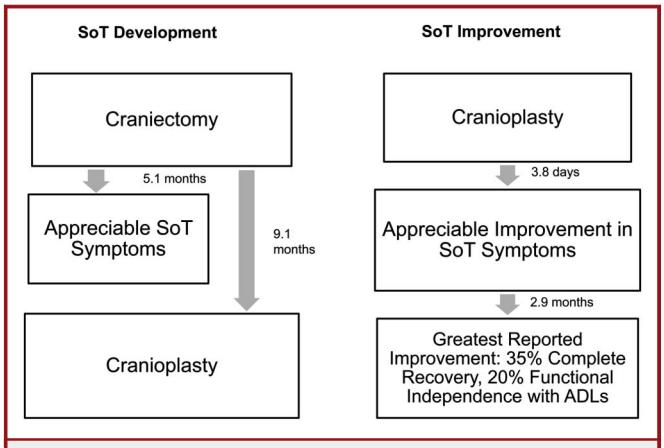

FIGURE 2. *Timeline graphic summarizing craniectomy to symptom onset, craniectomy to cranioplasty, and cranioplasty to symptom improvement. ADLs, activities of daily living; SoT, syndrome of the trephined.*

DISCUSSION

Patient Characteristics

According to our systematic review, we found that SoT symptoms can occur in adult patients of all ages, with an average reported age of 49 years and the youngest reported age of 19 years. We found a male predominance (60%), which is consistent with previous studies.[52] This may be due, in part, to the fact that the most common indication for craniectomy was neurotrauma, which in itself occurs more often in males. However, a substantial number of patients with aneurysm, meningioma, hemorrhage, and infarcts was also identified. Therefore, clinical suspicion should be high in all craniectomy patients with progressive neurological decline.

To our knowledge, this study helped to elucidate, for the first time, time intervals from craniectomy to symptom onset, craniectomy to cranioplasty, and cranioplasty to symptom improvement. An average time between craniectomy and onset of SoT symptoms was found to be ~5 months. However, due to

the extreme range of time variables until onset, it is reasonable for surgeons to consider the diagnosis for any unexplained neurological decline out of proportion to expected deficits after craniectomy, regardless of the elapsed time interval. For the SoT patient population, a mean time from craniectomy to cranioplasty was found to be ~9 months. This is longer than the current recommendations of early cranioplasty within 3 to 6 months. In many cases, delayed cranioplasty was attributed to infection. In other cases of cranioplasty performed after this recommended time, no specific reason was given. However, it is important to note that many cases included in this review are from as early as 1975, and these current recommendations did not exist. The time interval to cranioplasty is consistent with that in the literature but different from our team's published algorithm at ~3 to 4 months.[59] A potential confounding variable may be our distinct pericranial-onlay technique, which allows one to recruit greater scalp mobility using component separation compared with the more popular use of tissue expanders, for example.[60,61] A motivating factor for our team is the implication of prolonged intervals from craniectomy to cranioplasty in the development of SoT.[11,50,52] As such, our cranioplasty center tends to see a rare incidence of SoT compared with the average. The benefit of an early (ie, 3- to 4-month time interval) cranioplasty may outweigh the potential risks. In the case of previous bone flap infection/osteomyelitis, the use of a multidisciplinary care model incorporating a group of infectious disease experts seems equally critical.[59]

Interestingly, the overall craniectomy size was grossly underreported in the literature, with the average skull defect size hovering around 90 cm^2. Although there is a paucity of reported information on the relationship of craniectomy size to SoT development, making it impossible to suggest a correlation here, there is evidence in the literature of a trend, suggesting greater frequency in those patients with craniectomies of a critical size (>100 cm^2).[7] High-level prospective studies are required to determine the presence of a significant correlation.

Although SoT is classically associated with headache and motor weakness, the constellation of symptoms is poorly defined at this time. This review found motor weakness to be the most common symptom, with more than half of all patients experiencing some form of motor deficits (57%). However, in contrast, headache was reported in only <1 of every 5 patients (19%). In fact, the second most common symptom was cognitive decline, affecting a significant proportion of craniectomy patients (41%).

One explanation for this study's novel finding may be that motor weakness is more easily recognizable than new-onset cognitive deficits. In fact, only ~10% (7/58) of patients had undergone measures of cognitive function as an evaluative method post-craniectomy. Thus, it would be reasonable to deduce from this study that the craniectomy patient population is being grossly underdiagnosed and poorly screened for SoT.

