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The impact of skin allograft on inpatient outcomes in the treatment of major burns 20–50% total body surface area — A propensity score matched analysis using the nationwide inpatient sample[☆]

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ABSTRACT

Background: Human cadaveric skin (allograft) is used in treating major burns both as temporizing wound coverage and a means of testing wound bed viability following burn excision. There is limited information on outcomes, and clinicians disagree on indications for application in intermediate-sized burns. This study aims to improve understanding of allograft use in 20–50% total body surface burns by assessing current utilization and evaluating inpatient outcomes.

Methods: Discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality assessed 3557 major burn patients (>second degree depth and 20–50% TBSA) undergoing operative treatment. Outcomes were evaluated with propensity score matching. The primary outcome was mortality with secondary outcomes including complications, length of stay, total burn operations, and charges.

Results: After matching, 771 allografted patients were paired with 1774 controls. Covariate mean standard differences were all <11% after matching. The average treatment effect (ATE) of allograft on inpatient mortality was an increase of 2.8% (95% CI 0.2–5.3%, p = 0.041). Allograft ATEs were all significantly higher for secondary outcomes: composite complication index increased 0.13 (95% CI 0.07–0.20, p < 0.001), length of stay 8.4 days (95% CI 6.1–1.9 days, p < 0.001), total burn operations 1.6 (95% CI 1.4–1.9, p < 0.001), and total charges $139,476 [$100,716–178,236, p < 0.001).

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Conclusions: Allograft use in major burns 20–50% TBSA was associated with a significant increase in inpatient mortality. There was a notable correlation with increased inpatient complications, longer length of stay, more burn operations, and greater total charges. Better studies are needed to justify the use of this costly and limited resource in the intermediate sized major burn population.

1. Introduction

Early surgical excision and autologous skin grafting remain the standard of care in treating major burns [1]. Survival has dramatically improved since these techniques were adopted in the 1970s with many large burns now being routinely survivable [2]. This paradigm guides treatment at burn centers throughout the world, however the pathway from burn excision to skin grafting is not always linear. Uncertainty in depth of burn [3] and unavailability of donor skin [4] thwart the ability to autograft excised burns. In both scenarios, cadaveric human skin–allograft–can be used to cover excised wound beds. While cultured epidermal allografts have been shown in prospective studies to induce wound healing [5], the same has not been demonstrated with preserved sheet allografts. Retrospective single institution studies comprised of case series and cohorts suggest that allograft offers pain relief and may assist in healing [6].

However, the use of allograft is controversial—even in large burns [7]. While some burn centers routinely use, others refrain completely [8]. Opponents of allograft are critical of associated prolonged hospitalizations and additional operations [3]. Some suggest autografting should always be performed when feasible, and if donor skin is not available, alternative wound coverings ranging from animal skin, to synthetic products, to traditional dressings should be used instead [9]. Additionally, allograft is an expensive treatment option, and is a limited resource because its derivation from deceased humans. [10]. The processing and storing of allograft increases direct costs [11] with additional fees originating from distributer margins, hospital margins, and physician professional fees.

This study aims to improve information on allograft use by assessing utilization in the United States and looking at associated costs and outcomes. Given limited autograft donor sites in burns >50% TBSA, this study aims to focus on the major burn population for which there is sufficient donor skin to covered excised burns. Using a large national representative dataset, the Nationwide Inpatient Sample [NIS), this study will 1) characterize allograft use across the U.S., 2) evaluate clinical outcomes associated with allograft, and 3) determine whether allograft impacts inpatient length of stay and total cost of care.

2. Methods

2.1. Data

The NIS is produced by the Healthcare Cost and Utilization Project (HCUP) with support from the Agency for Healthcare Research and Quality (AHRQ). For each year, this dataset contains 5–8 million inpatient discharges from about 1000 hospitals sampled to approximate a 20% stratified sample of non-federal U.S. hospitals. Information is included from 44 states and the district of Columbia. The NIS sample was weighted to give national estimates and compare hospital types on a national scale. This study included 2002–2011. [12]. This evaluation of de-identified data was determined to be exempt by the institutional review board.

