Syndrome of the Trephined: Quantitative Functional Improvement after Large Cranial Vault Reconstruction

Joseph T. Tarr, M.D.
Matthew Hagan, M.D.
Ben Zhang, B.A.
Neil Tanna, M.D., M.B.A.
Brian T. Andrews, M.D.
Justine C. Lee, M.D., Ph.D.
James P. Bradley, M.D.

Philadelphia, Pa.; New York, N.Y.; Kansas City, Kan.; and Los Angeles, Calif.

Background: Large decompressive craniectomies may be life-saving; however, they may also result in syndrome of the trephined. This postrecovery sequela is characterized by dizziness, fatigue, depression, weakness, speech slowing, gait disturbance, and impaired mentation. Because this entity is poorly understood, the authors attempted to quantify the functional improvement in patients with syndrome of the trephined after cranial vault reconstruction.
Methods: Patients with cranial vault defects (>50 cm^2) from trauma, meningioma, and hemorrhage were studied preoperatively and postoperatively (6 months) after cranial vault reconstruction using (1) the Cognistat Active Form and (2) the Functional Independence Measure instrument ($n = 40$). Cranial vault reconstructive techniques varied from split cranial bone to alloplastic implants (polyetheretherketone or titanium mesh).
Results: Of the 143 patients treated with decompressive craniectomies, 28 percent ($n = 40$) developed symptoms of syndrome of the trephined. A larger craniectomy defect size correlated with development of syndrome of the trephined. Time from craniectomy to presentation of symptoms was 4.5 months. Time from craniectomy to cranial vault reconstruction was 6.1 months. Time from cranial vault reconstruction to symptom improvement was 4.3 days. Complete functional recovery of syndrome of the trephined was seen in 70 percent. Type of cranial vault reconstruction included polyetheretherketone implant (57.5 percent), split calvarial graft (22.5 percent), and titanium mesh (20 percent), and was not a determinant of functional improvement. Cognistat assessment score noted improvement (from 38 to 69); likewise, the Functional Independence Measure measurement tool showed improvement (from 38 to 98).
Conclusions: Syndrome of the trephined occurs more frequently than previously described in posttraumatic patients with large cranial vault defects. Cranial vault reconstruction leads to significant, quantifiable functional improvement in a large number of patients. (*Plast. Reconstr. Surg.* 145: 1486, 2020.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

PATIENT SAFETY

OUTCOMES
Patient-reported Health

4
THERAPEUTIC

The syndrome of the trephined is an underdiagnosed and underreported complication of decompressive craniectomy. It was first described by Grant and Norcross in 1939 as a cluster of symptoms including dizziness, undue fatigability, feeling of apprehension, and vague discomfort at the site of the cranial vault defect.[1] Today, the syndrome is more accurately described

From the Division of Plastic and Reconstructive Surgery, Lewis Katz School of Medicine at Temple University; the Division of Plastic and Reconstructive Surgery, Northwell Health Hofstra School of Medicine; the Division of Plastic and Reconstructive Surgery, University of Kansas; and the Division of Plastic and Reconstructive Surgery, University of California, Los Angeles David Geffen School of Medicine.
Received for publication October 30, 2018; accepted December 17, 2019.

DOI: 10.1097/PRS.0000000000006836

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

Related digital media are available in the full-text version of the article on www.PRSJournal.com.

By reading this article, you are entitled to claim one (1) hour of Category 2 Patient Safety Credit. ASPS members can claim this credit by logging in to PlasticSurgery.org Dashboard, clicking "Submit CME," and completing the form.

as a neurologic deterioration or behavioral disturbance after craniectomy with reversibility of symptoms following reconstructive cranioplasty.[2] These neurologic and behavioral changes include motor weakness, headaches, sensory changes, slowing of speech, impaired mentation, and gait disturbances and can occur either acutely or chronically.[2] The syndrome is most commonly seen in patients undergoing a craniectomy for trauma, infarction, hemorrhage, and infection.[1] These neurologic changes are independent of existing neurologic lesions from traumatic, vascular, or other insult. They are theorized to occur from direct brain compression caused by transmission of atmospheric pressure to the intracranial cavity by means of the skin flap.[3] This compression in turn changes cerebrospinal fluid hydrodynamics, resulting in decreased regional cerebral brain flow and cerebral metabolism.[3]

Because there are no detailed outcomes studies but merely anecdotal reports,[4] there remain unanswered questions surrounding this neurologic entity: Does the cranial vault defect size correlate to syndrome of the trephined symptoms? What is the timing of the development of syndrome of the trephined symptoms following craniectomy? What is the timing of improvement following cranioplasty? Can neurorehabilitation assessment scores be used to quantify development and resolution of syndrome of the trephined? To answer these questions, we critically looked at patients with large craniectomy defects who developed syndrome of the trephined symptoms, with particular emphasis on clinical outcomes and established neurorehabilitation functional assessment tools.

