

Cost differences between autologous and nonautologous cranioplasty implants: A propensity score–matched value driven outcomes analysis

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1. Introduction

Traumatic brain injuries or large-vessel occlusion strokes can lead to the development of medically refractory intracranial hypertension and malignant cerebral edema. Contained within the bony cranium, an engorging brain can become compressed, leading to catastrophic outcomes. Decompressive craniectomy can therefore be a life-saving intervention during states of high intracranial pressure.^{1,2} Once the causal pathology has been sufficiently treated and brain swelling has subsided, a cranioplasty is performed to provide renewed physical protection of neurological structures and to restore aesthetic cranial morphology.³ Traditionally, an autologous cranioplasty is fashioned using the patient's own cranial bone, which was stored in freezers or subcutaneously within the patient's abdominal wall. The bone is prepped and cleaned before being reapproximated and secured to its original place.^{4,5}

Complications such as infection, bone resorption, and skin flap breakdown are commonplace after autologous cranioplasties, with failure rates as high as 40%.^{6–8} To address these shortcomings, synthetic cranioplasty materials such as polymethylmethacrylate, hydroxyapatite implants, titanium mesh, and polyetheretherketone (PEEK) have been

developed. Many of these synthetic implants can be intricately fashioned with computer-aided design techniques that allow for a patient-specific custom fit.^{9,10} Although they are more expensive than autologous bone grafts, custom implants ideally offer multiple advantages, including faster operating times (because they are prefabricated and require no bone retrieval operations or bone preparation), alleviation of bone flap storage complexities, no potential for bone flap resorption, reduced postoperative infection rates, and a more precise fit, which reduces the likelihood of imbalanced skin pressures with resultant skin breakdown.^{6,11–18} These benefits suggest that custom implants could supersede autologous implants as the new gold standard. To this end, a limited number of studies have examined whether the increased initial costs of a custom cranioplasty can be economically justified by reducing the long-term complications, and thus total costs, more commonly observed among autologous grafts.^{11,19,20} Considering the many nuances such as synthetic material type, surface area required, and length of follow-up, it has been difficult to fully address this question. We examined our experience managing patients who underwent autologous or custom cranioplasty and assessed the comparative short- and aggregated long-term costs of the two techniques, using a proprietary institutional cost database. To enhance the robustness of our analysis and

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better isolate the effects of each implant modality, we employed propensity score-matching controlling for known risk factors for cranioplasty failure, an approach that has yet to be utilized in this arena.

2. Methods

2.1. Study cohort

This retrospective study was approved by the institutional review board with a waiver of informed consent. We queried the University of Utah billing records to identify all patient encounters between January 1, 2011, and June 1, 2022, that were coded with Common Procedural Terminology codes corresponding to cranioplasty (62,140, 62,141, 62,143, 62,146, 62,147). All autologous and custom implant types were included. To ensure that no patients were missed, we also reviewed the charts of all patients who had imaging reports with the keyword “cranioplasty.” Duplicate patients and pediatric cases (patients <18 years old) were excluded (Fig. 1). Likewise, all cranioplasties undertaken for reasons other than trauma or stroke were excluded. This was done to control for confounding pathologies like brain tumors, which might impart additional costs and long-term complication events that could bias our results. Lastly, patients were excluded if they were not discharged from the hospital between the hemispherectomy and cranioplasty or if there were no available cost data.

2.2. Assessed variables

Baseline demographics of the patients and clinical characteristics of the hemispherectomy and cranioplasty procedures were collected. These variables included age, sex, race, American Society of Anesthesiologists (ASA) class, and body mass index (BMI); history of diabetes mellitus (DM), hyperlipidemia (HLD), hypertension (HTN), smoking, and alcohol use; and procedures before hemispherectomy, shunts placed before hemispherectomy, ASA class at hemispherectomy, Glasgow Coma Scale (GCS) score at hemispherectomy, interval from hemispherectomy to cranioplasty, cranioplasty operation duration, length of hospital stay after cranioplasty, disposition after cranioplasty, and unplanned reoperation <30 days after cranioplasty. Additional data regarding cranioplasty size and materials and long-term outcomes were collected. These included rates of failure after initial cranioplasties but also after second and third revision operations, if applicable. Rates of implant resorption and infection were captured, and each patient’s length of clinical follow-up was noted.

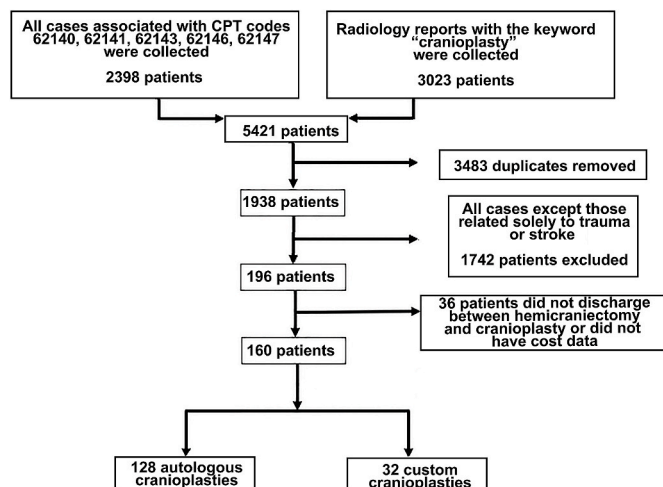


Fig. 1. Patient inclusion diagram.