2.2. Cohort

Subjects with burns were identified using diagnosis codes from the International Classification of Diseases (ICD), Ninth Edition. All burn codes were included for the initial cohort (Appendix A). The cohort was narrowed to only those who underwent operative treatment for a major burn. Major burn was defined using the American Burn Association (ABA) definition as any partial or full-thickness burn totaling 20% or greater total body surface area (TBSA) [13]. While smaller 2nd degree and 3rd degree burns may be treated with allograft during the course of treatment, these cases were excluded given smaller operative burns may be treated in the outpatient setting, and thus not captured in an inpatient discharge database. All patients with data missing for TBSA or depth of burn were excluded. The remainder of missing data was coded with a unique dummy variable following standard missing indicator methods [14].

2.3. Variables

Allograft use was identified by ICD-9 procedure code 86.66. Determination of burn-related operations included those undergoing excision (ICD-9 procedure codes 86.22, 86.91) with subsequent autologous tissue coverage (86.60, 86.61, 86.62, 8663, 86.69), xenograft placement (86.65), or use of dermal regenerative matrices (86.67). Patient level variables included: age, gender, %TBSA reported in intervals of 10% (based on ICD-9 codes), deepest burn, payer, and income quartile of patient residence zip code. Hospital-level variables included bed size, trauma center designation, U.S. Census regions and divisions, and a combined variable for teaching status and urban/rural location. Patient comorbidities were categorized based on the Elixhauser comorbidity score [15]. Complications were evaluated using a Patient Safety Indicator (PSI) composite score, as recommended by the Agency for Healthcare Research and Quality (AHRQ) [16]. The PSI variable consisted of post-admission diagnoses with a high-positive predictive value for complications in surgical populations [17]. The composite score (ranging from 1 to 5) included diagnoses related to five domains: hospital-acquired pneumonia, sepsis, venous thromboembolic disease, peri-procedural bleeding, and postoperative wound complications (see Appendix A for ICD-9 codes).

The primary outcome of interest was inpatient mortality. Secondary clinical outcome was measured using the PSI composite score [16]. Secondary health services outcomes included total burn-related operations, length of stay, and total charges.

2.4. Analysis

The proportion of major burn patients receiving an allograft procedure was used to assess variations in allograft utilization. After weighting, data were extracted at the state level and then aggregated into corresponding U.S. Census divisions. Geographic mapping was executed with Tableau (Tableau Software Inc. Seattle, Washington, USA). All baseline variables were evaluated including patient demographics and treating facility characteristics. Multivariable analysis was performed with logistic regression.

The treatment effect of allograft in major burns was evaluated using propensity score matching in order to minimize the effects of confounding by indication [18,19]. Outcomes were compared between the allografted and non-allografted cohorts using the standard reporting metric—average treatment effects (ATE). As the gold-standard comparator in observational studies attempting to adjust for confounding by indication, ATEs are the estimated effect of the entire untreated population receiving a treatment [19,20]. Any outcome variable can be modeled using ATEs; thus, ATEs assume the unit of the outcome of interest. For this analysis, the treatment was allograft, and the primary outcome was mortality (percentage), with secondary outcomes including length of stay (days), total burn-related operations (count), charges (dollars), and complications (composite PSI score). While ATEs yield a result generalizing to the entire burn population, the average treatment effect on the treated (ATET) models the treatment effect only on the allografted patients within the study. We report both ATE and ATET to offer results for the general burn population and comparisons to the patients contained within the NIS database.

The treatment group consisted of all patients who received allograft placement, and the control group consisted of all patients who received operative burn treatment without allograft placement. The modeling was performed using the Stata/IC 14.2 (StataCorp LLC, College Station, Texas, USA) command “teffects psmatch” [21]. All allografted patients were in the exposure group (regardless of timing during inpatient course), while non-allografted patients were in the control group [22]. Crossover was not possible using this paradigm. Covariates were chosen with a non-parsimonious model to account for all eligible variables [23]. For any variable with missing data, an additional “missing data” variable was generated using standard missing indicator methods [14]. The matching ratio was set at minimum 1:1 using greedy nearest-neighbor selection with replacement. The maximum caliper distance was set at 0.2. Regarding ties, because the model allows for replacement, multiple controls may match with cases if the propensity scores were within the caliper distance. This method of matching was used given evidence of bias minimization [24,25]. Standardized mean differences were calculated before and after matching to assess for pairing effectiveness. Additionally, propensity score box plots were generated to evaluate for balance before and after matching.