PATIENTS AND METHODS

After institutional review board approval, consecutive patients with large craniectomy defects (>20 cm^2) over an 8-year period were retrospectively reviewed for evidence of syndrome of the trephined (n = 143). Diagnosis of syndrome of the trephined was based on presence of symptoms described by Sedney et al. in 2015.[2] Patients with incomplete data were excluded from the study. Of the 143 patients identified with large cranial vault defects, 18 were eliminated because of incomplete data, including failure to make surgical and/or rehabilitation appointments for proper assessment. Those with the diagnosis of syndrome of the trephined were reviewed in detail (n = 40). Patients studied had the following recorded: age, gender, medical comorbidities, reason for craniectomy, presence of brain injury, ventriculoperitoneal shunt, size of craniectomy defect, presentation reason (i.e., deterioration during rehabilitation versus abrupt neurologic change), presenting syndrome of the trephined symptoms (i.e., headache, weakness, impaired mentation, speech slowing, gait disturbance, depression, altered level of consciousness), physical examination findings (i.e., presence of sunken skin flap, improvement in Trendelenburg position), seizures (i.e., before/after reconstruction), and magnetic resonance imaging findings (i.e., midline shift). Impaired mentation encompasses changes in areas such as memory, problem solving, social interactions, calculations, and naming.

The type of cranioplasty varied and consisted of split cranial bone grafts, banked cranial bone, polyetheretherketone implant reconstruction or titanium plate reconstruction based on location of defect, patient comorbidities, and surgeon preference. The following data on timing were specifically recorded: (1) time from initial craniectomy to presenting symptoms of syndrome of the trephined, (2) time from craniectomy to cranial vault reconstruction, (3) time from cranial vault reconstruction to improvement/resolution of syndrome of the trephined, and (4) time of greatest improvement in symptoms after cranioplasty.

Neurorehabilitation functional assessment was performed using both the Cognistat Active Form (Novatek, Montreal, Quebec, Canada) and the Functional Independence Measure (Uniform Data System for Medical Rehabilitation, Amherst, N.Y.) form (Fig. 1). Assessments were recorded in a serial fashion preoperatively, postoperatively, and during the rehabilitation process. The timeline for testing included assessment every 1 to 2 days as an inpatient, weekly during rehabilitation visits, and then monthly after 8 weeks. The Neurobehavioral Cognitive Status Examination (Cognistat Active Form) is a neurobehavioral-screening test that assesses the patient's level of consciousness, orientation, attention, language, constructional ability, memory, calculation skills, and executive skills. The form is completed by the practitioner in the above categories to tally a final score with the aim of objectively assessing the degree of cognitive impairment. Lower scores are associated with higher degrees of impairment. The Functional Independence Measure form measures overall independence during specific functional tasks, such as self-care, sphincter control, mobility, locomotion, communication, and social cognition. Scores range from 18 to 126, with the higher score being indicative of fully independent function.

Cognistat Active Form

	Level of Consciousness	Orientation	Attention	Language			Constructions	Memory	Calculations	Reasoning	
				Comprehension	Repetition	Naming				Similarities	Judgment
Average Range	Alert	12	(S)8	(S) 6	(S)	(S)	6 (S)5	12	(S)4	8 (S)6	6 (S)5
					12	8					
		10	6	5	11	7	4	10	3	5	4
Mild Impairment	Impaired	8	5	4	9	5	3	8	2	4	3
Moderate Impairment		6	3	3	7	3	2	6	1	3	2
Severe Impairment		4	1	2	5	2	0	4	0	2	1

*The validity of the Cognitive Status Profile depends on the administration in strict accordance with the Cognistat manual.

FIM® Instrument

LEVELS		
	7 Complete Independence (timely, safely) 6 Modified Independence (device)	NO HELPER
	Modified Dependence 5 Supervision (subject = 100%) 4 Minimal Assistance (subject = 75%+) 3 Moderate Assistance (subject = 50%+) **Complete Dependence** 2 Maximal Assistance (subject = 25%+) 1 Total Assistance (subject = less than 25%)	HELPER