2.3. Value driven outcomes cost data

The Value Driven Outcomes (VDO) database is an innovative resource that calculates healthcare-related costs based on the prices of instruments, drugs, and medical procedures, instead of patient or insurer charges. Its methodology has been described in previous studies.^{21,22} We employed the VDO tool to capture the relevant cranioplasty costs for the patients identified through the mechanisms described. Recorded cost data included initial cranioplasty total hospitalization costs as well as subsequent cranioplasty-related hospitalization costs. For each hospitalization, subcategory costs of pharmacy, imaging, supplies, laboratory, facility, and other were captured. All cost data are expressed as a percentage of the initial custom cranioplasty hospitalization total cost. Actual dollar amounts are not disclosed because of an agreement with University of Utah Health.

2.4. Statistical analysis

SPSS version 20 (IBM Corp.) was used for statistical analysis. Data normality was assessed using the Wilk–Shapiro test. Student’s T-test or the Mann–Whitney U test was used in assessment of continuous variables per distribution. The Pearson Chi-square test was used for comparison of categorical variables. Linear regression was used to perform multivariate analysis. The multivariate models were adjusted for clinically notable implant failure risk factors.^{23–27} Statistical significance was determined at $\alpha = 0.05$.

A 1:1 “nearest-neighbor” propensity-score matching scheme was completed using the *MatchIt* R package. Matches were based on predictors of cranioplasty failure and included age, interval from hemispherectomy to cranioplasty (days), smoking status, procedures performed before hemispherectomy, implant surface area, and post-operative length of stay.^{23–27} A caliper weight of 0.1 was used. Statistical significance remained at $\alpha = 0.05$.

3. Results

3.1. Unmatched demographic comparisons

A total of 32 patients with custom implants were compared with 128 patients with autologous grafts (Table 1). The custom cohort was more predominantly male (81.3% vs. 60.9%, $p = 0.03$) and had less hypertension (15.6% vs. 36.7%, $p = 0.02$) than the autologous cohort. There were no significant differences in other assessed demographic variables, including age (37.7 vs. 43.1 years), race, median BMI (25.8 vs. 28.4), DM (9.4% vs. 15.6%), HLD (9.4% vs. 20.3%), active smoker (25.0% vs. 28.9%), and alcohol abuse (9.4% vs. 11.7%) (all $p \geq 0.05$).

3.2. Unmatched hemispherectomy and initial cranioplasty management

Patients who underwent custom cranioplasties had a significantly longer median interval (80 days) between hemispherectomy and cranioplasty than autologous patients (61 days, $p = 0.04$) (Table 1). However, other variables were not significantly different between the custom and autologous groups, including procedures before hemispherectomy (18.8% vs. 7.9%), ASA class, mean GCS at hemispherectomy (9.3 vs 9.3), reason for cranioplasty (81.3%/18.8% vs. 64.8%/35.2% trauma/stroke), complication rate between hemispherectomy and cranioplasty (28.1% vs. 28.9%), median cranioplasty operation duration (125 vs. 127 min), disposition, and unplanned reoperation within 30 days of cranioplasty (9.4% vs. 8.6%) (all $p > 0.05$).

3.3. Unmatched long-term outcomes

The rate of initial graft failure was not significantly different between the custom (12.5%) and autologous (23.4%) graft groups ($p = 0.18$)

Table 1
Unmatched and matched comparisons of demographic and clinical variables for initial cranioplasty.