As opposed to cognitive dysfunction, a sunken flap is more readily identified and conspicuous. As such, an overwhelming number of authors (93%) noted a sunken skin flap in their SoT patients. However, the presence of reports of neurological decline without concave skin flaps suggests that this scalp contraction may not be an absolute precursor of SoT. As such, surgeons should remain cognizant of identifying SoT symptoms in patients with a symmetric physical appearance. Of note, some authors do claim that the presence of a sunken flap is the most sensitive positive predictor of SoT.[7]

Interestingly, in 18 separate cases, shunting and/or lumbar drainage were claimed to contribute to the development of SoT.[10,11,35,41,55-57] There are descriptions that craniectomy patients with hydrocephalus have shunts because CSF drainage causes a negative gradient between atmospheric pressure and intracranial pressure, thus worsening their neurological condition.[11] Thus, it may be justified to avoid VP shunting in all patients with cranial defects, especially because cranioplasty reliably improves CSF dynamics. In our review, 7 patients (39%) had undergone VP shunting, and 11 (61%) had serial lumbar puncture or lumbar drainage before the onset of SoT. Although limited, these data may suggest a greater prevalence of SoT in craniectomy patients undergoing lumbar drainage compared with VP shunting. Notably, similar literature exists for lumbar drainage after tumor resection, suggesting that CSF removal below the tentorium creates a pressure gradient between the supratentorial and lumbar cistern compartments, which in turn can lead to complications such as transtentorial herniation.[62] For this reason, intracranial drainage has been advocated in favor of lumbar drainage.[62,63]

The siphoning effect of drainage is also observed transiently in several reported patients who experienced orthostatic changes in symptoms of SoT. Ten reports indicated that the patients' neurological symptoms worsened with upright positioning and improved with horizontal positioning.[15,17,18,41,42,44,48,50] Only 1 of 10 had any form of CSF drainage (VP shunt). This seems to support the theory that an increased gradient between atmospheric and intracranial pressures caused by CSF flow contributes to the development of SoT.

Paradoxical herniation also rarely occurs in these patients, with 2 of the 58 reported patients experiencing deterioration because of this complication.[48,57] In 1 case, the patient eventually died of paradoxical herniation. In the other case, the final outcome was not documented. Therefore, further investigation of correlating the presence and outcomes of paradoxical herniation in SoT is necessary. Additionally, due to this complication's severity, all patients with SoT should be carefully screened for severe deterioration, especially as it can be easily reversed by placing the patient in the Trendelenburg position.

Evaluative Studies

Many authors have turned to objective studies and radiographic images to correlate clinical improvements with physiological changes after cranioplasty. We identified only 5 studies evaluating electroencephalographic results, both before and after cranioplasty, and, interestingly, all of them found improvement in seizure activity after cranioplasty.[10,18,23,39,54] Yamaura and

Makino[10] showed that 95% of patients with SoT had electroencephalographic changes, and 60% of patients experienced electroencephalographic improvement status post-cranioplasty. The greatest change was seen in paroxysmal abnormalities, suggesting improvement in the occurrence of clinical seizures. However, these data suggest that electroencephalography-related changes may be present even in patients not experiencing clinical seizures. For this reason, it may be a useful and underused tool for evaluating patients with neurological demise and suspected SoT.

Similarly, measures of cognitive impairment and tracking of ADLs may be underutilized tools in screening for SoT. As previously described, 41% of patients with clinically diagnosed SoT experienced cognitive decline. Thus, the data in this study suggest that cognitive and functional abilities may be negatively affected more frequently in SoT patients than currently recognized.[5] As such, cognitive and ADL screening may prove useful in future investigations.

Additionally, some authors have used dynamic phase-contrast magnetic resonance imaging (MRI) to show increased CSF flow after cranioplasty.[2,3] This study can elucidate patterns of arterial, venous, and CSF flow before and after cranioplasty. Changes in oscillatory flow of CSF can be indicative of changes in compliance with the craniospinal system resulting from the cranial defect.[2] Considering the suggested exaggeration of SoT with a VP shunt or lumbar drain, it may be prudent to evaluate craniectomy patients with phase-contrast MRI before CSF drainage. Computed tomography (CT) perfusion scans have also proved to be valuable for evaluating postcraniectomy changes and improvements after cranioplasty. Bilateral increases in cerebral blood flow (CBF) after cranioplasty are well established in the existing literature[6,37,53]; however, studies to date have compared pre- and postcranioplasty CBF and have not offered precranioplasty CBF levels suggestive or diagnostic of SoT. Therefore, wider use of CT perfusion may provide better diagnostic criteria for SoT.