2.5. Sensitivity analysis

In order to further parse our results, we performed a sensitivity analysis evaluating our primary and secondary outcomes over

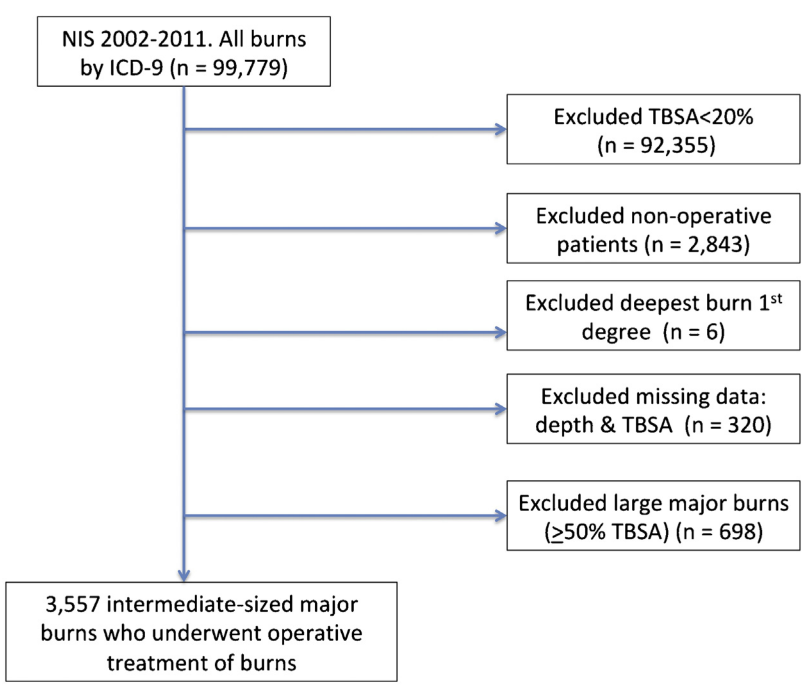

Fig. 1 – Inclusion and exclusion flow diagram for selecting the cohort of acute major burn patients who underwent surgical treatment.

Table 1 – Baseline variables with logistic model for allograft vs. no-allograft in major burns 20-50% TBSA.