Variable	Unmatched			Matched		
	Autologous (n = 128)	Custom (n = 32)	P value	Autologous (n = 29)	Custom (n = 29)	P value
Age at HC	43.1 ± 15.1	37.7 ± 16.2	0.07	30 (23–50)	39 (24–53)	0.76
Male sex	78 (60.9)	26 (81.3)	0.03	16 (55.2)	24 (82.8)	0.02
Race			0.47			0.23
White	100 (78.1)	27 (84.4)		22 (75.9)	25 (86.2)	
Black	2 (1.6)	1 (3.1)		0	1 (3.4)	
Asian or Pacific Islander	8 (6.3)	0		3 (10.3)	0	
Other	18 (14.1)	4 (12.5)		4 (13.8)	3 (10.3)	
BMI ^a	28.4 (23.5–31.5)	25.8 (23.0–30.8)	0.54	26.1 (23.3–30.2)	25.9 (23.4–30.7)	0.70
DM	20 (15.6)	3 (9.4)	0.37	2 (6.9)	3 (10.3)	0.64
HLD	26 (20.3)	3 (9.4)	0.15	4 (13.8)	3 (10.3)	0.69
HTN	47 (36.7)	5 (15.6)	0.02	9 (31.0)	5 (17.2)	0.22
Active smoker	37 (28.9)	8 (25.0)	0.66	6 (20.7)	7 (24.1)	0.75
Alcohol abuse	15 (11.7)	3 (9.4)	0.71	3 (10.3)	2 (6.9)	0.64
Procedures prior to HC	10 (7.9)	6 (18.8)	0.07	4 (13.8)	6 (20.7)	0.49
Perioperative shunt for HC	26 (20.3)	6 (18.8)	0.84	7 (24.1)	5 (17.2)	0.52
ASA class at HC			0.18			0.36
Class I	3 (2.3)	0		0	0	
Class II	5 (3.9)	4 (12.5)		1 (3.4)	2 (6.9)	
Class III	24 (18.8)	9 (28.1)		4 (13.8)	9 (31.0)	
Class IV	56 (43.8)	12 (37.5)		15 (51.7)	12 (41.4)	
Class V	40 (31.3)	7 (21.9)		9 (31.0)	6 (20.7)	
GCS score at HC	9.3 ± 3.7	9.3 ± 4.3	0.99	7 (6–10)	9 (5–13)	0.34
Time from HC to CP (days) ^a	61 (44–81)	80 (61–131)	0.04	49 (41–80)	80 (57–123)	<0.01
Reason for HC			0.08			0.75
Trauma	83 (64.8)	26 (81.3)		22 (75.9)	23 (79.3)	
Stroke	45 (35.2)	6 (18.8)		7 (24.1)	6 (20.7)	
Interval complication between HC and CP	37 (28.9)	9 (28.1)	0.93	6 (20.7)	8 (27.6)	0.54
CP operation duration ^a	127 (96–142)	125 (90–162)	0.87	124 (100–138)	128 (97–160)	0.45
Length of stay (days) ^a	3 (2–5)	3 (2–4)	0.60	3.0 (2.0–5.0)	3 (1.8–4.5)	0.74
Disposition following CP			0.66			0.29
Home	70 (54.7)	19 (59.4)		18 (62.1)	18 (62.1)	
Rehab	24 (18.8)	4 (12.5)		2 (6.9)	4 (13.8)	
SNF	23 (18.0)	8 (25.0)		5 (17.2)	1 (3.4)	
Long-term acute care	10 (7.8)	1 (3.1)		4 (13.8)	6 (20.7)	
Prison	1 (0.8)	0		2 (6.9)	3 (10.3)	0.64
Unplanned reoperation <30 days after CP	11 (8.6)	3 (9.4)	0.89			

Values reported as number (%), mean ± standard deviation.

Boldface font indicates statistical significance.

ASA, American Association of Anesthesiologists; BMI, body mass index; CP, cranioplasty; DM, diabetes mellitus; GCS, Glasgow coma scale; HC, hemicraniectomy; HLD, hyperlipidemia; HTN, hypertension; SNF, skilled nursing facility.

^a Non-parametric continuous data reported as median (interquartile range).

Table 2
Unmatched and matched comparisons of initial cranioplasty outcomes.

	Unmatched			Matched		
	Autologous (n = 128)	Custom (n = 32)	P value	Autologous (n = 29)	Custom (n = 29)	P value
Initial CP failure	30 (23.4)	4 (12.5)	0.18	5 (17.2)	4 (13.8)	0.72
Median time from CP to failure (days) ^a	170 (56–475)	256 (60–523)	0.60	163 (28–448)	256 (60–523)	0.87
Reason for CP failure						
Infection	16 (12.5)	4 (12.5)	1.00	2 (6.9)	4 (13.8)	0.39
Bone resorption	18 (14.1)	0	0.02	3 (10.3)	0	0.08
CP surface area (cm ²)	152.7 ± 27.3	143.7 ± 40.6	0.14	155 (135–172)	150 (132–164)	0.62
Second CP	29 (22.7)	4 (12.5)	0.20	5 (17.2)	4 (13.8)	0.72
Second CP failure	10 (7.8)	2 (6.3)	0.76	3 (10.3)	2 (6.9)	0.64
Third CP	9 (7.0)	2 (6.3)	0.88	3 (10.3)	2 (6.9)	0.64
Time to last clinical follow-up (months) ^a	5.2 (1.4–19.3)	5.0 (1.1–10.7)	0.26	3.9 (1.1–11.7)	4.9 (1.1–11.6)	0.87

Values reported as number (%) or mean ± standard deviation.

Boldface font indicates statistical significance.

CP, cranioplasty.

^a Non-parametric continuous data reported as median (interquartile range).

(Table 2). Understandably, however, the rates of implant failure resulting from bone resorption were significantly higher in the autologous cohort (14.1%) than in the custom group (0%) (p = 0.02). Differences in other long-term outcomes between custom and autologous groups also failed to reach levels of significance, including median days from cranioplasty to failure (256 vs. 170 days), failure due to infection

(12.5% vs. 12.5%), mean implant surface area (144 vs. 153 cm²), second cranioplasty (12.5% vs. 22.7%), second cranioplasty failure (6.3% vs. 7.8%), third cranioplasty (6.3% vs. 7.0%), and median clinical follow-up (5.0 vs. 5.2 months) (all p > 0.05).