Based on our comprehensive assessment of the literature, we recommend a multifaceted approach to evaluating SoT patients that may prove useful in detecting symptoms that otherwise would go unrecognized (Figure 3). In patients with difficult-to-detect deficits, such as cognitive or language disturbance, CT perfusion scanning can aid in detecting anatomic changes and disturbances in CBF that may contribute to neurological impairment. Phase-contrast MRI can be a useful adjuvant in contributing more information to the elucidation of the pathophysiology of SoT. Additionally, use of cognitive impairment and electroencephalography in craniectomy patients with halted progress or deterioration in recovery is suggested to detect possible subclinical effects of SoT.

Postcraniotomy Course

In summary, all patients showed some form of rapid improvement after cranioplasty, with some demonstrating early significant reversals at an average of 4 days after surgery. In many cases, improvement was seen within 24 hours. After the initial signs of improvement, SoT patients recovered further neurological function during their rehabilitation phase. Of note, the most common time interval after cranioplasty for symptom reversal was ~3 months. Extended follow-up was not always reported, and, therefore, the time to plateaus in recovery is not clearly defined in the literature.

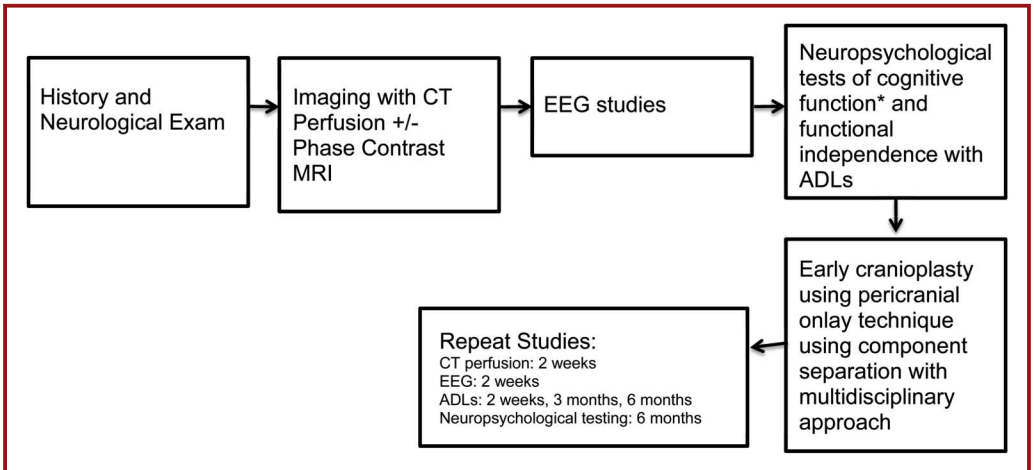

FIGURE 3. *Flowchart of objective evaluation of SoT patients before and after cranioplasty and ideal management. *Previously reported tests used before and after cranioplasty: Wechsler Memory Scale–Revised, Rey Auditory Verbal Learning Test, Controlled Oral Word Association Test–FAS; the Verbal Fluency Test–Animal Category, VST, WMI, and Wechsler Adult Intelligence Scale, Wechsler Memory Scale and Wechsler Adult Intelligence Scale, Trail Making Tests A and B, POD, the Rey Complex Figure Test, Beck Depression Inventory, BAI, BHS, ISSL, and Mini-Mental State Examination. The modified Rankin Scale and Barthel Index were recorded to evaluate global functional status. BAI, Beck Anxiety Inventory; BHS, Beck Hopelessness Scale; COWAT-FAS, Controlled Oral Word Association Test; ISSL, Lipp's Inventory of Stress Symptoms for adults; POD, Pfeffer Outpatient Disability Scale; VST, Victoria Stroop Test; WMI, working memory index.*