	ADMISSION	DISCHARGE	FOLLOW-UP
Self-Care			
A. Eating			
B. Grooming			
C. Bathing			
D. Dressing: Upper Body			
E. Dressing: Lower Body			
F. Toileting			
Sphincter Control			
G. Bladder Management			
H. Bowel Management			
Transfers			
I. Bed, Chair, Wheelchair			
J. Toilet			
K. Tub, Shower			
Locomotion			
L. Walk, Wheelchair	W Walk C Wheelchair B Both	W Walk C Wheelchair B Both	W Walk C Wheelchair B Both
M. Stairs			
Motor Subtotal Rating			
Communication			
N. Comprehension	A Auditory V Visual B Both	A Auditory V Visual B Both	A Auditory V Visual B Both
O. Expression	V Vocal N Nonvocal B Both	V Vocal N Nonvocal B Both	V Vocal N Nonvocal B Both
Social Cognition			
P. Social Interaction			
Q. Problem Solving			
R. Memory			
Cognitive Subtotal Rating			
TOTAL FIM® RATING			

NOTE: Leave no blanks. Enter 1 if patient is not testable due to risk.

Fig. 1. Neurorehabilitation functional assessment. (*Above*) Cognistat Active Form evaluates attention, language, memory, and calculation skills. (*Below*) The Functional Independence Measure (*FIM*) evaluates independence during tasks with regard to self-care, mobility, communication, and social cognition. (Copyright © 1997 Uniform Data System for Medical Rehabilitation, a division of UB Foundation Activities, Inc. Reprinted with permission).

Statistical analysis was performed, with a value of $p < 0.05$ being considered significant. Univariate linear regression analysis was performed when a single response variable was assessed for linear trends. Mean values between two groups were compared using a *t* test. Three or more mean values were compared using an analysis of variance test. Figures were produced using GraphPad Prism v7 (GraphPad Software, Inc., San Diego, Calif.) and Microsoft Excel (Microsoft Corp., Redmond, Wash.).

RESULTS

Of the 143 patients who underwent decompressive craniectomies, 40 patients (28 percent) were clinically diagnosed with syndrome of the trephined. [**See Figure, Supplemental Digital Content 1,** which shows a patient with syndrome of the trephined after craniectomy. (*Left*) Intraoperative view demonstrating large craniectomy defect after skull resection for meningioma and (*right*) postcranioplasty view after polyetheretherketone implant restored normal skull shape resulting in alleviation of syndrome of the trephined symptoms, ***http://links.lww.com/PRS/E94***.] Demographic analysis showed a mean age of 38.4 ± 12.3 years, 60 percent male gender, and comorbidities present in 55 percent, including hypertension (27.5 percent), smoking (10 percent), diabetes mellitus (5 percent), coronary artery disease, arrhythmias, intravenous drug abuse, and gout. Craniectomies were performed because of trauma (37 percent), meningioma (32 percent), hemorrhage (10 percent), or aneurysm (1 percent). Bone grafts were saved from one-third of the trauma cases for reconstruction. Thirty-five percent had a concomitant brain injury and 10 percent had a ventriculoperitoneal shunt.

Diagnosis of syndrome of the trephined was based on the presence of two criteria: (1) history of either slow neurologic deterioration in rehabilitation [$n = 30$ (75 percent)] or an abrupt change in neurologic findings [$n = 10$ (25 percent); and (2) a constellation of symptoms including weakness [$n = 24$ (60 percent)], impaired mentation [$n = 14$ (35 percent)], gait disturbance [$n = 13$ (33 percent)], slowed speech [$n = 12$ (30 percent)], depression [$n = 11$ (28 percent)], altered level of consciousness [$n = 10$ (25 percent)], and headache [$n = 8$ (20 percent)]. On examination, 36 patients (90 percent) had a sunken skin flap and 18 patients (45 percent) had improvement in symptoms with Trendelenburg position (Trendelenburg position will reverse the pressure changes on the cerebrospinal fluid caused by the atmospheric pressure and may alleviate some of the symptoms of syndrome of the trephined). Seizures were seen in seven patients (18 percent) before cranioplasty and in one patient (2.5 percent) after cranioplasty. A midline shift was seen in preoperative magnetic resonance imaging in 34 patients (85 percent).

Size of Cranial Defect

The 143 patients reviewed had craniectomy defects greater than 20 cm^2. All of the 40 patients diagnosed with syndrome of the trephined had defects greater than 50 cm^2. The defect size range for syndrome of the trephined patients was 55 to 105 cm^2, with a mean of 83.2 ± 17.5 cm^2. A larger craniectomy defect size positively correlated with development of syndrome of the trephined (Fig. 2). With a defect size of 55 to 75 cm^2, 15 of 68 patients (22 percent) developed syndrome of the trephined; with a defect size of 76 to 100 cm^2, 19 of 30 patients (63 percent) developed syndrome of the trephined; and with a defect size greater than 100 cm^2, six of six patients (100 percent) developed syndrome of the trephined.