3.4. Unmatched custom graft types

For the initial cranioplasty, 32 patients received custom grafts. In these cases, PEEK was used most often for initial cranioplasty (34.4%), with fewer patients receiving a calcium phosphate graft reinforced with 3D printed titanium (21.9%), titanium mesh (18.8%), porous polyethylene sheet (15.6%), and calcium phosphate bone cement (9.4%) (Supplemental Table 1). In the 33 patients (including both originally autologous and custom grafts) who required a second cranioplasty, titanium mesh was used most frequently (48.5%), followed by calcium phosphate graft reinforced with 3D printed titanium (27.3%), porous polyethylene sheet (12.1%), PEEK (9.1%), and methyl methacrylate (3.0%). In the 11 patients who required a third cranioplasty, titanium mesh was used most often (72.7%), followed by equal numbers of calcium phosphate graft reinforced with 3D printed titanium (9.1%), porous polyethylene sheet (9.1%), and methyl methacrylate (9.1%).

3.5. Unmatched cost analysis of initial cranioplasty implants

Assessment of initial cranioplasty costs found that custom cranioplasties (100%) were significantly more expensive than autologous grafts (46.8%, $p < 0.01$) (Table 3, Fig. 2, top). Cost subcategories with statistically significant differences between groups included implant costs (89.2% vs. 12.2%, $p < 0.01$) and pharmacy costs (3.1% vs. 4.4%, $p = 0.03$). Other subcategories had nonsignificant costs differences, including other costs (1.6% vs. 2.1%, $p = 0.42$), laboratory costs (1.0% vs. 1.0%, $p = 0.55$), imaging costs (0.2% vs. 0.2%, $p = 0.18$), supply costs (2.7% vs. 2.4%, $p = 0.88$), and facility costs (26.0% vs. 24.0%, $p = 0.80$).

3.6. Longitudinal cost analysis of custom vs. autologous implants

After univariate aggregation of all initial and long-term cranioplasty hospital costs, using initial custom cranioplasty hospitalization costs as a baseline, custom cranioplasties remained significantly more expensive than autologous grafts (101.8% custom vs. 58.7% autologous, $p = 0.03$) (Table 3, Fig. 2, bottom). Cost subcategories with significant differences included implant costs (89.2% vs. 18.5%, $p < 0.01$), pharmacy costs (3.2% vs. 12.2%, $p < 0.01$), and imaging costs (0.2% vs. 0.3%, $p = 0.04$). Subcategories that were not significantly different between the two groups included other costs (1.7% vs. 2.9%, $p = 0.07$), laboratory costs (1.0% vs. 1.4%, $p = 0.74$), supply costs (2.8% vs. 3.3%, $p = 0.47$), and facility costs (29.4% vs. 29.5%, $p = 0.23$).

Table 3

Unmatched and matched comparisons of initial and long-term costs reported as median percent of the custom approach (interquartile range).

Costs type	Unmatched			Matched		
	Autologous (n = 128)	Custom (n = 32)	P value	Autologous (n = 29)	Custom (n = 29)	P value
Initial surgery costs						
Other	2.1 (1.0–7.5)	1.6 (1.1–3.8)	0.42	1.6 (0.9–4.5)	1.6 (1.0–4.2)	0.97
Lab	1.0 (0.5–2.0)	1.0 (0.6–2.2)	0.55	1.2 (0.6–3.0)	0.9 (0.6–1.9)	0.37
Pharmacy	4.4 (3.2–6.7)	3.1 (2.2–5.3)	0.03	3.6 (2.2–4.8)	3.3 (2.0–6.1)	0.99
Imaging	0.2 (0.2–0.6)	0.2 (0.1–0.4)	0.18	0.2 (0.1–0.6)	0.2 (0.1–0.4)	0.78
Implant	12.2 (4.9–27.7)	89.2 (24.2–133.6)	<0.01	6.5 (4.2–26.8)	88.5 (30.7–132.5)	<0.01
Supply	2.4 (1.3–5.3)	2.7 (1.4–5.0)	0.88	2.9 (1.4–4.8)	2.9 (1.6–5.4)	0.62
Facility	24.0 (18.8–36.6)	26.0 (17.1–31.2)	0.80	21.2 (19.1–33.9)	26.1 (17.4–31.6)	0.70
Total direct	46.8 (36.0–71.1)	100.0 (76.3–131.5)	<0.01	58.3 (31.8–68.9)	100.0 (76.3–126.6)	<0.01
Initial plus long-term costs						
Other	2.9 (1.2–10.2)	1.7 (1.1–4.1)	0.07	1.7 (1.0–4.9)	1.7 (1.0–4.3)	0.73
Lab	1.4 (0.6–4.1)	1.0 (0.7–2.8)	0.74	1.3 (0.7–3.0)	1.0 (0.7–2.5)	0.32
Pharmacy	12.2 (3.4–9.8)	3.2 (2.3–6.4)	<0.01	3.8 (2.3–7.0)	3.7 (2.2–6.8)	0.41
Imaging	0.3 (0.2–0.7)	0.2 (0.1–0.4)	0.04	0.3 (0.2–0.6)	0.3 (0.1–0.4)	0.41
Implant	18.5 (6.0–46.6)	89.2 (46.0–133.6)	<0.01	44.7 (5.4–112.4)	96.3 (49.6–132.1)	<0.01
Supply	3.3 (1.4–7.2)	2.8 (1.4–7.2)	0.47	2.9 (1.5–5.9)	2.9 (2.1–6.0)	0.76
Facility	29.5 (19.7–65.4)	29.4 (18.7–33.21)	0.23	26.6 (19.3–38.4)	29.9 (21.0–33.2)	0.77
Total direct	58.7 (35.5–136.8)	101.8 (78.2–133.2)	0.03	86.3 (36.5–134.8)	101.9 (78.9–125.5)	0.03