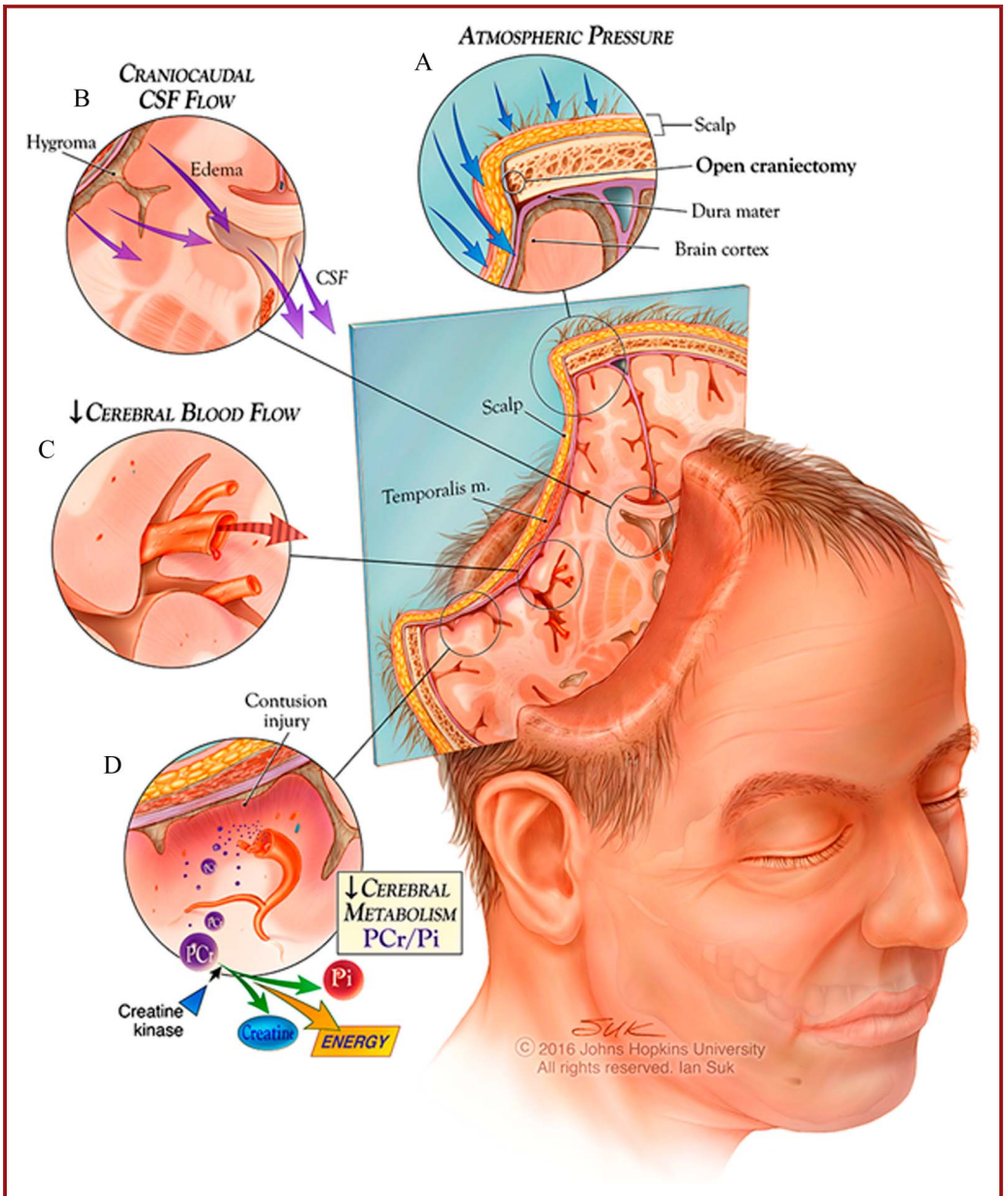

FIGURE 4. *Illustration demonstrating 4 theoretical mechanisms contributing to syndrome of the trephined:* **A**, *Atmospheric pressure,* **B**, *Craniocaudal CSF flow,* **C**, *Decreased cerebral blood flow, and* **D**, *Decreased cerebral metabolism. CSF, cerebrospinal fluid; PCr/Pi, phosphocreatine to inorganic phosphate ratio. ©2016 JHU Neurosurgery–Ian Suk, reproduced, with permission. Color version available online only.*

After cranioplasty, all but 1 patient exhibited marked improvement of neurological symptoms. In 51 cases, the extent of improvement of neurological symptoms was specifically reported. Fifty-five percent of patients were able to achieve functional independence with ADLs, with 35% showing no neurological symptoms after cranioplasty. The remainder exhibited dramatic improvements in cognitive and/or motor function that greatly increased the quality of life. Due to a lack of standardized methods for reporting neurological improvements after craniectomy, it is difficult to draw any reliable conclusions. However, those patients not reaching neurological intactness frequently began with greater deficits. A study with standardized and detailed documentation of pre- and post-SoT symptoms as well as postcranioplasty symptoms would be

necessary to conclusively demonstrate the correlation between starting symptoms and outcomes. One patient died of complications of paradoxical herniation, which might have been prevented with earlier cranioplasty before herniation occurred.

Pathophysiology

The mechanism of the SoT has not been fully elucidated. However, there are several interrelated theories on the cause (Figure 4).