	Allograft n=771	No-allograft n=2786	Odds ratio	95% Confidence interval	p-value
Age, mean (SD)	39.9 (23.0)	36.42 (21.11)	1.00	1.00–1.01	0.374
Gender					
Female, n (%)	351 (45.5%)	1,201 (43.1%)	1.26	1.05–1.53	0.015
TBSA					
20-29%	391 (50.7%)	1701 (61.1%)	Ref		
30-39%	193 (25.0%)	760 (27.3.%)	1.05	0.86–1.28	0.648
40-49%	187 (24.3%)	325 (11.7%)	2.46	1.97–3.07	<0.001
Deepest depth					
Second degree	71 (9.2%)	547 (19.6%)	Ref		
Third degree	700 (90.8%)	2239 (80.4%)	2.09	1.59–2.75	<0.001
Inhalation injury	23 (3.0%)	65 (2.3%)	1.39	0.83–2.33	0.204
Elixhauser comorbidity					
<1	428 (55.5%)	1923 (69.0%)	Ref		
2	178 (23.1%)	486 (17.4%)	1.44	1.16–1.79	0.001
3	95 (12.3%)	221 (7.9%)	1.51	1.13–2.01	0.005
>4	70 (9.1%)	156 (5.6%)	1.56	1.12–2.16	0.009
Race					
White	350 (45.4%)	1274 (45.6%)	Ref		
Black	102 (13.2%)	340 (12.2%)	1.21	0.93–1.59	0.158
Hispanic	105 (13.6%)	298 (10.7%)	1.07	0.80–1.43	0.635
Other	47 (6.1%)	158 (5.7%)	1.26	0.87–1.82	0.229
Missing	167 (21.7%)	716 (25.7%)	0.87	0.70–1.10	0.245
Payer					
Medicare	143 (18.6%)	337 (12.1%)	Ref		
Medicaid	198 (25.7%)	747 (26.8%)	0.69	0.50–0.95	0.022
Private	223 (28.9%)	875 (31.4%)	0.71	0.52–1.18	0.620
Self-pay	71 (9.2%)	321 (11.5%)	0.58	0.40–0.85	0.005
Pay other	128 (16.6%)	481 (17.3%)	0.66	0.48–0.91	0.012
Missing	8 (1.0%)	25 (0.9%)	0.97	0.41–2.34	0.592
Income quartile					
1	223 (28.9%)	866 (31.1%)	Ref		
2	157 (20.4%)	718 (25.8%)	0.79	0.62–1.01	0.060
3	169 (21.9%)	509 (18.3%)	1.20	0.94–1.53	0.148
4	133 (17.3%)	276 (9.9%)	1.48	1.12–1.96	0.006
Missing	89 (11.5%)	417 (15.0%)	0.97	0.72–1.31	0.846
Bed-size					
Small	22 (2.9%)	170 (6.1%)	Ref		
Medium	212 (27.5%)	466 (16.7%)	5.21	3.08–8.83	<0.001
Large	537 (69.7%)	2,150 (77.2%)	2.79	1.69–4.60	<0.001
Geography					
Northeast	70 (9.1%)	402 (14.4%)	Ref		
Midwest	145 (18.8%)	592 (21.3%)	1.53	1.09–2.14	0.014
South	327 (42.4%)	1,361 (48.9%)	1.13	0.84–1.53	0.412
West	229 (29.7%)	431 (15.5%)	3.44	2.48–4.78	<0.001
Trauma Center	80 (10.4%)	183 (6.6%)	1.71	1.27–2.30	<0.001

SD, Standard deviation; C-statistic 0.86.

a range of burn severities. Using the Abbreviated Burn Severity Index (ABSI) [26,27,28] calculated in standard fashion, we stratified our results by literature derived inflection points in survival. The propensity score matching models were executed in the same fashion as original model drawing both cases and controls from a pool meeting the definitions. We report the ABSI intervals 2-5 (low-moderate threat to life), 6-9 (moderately severe to serious), and >10 (severe).

3. Results

A total of 99,779 acutely burned patients were identified in the NIS from 2002–2011 (Fig. 1). After excluding burns <20% TBSA, burns >50% TBSA, non-operative patients, deepest burns first degree, and those with missing data for depth or TBSA, 3557 patients were included in the cohort. A total of 771 patients received allograft during their admission while 2786 patients did not. Baseline patient and treating facility characteristics were assessed with multivariable analysis (Table 1); the multivariable logistic regression yielded a C-statistic of 0.86.

Patient characteristics independently associated with increased allograft use included female gender, burns 40–49% TBSA, deepest burn third degree, Elixhauser comorbidity scores greater than one, and income in the highest quartile. There was decreased allograft use with Medicaid as payer. Treating hospital characteristics independently associated with allograft use included medium to large hospital size, trauma centers, the Midwest Census Region, and the West Census Region. Further analyzing weighted regional differences at the level of U.S. Census Divisions showed wide variation across the country (Fig. 2). The region of lowest use was Division 4 (West North Central) at 18.3%, while Division 8 (Pacific) used allograft the most frequently in 36.2% of cases.

Unadjusted outcomes between the two cohorts (before matching) showed higher mortality in the allografted group along with longer length of stay, more operations, a worse composite patient safety indicator index, and increased charges (Table 2). These figures do not account for confounding; therefore, comparative statistics were not performed.

After propensity score matching, all 771 allografted patients had at least one match within the designated caliper distance. Of the 2786 controls, 1774 met matching criteria, which generated 2757 matches (Fig. 3). Standardized mean differences (SMD) were compared before and after matching to assess for covariate balance (Table 3). Pre-match, many covariates had SMDs over 0.1 with some upwards of 0.3, such as TBSA 40–49%. Post-match, SMDs were below 0.11. This confirmed robust and effective matching. The box plot of propensity scores before and after matching demonstrated the initial propensity towards allograft use, with balance after matching (Fig. 4).