Boldface font indicates statistical significance. Data reported as median percent (interquartile range).

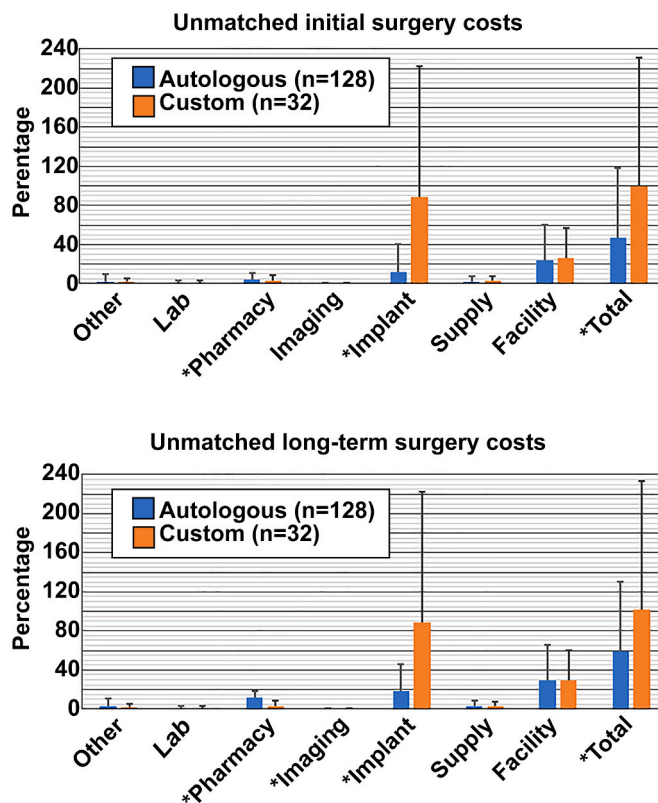


Fig. 2. Unmatched initial (top) and long-term (bottom) hospitalization costs related to cranioplasty surgery are illustrated. For the unmatched initial surgery costs, custom cranioplasty was significantly cheaper in pharmacy costs, but more expensive in imaging and total direct costs. Upon long-term analysis, custom cranioplasty was less costly in pharmacy and imaging costs, but increased in implant and total direct costs (all $p < 0.05$). All costs (initial and long-term) are represented as a percentage of unmatched initial total custom cranioplasty costs (Statistical significance indicated with asterisk.)

A subanalysis was performed to assess whether differences in initial and long-term costs exist depending upon injury cause (i.e., trauma vs. stroke) (Supplemental Table 2). No differences were detected among the custom or autologous cohorts regardless of timeframe (all $p > 0.05$).

3.7. Multivariate analysis of longitudinal total direct costs for autologous and nonautologous implants

Multivariate linear regression was performed to isolate the independent effects of cranioplasty implant type on initial and long-term costs. The model was adjusted for age, sex, smoking status, HTN, GCS, trauma vs. stroke cause, graft surface area, interval (days) from hemi-craniectomy to cranioplasty, cranioplasty operation duration, and length of stay. For initial costs, custom cranioplasty implants were significantly associated with higher costs (standardized $\beta = 0.20$, $p < 0.01$) (Table 4). The other significant contributor to initial cost was length of stay (standardized $\beta = 0.92$, $p < 0.01$). A similar multivariate linear regression was performed for long-term costs (Table 4). Notably, custom cranioplasty was not an independently significant contributor to the aggregated long-term total costs (standardized $\beta = 0.10$, $p = 0.13$), whereas initial cranioplasty operation time (standardized $\beta = 0.13$, $p = 0.03$) and initial cranioplasty length of stay (standardized $\beta = 0.63$, $p < 0.01$) were.

3.8. Matched analysis of demographic and clinical variables

After a 1:1 propensity-score matching based on implant type, 29 patient pairs were available for analysis. Comparisons for baseline demographics and clinical course were performed as previously described (Tables 1–2). Statistically significant differences included custom implants being used more often in male patients (82.8% vs. 55.2%, $p = 0.02$) and a longer interval from hemi-craniectomy to cranioplasty in

Table 4
Unmatched multivariate linear regression for initial cranioplasty and long-term total direct costs (\$).