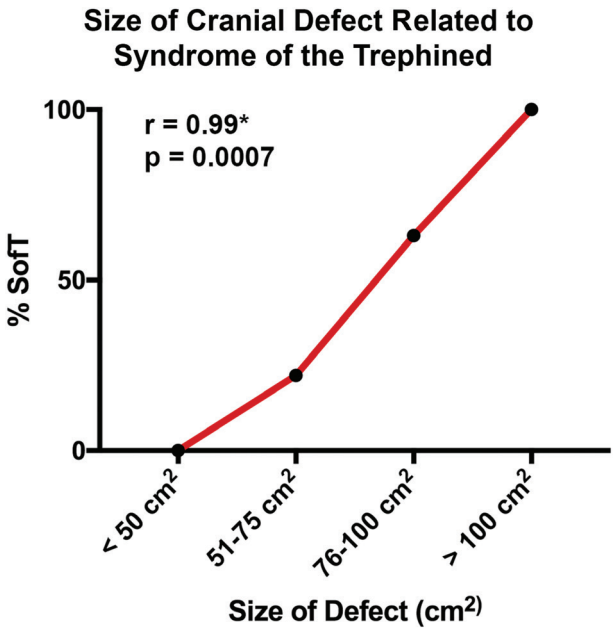

Fig. 2. Graphic depiction of relationship between cranial defect size (in millimeters) and development of syndrome of the trephined (in percent). Development of syndrome of the trephined (*SoFT*) is positively correlated with defect size ($r = 0.99$): under 50 cm^2, no patients ($n = 39$); between 51 and 75 cm^2, 22 percent of patients ($n = 68$); between 76 and 100 cm^2, 63 percent of patients ($n = 30$); and greater than 100 cm^2, all patients developed syndrome of the trephined ($n = 6$) (*$p < 0.05$).

Outcomes in Different Implant Type Used in Reconstruction				
Implant Type	**Percentage of Patients (%)**	**OR Time (min)**	**EBL (cc)**	**Complications (%)**
Split Calvarial Bone	22.5	198	410	0%
PEEK	57.5	104*	240*	17%*
Titanium	20	110*	252*	25%*

Fig. 3. Outcomes based on type of cranial vault reconstruction. Autogenous reconstruction (split calvarial bone) had the longest average operating room (*OR*) times and blood loss, but alloplastic reconstruction (custom polyetheretherketone and titanium implants) had more exposure and more infectious complications. *$p < 0.05$ compared with split calvarial bone. *PEEK*, polyetheretherketone; *EBL*, estimated blood loss.

Type of Reconstruction

When bone graft was not saved from initial decompression (88.2 percent), cranial vault reconstruction consisted of polyetheretherketone implantation (57.5 percent), split cranial bone graft (22.5 percent), and titanium plating (20 percent) (Fig. 3). Type of cranioplasty reconstruction was based on surgeon preference (the craniofacial surgeon preferred split bone reconstruction, whereas neurosurgeons preferred custom polyetheretherketone implants) and other patient-specific factors, including patient preference. Split calvarial bone grafting had the longest operating room time (198 minutes versus 104 minutes and 110 minutes for polyetheretherketone and titanium, respectively) and the greatest blood loss (410 cc versus 240 cc and 252 cc for polyetheretherketone and titanium, respectively). Both polyetheretherketone and titanium mesh implants had higher complication rates, with exposure of implant, infection, and reoperation, compared with split cranial bone graft (17 percent and 25 percent for polyetheretherketone and titanium, respectively, versus 0 percent). No outcome differences were seen between reconstruction options (Fig. 4).

Timing

The mean amount of time from craniectomy to presentation of syndrome of the trephined symptoms was 4.5 ± 1.1 months (range, 2.4 to 7.2 months) (Fig. 5). The mean time from decompressive craniectomy to cranial vault reconstruction was 6.1 ± 1.4 months (range, 3.3 to 9.0 months).