There was a significant increase in mortality for patients receiving allograft, with an average treatment effect (ATE) of 2.8% (95% CI 0.2–5.3%, p=0.041)(Table 4). Evaluating secondary outcomes, the use of allograft was associated with a significantly longer length of stay by 8.4 days (95% CI 6.1–10.7, p<0.001), more total burn operations by 1.6 operations (95% CI 1.4–1.9, p<0.001), higher charges at $139,476 (95% CI $100,716–$178,236, p<0.001), and greater composite PSI score at 0.13 (95% CI 0.07–0.20, p<0.001). The average treatment effects on the treated (ATET) were similar with the same pattern of significance.

Stratifying by ABSI, the overall mortality increase associated with allograft was only present in the higher ABSI group (i.e.>10), with a 9.2% increase (95% CI 1.0–17.3%, p=0.028) (Table 5). The other cohorts saw no significant differences. The ABSI <5 cohort yielded an insignificant mortality decrease of

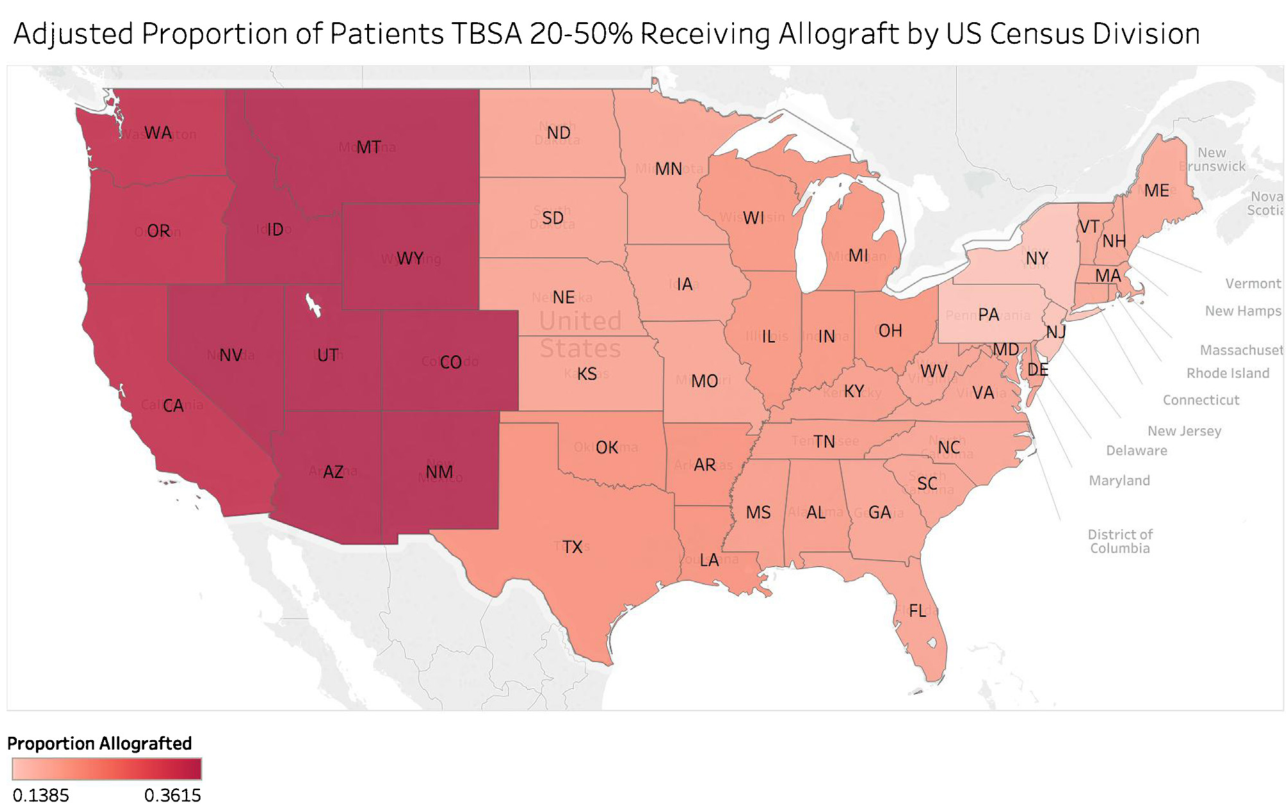

Fig. 2 – Proportion of major burn patients who received allograft during their inpatient burn treatment. Data were pulled from available states and aggregated into U.S. census divisions. Note that only 44 states are represented in the NIS, and thus data should only be interpreted at the census level.