Variable	Standardized Coefficients	95% confidence intervals		P value
		Lower bound	Upper bound	
Initial surgery total direct costs				
Custom CP	0.20	0.13	0.26	<0.01
Smoker	-0.02	-0.08	0.04	0.52
HTN	-0.03	-0.09	0.04	0.44
Age	0.04	-0.03	0.11	0.23
Male sex	0.00	-0.06	0.06	0.93
GCS score	-0.01	-0.08	0.05	0.68
Reason for HC (stroke)	-0.01	-0.07	0.05	0.80
CP surface area (cm ²)	0.02	-0.04	0.08	0.51
Time from HC to CP (days)	0.02	-0.04	0.08	0.48
CP operative duration (min)	0.03	-0.03	0.03	0.30
Length of stay (days)	0.92	0.86	0.98	<0.01
Initial plus long-term total direct costs				
Custom CP	0.10	-0.03	0.22	0.13
Smoker	-0.02	-0.14	0.10	0.75
Hypertension	0.02	-0.11	0.16	0.76
Age	0.13	0.00	0.27	0.04
Male sex	-0.10	-0.22	0.03	0.12
GCS score	-0.02	-0.14	0.11	0.80
Reason for HC (stroke)	0.00	-0.12	0.13	0.97
CP surface area (cm ²)	0.07	-0.05	0.20	0.25
Time from HC to CP (days)	-0.03	-0.16	0.09	0.59
CP operative duration (min)	0.13	0.01	0.25	0.03
Length of stay (days)	0.63	0.51	0.75	<0.01

For initial cranioplasty costs, $R^2 = 0.87$, $p < 0.01$. For long-term cranioplasty costs, $R^2 = 0.50$, $p < 0.01$. CP, cranioplasty; GCS, Glasgow Coma Scale; HC, hemi-craniectomy; HTN, hypertension. Boldface font indicates statistical significance.

patients undergoing custom cranioplasty (80 vs. 49 days, $p < 0.01$). There were no significant differences in outcomes between the two groups (all $p > 0.05$).

3.9. Matched initial cranioplasty and long-term cost analyses

Univariate analysis of the matched cohorts likewise found custom grafts were more expensive in the initial surgery (100.0% custom vs. 58.3% autologous, $p < 0.01$) and in the long term (101.9% vs. 86.3%, $p = 0.03$) (Table 3, Fig. 3, top). In the matched cohorts, multivariate linear regression also demonstrated that costs for initial surgeries were greater in the custom group (standardized $\beta = 0.56$, $p < 0.01$) but long-term costs were not (standardized $\beta = 0.22$, $p = 0.11$) (Table 5, Fig. 3, bottom).

4. Discussion

Decompressive hemicraniectomy and subsequent cranioplasty surgery are fundamental, life-saving procedures in the care of neurosurgical patients, but rates of implant failure remain quite high. To improve implant longevity, enhance cosmesis, and mitigate complication profile, multiple custom implant materials have been developed. However, the cost implications of these synthetic implants remain insufficiently described, and questions remain as to whether custom grafts are economically justified as a primary treatment. In this study, we compared cranioplasty patients with custom or autologous implants to evaluate for cost differences in the short- or long-term using a well-validated tool that tracks costs at our institution.

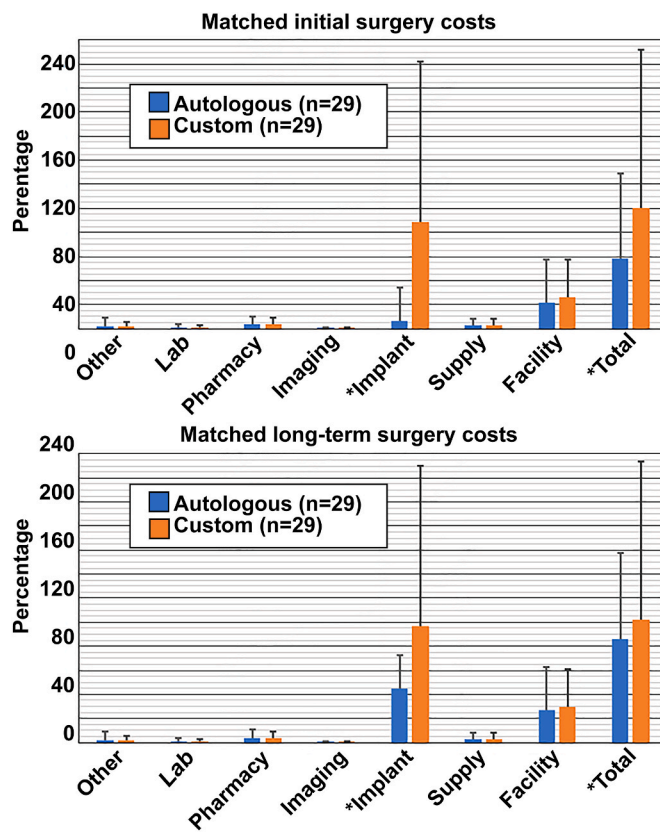


Fig. 3. Matched initial (top) and long-term (bottom) hospitalization costs related to cranioplasty surgery and are shown. For the matched initial surgery costs, custom cranioplasty was statistically more costly for implant and total direct costs. Upon long-term analysis, implant and total direct costs remained statistically more expensive for custom grafts (all $p < 0.05$). All costs (initial and long-term) are represented as a percentage of matched initial total custom cranioplasty costs (Statistical significance indicated with asterisk.)