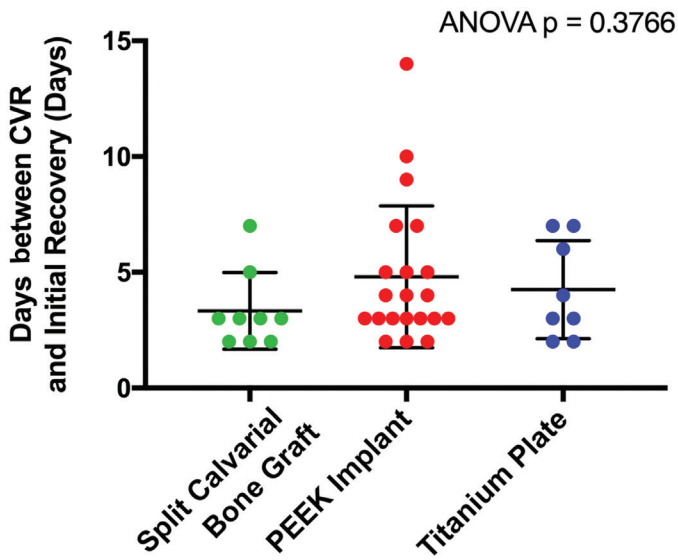

Fig. 4. Resolution of syndrome of the trephined symptoms after different types of cranial vault reconstruction (*CVR*): use of split calvarial bone grafts (*green circles*), polyetheretherketone (*PEEK*) implants (*red circles*), or titanium plates (*blue circles*) did not alter time from cranial vault reconstruction to initial recovery (*circles* represent individual patients). *ANOVA*, analysis of variance.

Timeline of Clinical Events	
Timing: From ➔ To	**Duration**
Craniectomy ➔ SofT Symptoms	4.5 ± 1.1 months
Craniectomy ➔ Cranioplasty	6.1 ± 1.4 months
Cranioplasty ➔ Improvement of Symptoms	4.3 ± 2.6 days
Cranioplasty ➔ Maximum Improvement	6.8 ± 3.3 weeks

Fig. 5. Chart with timing of key clinical events.

The mean time from cranial vault reconstruction to improvement in symptoms of syndrome of the trephined based on neurologic evaluation was 4.3 ± 2.6 days (range, 2 to 14 days); however, two patients did not exhibit improvement. The mean time to the greatest improvement in symptoms after cranial vault reconstruction based on evaluations and neurofunctional tests was 5.2 ± 3.3 weeks.

Functional Assessment

After cranial vault reconstruction, 38 patients (95 percent) showed improvement, with 27 (71 percent) of those who improved showing complete resolution of syndrome of the trephined symptoms and the remaining 11 (29 percent) demonstrating improvement to a lesser degree. Patients who required removal or explantation of alloplastic implants because of exposure or infection redeveloped syndrome of the trephined shortly after removal (n = 6). Protocol required 3 to 6 months before subsequent reconstruction. Secondary cranial vault reconstructions (performed with split cranial bone graft in all but one case) led to resolution of syndrome of the trephined in all patients.

The neurologic functional level of patients improved from the time when the patient had a large cranial defect and syndrome of the trephined to the time when the patient recovered from cranioplasty. The Cognistat Active Form showed improved scoring in all areas, including naming, memory, and judgment (Fig. 6). The mean total preoperative score of 38 ± 9 increased

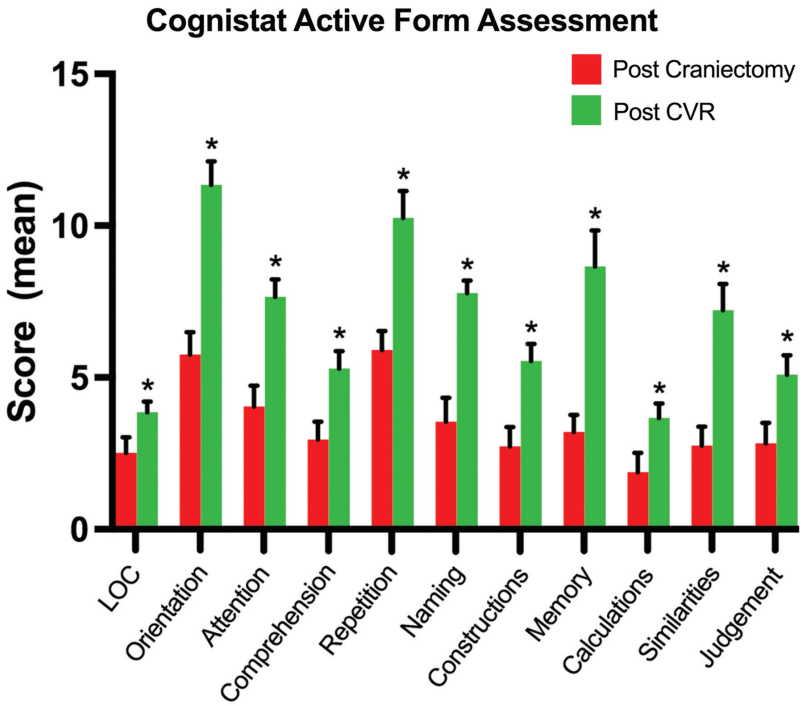

Fig. 6. Cognistat Active Form assessment. Improvement in all mean scores when comparing functional evaluations after (*green*) to before (*red*) cranioplasty (n = 40) (*$p < 0.05$). *CVR*, cranial vault reconstruction; *LOC*, level of consciousness.

to a mean total postoperative score of 69 ± 11. The Functional Independence Measure form (Fig. 7) also resulted in significant improvements in functional scores from a mean score of 38 ± 7 to a mean score of 98 ± 10, such that patients went from a condition of modified/complete dependence (moderate to maximal assist) to near or full independence. The mean follow-up was 28.2 ± 4 months (range, 15 to 41 months).