Atmospheric Pressure

Atmospheric pressure, often associated with sinking of the skin flap, suggests that a cranial defect allows external pressure to act on the brain.[6,7] It is argued that external barometric pressure on the scalp is transmitted to the cerebral vasculature, causing decreased blood flow to the area of the defect.[64] In theory, then, the larger the area of the cranial defect is, the lower the flow.[65] It has been postulated that this mechanical pressure also decreases the CSF flow.[3]

Cerebral Blood Flow

Decreases in CBF have been extensively shown using xenon-enhanced perfusion CT. These changes have been found both at the site of the defect as well as distant sites.[52,53] This has been attributed to both atmospheric pressure and impairment of venous blood flow through the brain.[10,14]

CSF Flow

CSF dynamics have played an integral role in the existing theories behind the incidence of SoT. Many studies have shown low CSF flow after craniectomy.[3,10] Dujovny et al[2] noted a 2-fold increase in craniocaudal CSF systolic flow velocity after cranioplasty, which, they argue, may be explained by changes in compliance of the craniospinal system with the closure of a cranial defect. Stiver et al[52] suggested that impaired CSF circulation in the setting of contusion injury causes transgression of CSF and edema into the parenchyma underlying the skull defect. This was evidenced by the fact that patients had statistically a significantly higher incidence of CSF hygromas during the first month after decompressive hemicraniectomy (P = .02).

Cerebral Metabolism

Some evidence has shown that cerebral glucose metabolism is deficient in the injured hemisphere, contributing to cortical dysfunction. This was suggested by determining the ratio of phosphocreatine to inorganic phosphate, which is a sensitive index of cerebral energy depletion.[9]

CONCLUSION

SoT is a rare and serious complication, most often described in male patients after neurotrauma, manifesting as an unexplained motor function decline after craniectomy. However, it has been poorly characterized to date. We conclude that SoT is underdiagnosed and further recommend a new multifaceted approach to evaluating craniectomy patients, including CT perfusion, cognitive impairment measurements, measures of ADLs, and electroencephalography. SoT is important to recognize as it may indicate the need for earlier intervention, help improve patients' overall outcome,[59,66] and provide evidence-based recommendations for craniectomy patients receiving unjustified insurance denials for their much-needed secondary cranial reconstruction. Furthermore, to contribute to the understanding of this rare syndrome, we aim to improve our team's documentation of patient characteristics, including cranial defect size and the amount of time elapsed until the cranioplasty, as well as a more detailed postcranioplasty course outlining patient improvements for all cases suggestive of SoT.

Disclosures

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COMMENT

The authors are to be commended for bringing together the literature describing syndrome of the trephined. I suspect this is an underreported complication of delayed cranioplasty in the cases of large decompressive craniectomies. This review addresses the varied presentations of syndrome of the trephined in a clear and concise fashion: motor, 57%; cognitive,41%; and language deficits, 28%. Cognitive deficits reported by the authors include decreased attention (37.5%), memory impairment (37.5%), and executive function difficulties (25%). The compelling clinical symptom is typically severe position-related headaches, which are exacerbated by dehydration, as the authors discuss. Overall, these patients demonstrate a significant psychomotor slowing with decreased animation, activity, and a paucity of response to their environment over time. This becomes particularly concerning in patients who were previously progressing well during rehabilitation. In military experience, we saw a higher incidence due to the delay mandated by recurrent infections, combined skull base and frontal sinus injuries, and defects in scalp and soft-tissue coverage due to high-energy ballistic and blast injuries. A multidisciplinary approach to these patients was best coordinated from the initial time of their injury. This report supports the role of a time delay of typically 5 to 9 months as a prerequisite for the development of the syndrome. In our experience, proper planning of the scalp flap in the face of tissue loss may help to prevent further delayed defects that then lead to infections and the delay in cranioplasty and subsequent syndrome. The recovery of symptoms post-cranioplasty is an essential part of the diagnosis and may need to be separated from underlying hydrocephalus, seizure, or delayed strokes. Disruption of cerebrospinal fluid circulation may also significantly contribute to this syndrome when combined with the application of atmospheric pressure on the cortical mantle, ventricles, and subarachnoid space. The loss of the absorptive capacity of the subarachnoid space to cardiac pulsations may be the culprit for ventricular enlargement. Once the cranial vault is closed, the subarachnoid space expands, allowing a decrease in the ventricular size in select, but not all, patients. Perhaps in the future, protective head gear can be designed that protects the brain from atmospheric pressure effects. Such patient-specific head gear would need to recreate a closed vault externally without exerting increased suction pressure on the cortical vessels, cortex, or scalp. This review gives ample evidence of the deleterious but reversible effects of syndrome of the trephined and should be read by neurosurgeons, rehabilitation physicians, and neurologists involved in the care of the postcraniectomy patient.

Rocco A. Armonda
Bethesda, Maryland