Table 5
Matched multivariate linear regression for initial cranioplasty and long-term total direct costs.

Variable	Unstandardized Coefficients	95% confidence intervals		P value
		Lower bound	Upper bound	
Initial surgery total direct costs				
Custom CP	0.56	0.39	0.74	<0.01
Smoker	-0.02	-0.21	0.16	0.80
HTN	-0.02	-0.21	0.17	0.84
Age	0.02	-0.18	0.23	0.83
Sex	-0.11	-0.29	0.07	0.24
GCS	-0.18	-0.36	0.01	0.06
Reason for HC (stroke)	0.01	-0.22	0.25	0.92
CP surface area (cm ²)	0.01	-0.17	0.19	0.91
Time from HC to CP (days)	0.12	-0.08	0.32	0.24
CP operative duration (min)	0.04	-0.13	0.21	0.63
Length of stay (days)	0.66	0.47	0.85	<0.01
Initial plus long-term total direct costs^a				
Custom CP	0.22	-0.05	0.49	0.11
HTN	0.18	-0.10	-0.10	0.46
Age	0.16	-0.15	0.48	0.30
Sex	-0.27	-0.53	-0.01	0.04
GCS	-0.15	-0.44	0.13	0.28
Reason for HC (stroke)	0.09	-0.25	0.43	0.60
Cranioplasty surface area (cm ²)	0.04	-0.23	0.32	0.75
Time from HC to CP (days)	-0.01	-0.31	0.30	0.97
CP operative duration (min)	0.21	-0.06	0.47	0.12
Length of stay (days)	0.21	-0.08	0.49	0.16

For initial cranioplasty costs, $R^2 = 0.72$, $p < 0.01$. For long-term cranioplasty costs, $R^2 = 0.32$, $p = 0.03$.

CP, cranioplasty; GCS, Glasgow coma score, HC, hemicraniectomy; HTN, hypertension.

Boldface font indicates statistical significance.

^a Smoking status removed to achieve adequate goodness of fit.

4.1. Cost comparison of custom vs. autologous implants

Our unmatched multivariate cost analysis demonstrated significant differences in favor of autologous grafts in the initial surgery period (custom implants: standardized $\beta = 0.20$, $p < 0.01$) while no statistical difference was observed in the long term (custom implants: standardized $\beta = 0.10$, $p = 0.13$). These findings were replicated upon matched analysis (standardized $\beta = 0.56$, $p < 0.01$; standardized $\beta = 0.22$, $p = 0.11$; respectively). It is difficult to contextualize and directly compare these findings with those of other reports given the limited number of available studies and the heterogeneity in custom implant materials and follow-up protocols. Typically, however, although cost analysis results have been mixed, autologous grafts have often been favored in the short term and custom implants in the long term.

For example, in a randomized controlled trial assessing the cost disparity between titanium implants ($n = 32$) and autologous grafts ($n = 32$), Honeybul et al²⁸ demonstrated that healthcare costs were statistically equivalent in the initial cranioplasty encounter regardless of graft type (\$3281 mean difference in favor of titanium cranioplasty; $p = 0.327$). However, upon 24-month follow-up, this same trial demonstrated a significant cost advantage favoring titanium implants, with average healthcare savings of \$9999 ($p = 0.015$) compared with autologous grafts.²⁹ In an analysis of 33 patients (17 custom and 16 autologous), Lethaus et al³⁰ found that patient-specific implants (10 PEEK, 7 titanium) were more costly than autologous grafts in the initial surgery (€15,532 vs. €10,850); however, once long-term subsequent costs were

factored in, custom implants became the cheaper option (€15,532 vs. €26,086). Conversely, other analyses such as that by Binhammer et al¹⁹ have reported mixed results. In their analysis, titanium mesh grafts were more cost-effective than autologous grafts in the setting of smaller cranial defects; however, autologous materials were more financially favorable for larger defects (>5 cm).

In our analysis, 6 different synthetic material types were used and follow-up was variable.

As reflected in the previously discussed studies,^{19,28,29} the most significant contributor to custom cranioplasty costs in the present analysis were the implants themselves. In the unmatched analysis, custom implants accounted for 89.2% of the total initial custom cranioplasty hospitalization costs. This drastically contrasted with the median percentage cost of autologous grafts, which was only 12.2% of the total initial custom cranioplasty hospitalization costs ($p < 0.01$). Although median initial implant costs were significantly higher in custom grafts, other hospitalization subcategory costs that were statistically equivalent to that of autologous grafts included other costs, laboratory costs, supply costs, and facility costs. Moreover, custom grafts were comparatively significantly cheaper in initial pharmacy costs and imaging costs (although these were still much smaller than the cost of the implants).