DISCUSSION

The syndrome of the trephined is a potentially devastating sequela of decompressive craniectomy. This syndrome is seemingly underreported and underdiagnosed. [**See Video (online)**, which shows a visual summary of study with a single patient example of cranioplasty and functional recovery. (Syndrome of the trephined mechanism illustration used from Ashayeri K, Jackson EM. Syndrome of the trephined: A systematic review. *Neurosurgery* 2016;79:525–534 by permission of Oxford University Press.)] Earlier case reports noted an incidence of 1 to 2 percent, whereas recent case reports noted an incidence as high as 24 percent.[5] Patients with syndrome of the trephined may experience a variety of symptoms that impair function and can severely affect their daily lives. Symptoms span from headache to severe mental impairment and can be life-altering. Surprisingly, there are many unanswered questions regarding syndrome of the trephined that may impact patients who would ultimately benefit from corrective surgery. We attempted to address four questions in our clinical outcomes study that involve (1) cranial defect size, (2) timing of development, (3) timing of improvement (after reconstruction), and (4) quantification of neurorehabilitation function.

The pathophysiology behind syndrome of the trephined is understood by related mechanisms of alteration of (1) atmospheric pressure, (2) cerebral blood flow, (3) cerebrospinal fluid flow, and (4) cerebral metabolism.[2,3,5,6] With large craniectomy defects, there is direct transference of atmospheric pressure through the sunken skin flap to the intracranial cavity, causing brain compression. This compression creates changes in cerebrospinal fluid hydrodynamics, such as hypovolemia and decreased pressure.[6,7] There is

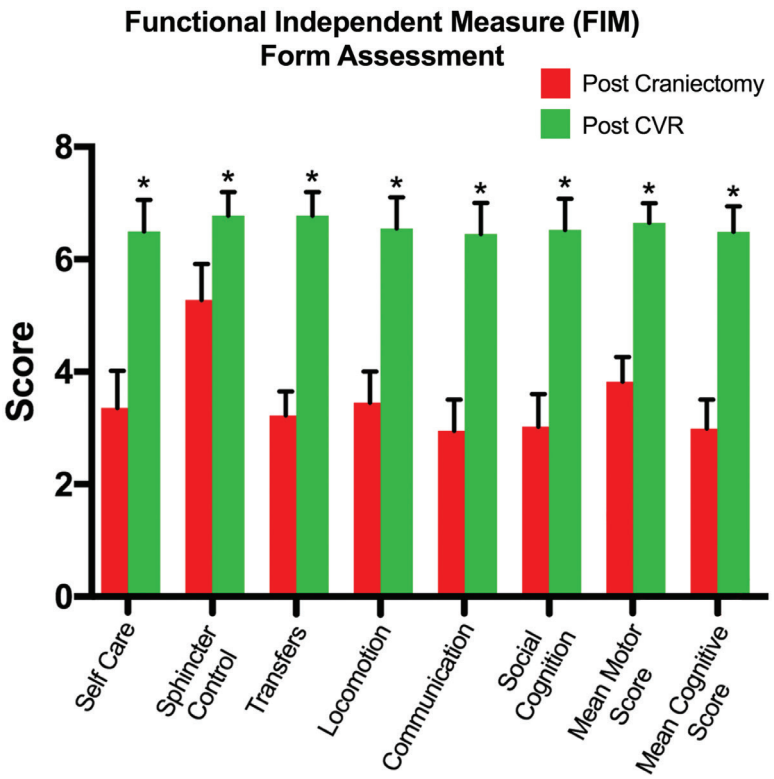

Fig. 7. Functional Independent Measure (*FIM*) assessment. Improvement in mean scores including motor and cognitive scores when comparing after (*green*) to before (*red*) cranioplasty ($n = 40$) (*$p < 0.05$). *CVR*, cranial vault reconstruction.

also compression of cerebral vasculature, venous return impairment, and deformity of intracranial structures.[5,8] This decrease in regional cerebral blood flow, as seen on computed tomographic perfusion studies and xenon computed tomography and magnetic resonance spectroscopy, creates metabolic derangements leading to cortical dysfunction that is manifested as syndrome of the trephined.[7,8] As an extension of these theories of cause, cranioplasty correction should eliminate alterations of atmospheric pressure, cerebral blood flow, cerebrospinal fluid flow, and cerebral metabolism, thereby reversing the syndromic symptoms.[9–11]

Our patients, and patients in other studies, had large craniectomy defects created for pathologic entities, including trauma, infarction, hemorrhage, and infection.[3–5,12] They developed syndrome of the trephined, which presented as symptoms that included weakness, hemiparesis, paralysis, headaches, sensory changes, slowing of speech, impaired mentation, and/or gait disturbances.[5] In our study, development of symptoms manifested as either a gradual deterioration in rehabilitation (75 percent of patient) or an abrupt change in neurologic findings (25 percent of patients).

An exact correlation between craniectomy size and the development of syndrome of the trephined has not been described. Dujovny et al. reported, in a small study of seven patients, an average surface area of 88.3 cm^2 in patients who developed the syndrome of the trephined symptoms.[8] Contrary to other studies, we observed a correlation between defect size and the development of syndrome of the trephined. None of our initial 143 patients observed to have defects smaller than 50 cm^2 ($n = 39$) developed syndrome of the trephined, but all patients with defects greater than 100 cm^2 developed syndrome of the trephined. The mean cranial defect area of our patients with syndrome of the trephined was 83.2 cm^2.

Timing of development of syndrome of the trephined from the time of craniectomy varies greatly in published reports from 3 days to 7 years.[5,12,13] In our patients, it took an average of 4.5 months between craniectomy and syndrome of the trephined symptom development. In other studies, the time interval between craniectomy and the development of symptoms was 5 months.[12,14] Improvement of symptoms after cranial reconstruction may be complete (return to the presyndrome baseline) or partial. Some case reports note immediate reversal with significant clinical improvements in cognition and motor skill, such as improved sensorium, gait balance, memory, speech, and social interaction.[13,15] Ashayeri et al. noted that 34.6 percent of patients experienced complete resolution of symptoms.[12] This appreciable resolution of symptoms occurred at 3.8 days after cranioplasty.[12] We found that the mean time from cranial vault reconstruction to symptomatic improvement was 4.3 days; however, two patients had no improvement. Interestingly, the time to the greatest improvement in symptoms was not until 6.8 weeks. Thus, in our study, many patients took time to gain maximal neurologic benefit. This slower full recovery is different from reports suggesting that complete neurologic recovery occurs between 24 hours and 2 weeks postoperatively.[5,12,14]

Current practice guidelines recommend cranioplasty 3 months after initial craniectomy to let cerebral edema resolve and to allow for hematoma resolution. Some surgeons have a more aggressive timeline and perform the operation at 1 month. Studies suggest that patients with early cranioplasty (<85 days) have a better functional outcome and no difference in complication rates.[16] However, in our study, the mean time to cranial vault reconstruction would not be considered an early cranioplasty at 6.1 months. The mean elapsed time interval in the literature was 9.1 months.

Cranial vault reconstruction options for large decompressive craniectomy defects include autogenous bone grafting (split cranial, rib, or iliac crest) and alloplastic implants (titanium, polymethylmethacrylate, hydroxyapatite components, or other material). Custom-made polyetheretherketone and titanium implants predominated our reconstruction, together accounting for 77.5 percent; split cranial bone grafts accounted for the rest (22.5 percent). When the cranial defect involved the frontal sinus region, we exclusively used bone after cranialization or obliteration of the sinus. Although implants had shorter operating room times and less blood loss, they had more complications, such as exposure, infection, and reoperation. When implants required removal, syndrome of the trephined symptoms returned in all patients and remained until revision surgery could be performed. In our study, all types of structural reconstruction resulted in similar resolution of syndrome of the trephined symptoms. Soft-tissue vascularized coverage is paramount for healing following reconstruction. Local closure with rotation scalp flaps is generally adequate. When wound breakdown occurred over

an implant, removal was performed expediently, whereas exposure over incorporated bone grafts was managed with débridement and reclosure.

More sophisticated neurologic testing now exists that is useful in determining (1) the extent of neurologic recovery after a neurologic event, (2) rehabilitation progress after neurologic surgery, or (3) deterioration during the rehabilitation process. Our patients underwent Cognistat and Functional Independence Measure testing to document the functional neurologic changes associated with syndrome of the trephined and resolution following cranioplasty. Honeybul et al. measured preoperative and postoperative functional and cognitive ability scores on 25 patients undergoing cranioplasty.[11] They were able to demonstrate significantly improved in scores in 16 percent of cranioplasty patients.[11] We were able to show significant improvement in 95 percent of patients after cranioplasty.