4.2. Failure rates

A key element in evaluating cost differences is ensuring that the outcomes in the comparison group are noninferior to those in the control group. Complicating variables related to patient age, cause of the bony defect, condition of the flap or implant, size and location of the cranial defect, or other concurrently existing pathologies can impede proper cranioplasty formation or otherwise predispose to ultimate implant failure.³¹ Partly because of their biological nature and capacity for resorption, autologous implants have demonstrated greater risk of implant failure compared with custom materials.²⁹ In our study, 14.1% of initial autologous cranioplasties failed because of bone resorption (Table 2). Likewise, some custom cranioplasty materials are lauded for their nonbiologic nature and other properties that reduce infection risk.³² For example, PEEK is built with a porous design that facilitates tissue integration, thereby reducing residual empty space that can act as a nidus for infection.³³ In our study, autologous implants generally demonstrated elevated, though statistically insignificantly, rates of initial cranioplasty failure (12.5% custom vs. 23.4% autologous; $p = 0.18$). The lack of significant differences between failure rates is likely a limitation of our study's sample size. However, our autologous failure rate falls within the range of other published reports, which describe autologous cranioplasty failure rates of 7–40%.^{6–8,17,34–36} Significant efforts are being made within both autologous and custom cranioplasty protocols/materials to lessen rates of postimplantation infection, necrosis, and resorption.^{37,38}

4.3. Future directions

Growing clinical evidence strongly suggests that currently available custom materials demonstrate notable clinical advantages over autologous implants.¹⁷ A major concern impeding a more widespread use of custom implants has been related to cost.¹³ Although the present analysis suggests that in select contexts, presently available materials may be economically noninferior to traditional autologous implants, streamlined manufacturing pipelines, on-site 3-D printing, and continued optimization of low-cost graft materials should further reduce custom implant costs and allow for increased popularity as a primary cranioplasty approach.^{39,40}

In all, the mixed results reported in the literature demonstrate the high complexity of cranioplasty cost analysis, which is complicated by highly diverse clinical presentations, varying surgical indications, numerous custom implant materials, and heterogeneity in follow-up

duration. Future, high-quality retrospective meta-analyses or prospective randomized clinical trials with consistent surgical techniques and periprocedural protocols from surgeon to surgeon will be required to adequately characterize the cost profile associated with each graft material and to define the clinical scenarios in which custom or autologous implants yield greater economic advantage. At present, and in the absence of convincing cost data for one approach over the other, the decision to use autologous or custom grafts is left to surgeon and patient discretion, factoring in elements such as bone flap integrity, cosmesis projections, local resources, insurance requirements, and surgeon experience.

5. Limitations

Among this study's limitations, our analysis only included patients who underwent reconstructive cranioplasty after either stroke or trauma. In cases of trauma, our study did not capture fracture severity or type. For this reason, our analysis may conflict with other published reports that may have included patients who required cranioplasty after tumor removal or aneurysm occlusion. Additionally, our study—and particularly our matched comparison—contains a limited sample size, which inhibited our ability to robustly assess wide-ranging cost data or potentially detect differences in failure rates or operative times, increasing the possibility of a type 2 error. Likewise, because of the sample size limitations, we were unable to thoroughly assess the various custom implant materials—e.g., titanium mesh, PEEK—in comparison with one another. Finally, our assessments are largely dependent on the charges for the custom implant. Our analysis may or may not apply to systems where because of competition or other factors different implant cost negotiations have decreased custom graft costs.

6. Conclusion

Our results suggest that during the initial cranioplasty surgery, autologous implants are significantly cheaper; however, upon unmatched and matched analyses, multivariate assessment of long-term costs data suggested that custom cranioplasty may be economically noninferior to autologous grafts. Similarly, patient outcomes were not significantly different in the two groups. From a financial perspective, it may be reasonable to consider custom cranioplasty implants as a primary approach for individuals requiring surgical correction of cranial defects, although more study is required.

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CRediT authorship contribution statement

Matthew Findlay: Writing – original draft, Formal analysis, Data curation. **Sawyer Z. Bauer:** Data curation. **Diwas Gautam:** Data curation. **Matthew Holdaway:** Data curation. **Robert B. Kim:** Writing – review & editing, Conceptualization. **Walid K. Salah:** Formal analysis. **Spencer Twitchell:** Data curation. **Sarah T. Menacho:** Writing – review & editing. **Gurpreet S. Gandhoke:** Writing – review & editing, Formal analysis. **Ramesh Grandhi:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

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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Appendix A. Supplementary data

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Abbreviations

ASA: American Society of Anesthesiologists
 BMI: body mass index
 DM: diabetes mellitus
 GCS: Glasgow Coma Scale
 HLD: hyperlipidemia
 HTN: hypertension
 PEEK: polyetheretherketone
 VDO: Value Driven Outcomes