In summary, patients with large craniectomy defects are more likely to develop syndrome of the trephined, but the severity of symptoms may not correlate. After any type of cranioplasty (implant or bone), patients with syndrome of the trephined will have symptomologic improvement within days (approximately 5 days), with a maximum neurologic improvement in weeks (approximately 5 weeks). Functional improvements in naming, memory, and judgment (Cognistat Active Form) and in need for assistance (Functional Independence Measure) were quantified after cranioplasty. The retrospective nature and single-center design of this study are limitations that will be addressed with future multicenter prospective studies. Future studies will also focus on additional factors, such as inciting event necessitating craniectomy, location of craniectomy, time from trauma to craniectomy, and radiation status in meningioma patients.

CONCLUSIONS

Syndrome of the trephined is an underdiagnosed sequela of craniectomy with significant neurologic disability. Its reversibility is evident in patients with large cranial vault defects who undergo cranial vault reconstruction. Neurosurgeons and craniofacial surgeons should have heightened suspicion for the diagnosis in the postsurgical craniectomy patient, as appropriate treatment of this sequela can provide significant and life-altering improvements in these patients beyond cosmetic appearance and cerebral protection.

James P. Bradley, M.D.
Division of Plastic and Reconstructive Surgery
Northwell Health Hofstra Zucker Medical School
1991 Marcus Avenue
Lake Success, N.Y. 11042
jpbradley4@mac.com
Instagram: @jamespbradleymd
Facebook: @DrJamesPBradley
Twitter: @DrJamesPBradley

PATIENT CONSENT

The patient provided written consent for use of the patient's images.

REFERENCES

1. Grant FC, Norcross NC. Repair of cranial defects by cranioplasty. *Ann Surg.* 1939;110:488–512.
2. Sedney CL, Dillen W, Julien T. Clinical spectrum and radiographic features of the syndrome of the trephined. *J Neurosci Rural Pract.* 2015;6:438–441.
3. Yamaura A, Makino H. Neurological deficits in the presence of the sinking skin flap following decompressive craniectomy. *Neurol Med Chir (Tokyo)* 1977;17:43–53.
4. Choi JJ, Cirivello MJ, Neal CJ, Armonda RA. Paradoxical herniation in wartime penetrating brain injury with concomitant skull-base trauma. *J Craniofac Surg.* 2011;22:2163–2167.
5. Annan M, De Toffol B, Hommet C, Mondon K. Sinking skin flap syndrome (or syndrome of the trephined): A review. *Br J Neurosurg.* 2015;29:314–318.
6. Fodstad H, Love JA, Ekstedt J, Fridén H, Liliequist B. Effect of cranioplasty on cerebrospinal fluid hydrodynamics in patients with the syndrome of the trephined. *Acta Neurochir (Wien)* 1984;70:21–30.
7. Yoshida K, Furuse M, Izawa A, Iizima N, Kuchiwaki H, Inao S. Dynamics of cerebral blood flow and metabolism in patients with cranioplasty as evaluated by 133Xe CT and 31P magnetic resonance spectroscopy. *J Neurol Neurosurg Psychiatry* 1996;61:166–171.
8. Dujovny M, Agner C, Aviles A. Syndrome of the trephined: Theory and facts. *Crit Rev Neurosurg.* 1999;9:271–278.
9. Richaud J, Boetto S, Guell A, Lazorthes Y. Effects of cranioplasty on neurological function and cerebral blood flow (in French). *Neurochirurgie* 1985;31:183–188.
10. Winkler PA, Stummer W, Linke R, Krishnan KG, Tatsch K. Influence of cranioplasty on postural blood flow regulation, cerebrovascular reserve capacity, and cerebral glucose metabolism. *J Neurosurg.* 2000;93:53–61.
11. Honeybul S, Janzen C, Kruger K, Ho KM. The impact of cranioplasty on neurological function. *Br J Neurosurg.* 2013;27:636–641.
12. Ashayeri K, Jackson EM, Huang J, Brem H, Gordon CR. Syndrome of the trephined: A systematic review. *Neurosurgery* 2016;79:525–534.
13. Joseph V, Reilly P. Syndrome of the trephined. *J Neurosurg.* 2009;111:650–652.
14. Stiver SI, Wintermark M, Manley GT. Reversible monoparesis following decompressive hemicraniectomy for traumatic brain injury. *J Neurosurg.* 2008;109:245–254.
15. Abdou A, Liu J, Carroll M, Vivaldi G, Rizzo JR, Im B. Motor and neurocognitive recovery in the syndrome of the trephined: A case report. *Ann Phys Rehabil Med.* 2015;58:183–185.
16. Cho YJ, Kang SH. Review of cranioplasty after decompressive craniectomy. *Korean J Neurotrauma* 2017;13:9–14.