Table 2 – Unadjusted outcomes between allografted and non-allografted patients.

Outcome	allograft (n=771) Mean (SD)	non-allograft (n=2786) Mean (SD)
Inpatient mortality, n (%)	88 (11.4%)	179 (6.4%)
Length of stay (days)	39.0 (28.2)	26.0 (22.0)
Total burn operations	4.0 (2.3)	2.1 (1.7)
Charges (U.S. dollars)	$407,724 ($34,791)	$218,108 ($26,361)
Composite PSI	0.57 (0.74)	0.33 (0.60)

SD, Standard deviation.
PSI, Patient safety indicator.

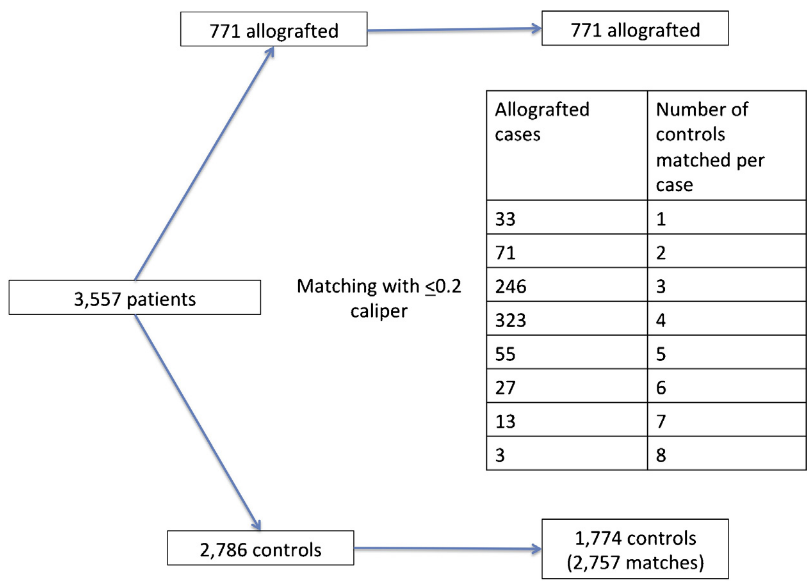

Fig. 3 – Matching diagram.

−1.3% (95% CI −2.8-0.1%, p=0.078), and the ABSI 6-9 cohort showed an insignificant mortality increase of 0.7% (95% CI −1.8-3.3%, p=0.541). The secondary outcomes were all significantly higher in the allografted group regardless of ABSI stratification.

4. Discussion

Similar to prior single institution studies [3], this national analysis demonstrated heightened odds of allograft use in larger and deeper burns. Specifically, the odds of receiving allograft were significantly higher when TBSA was 40-49%. With third degree burns, the odds of being allografted were over 2 compared to partial thickness injuries. Regarding other patient factors, novel findings include greater odds of allograft use in women and patients from higher socioeconomic backgrounds. While there are no obvious explanations for these patterns; perhaps in these populations, burn surgeons have less tolerance for failed autografts, and thus are more conservative in autografting timing. Of note, allograft use was not associated with age, inhalation injury, payer status, or race. Patients with elevated Elixhauser comorbidity scores showed increased odds of allograft use.

In terms of treatment facility factors, as the first national evaluation of allograft, the study demonstrated independent predictors of use including trauma center status and larger-sized facilities. The higher use of allograft at larger trauma centers could possibly result from greater access to allograft. Many ABA verified burn centers are connected with trauma centers, so this could also reflect a preference of burn centers, although this data cannot confirm this hypothesis. Repeating a similar analysis with the National Burn Repository [29] could help answer whether ABA verified burn centers are more likely to use allograft.

Regarding the impact of allograft use on inpatient survival, this analysis showed an increase in mortality with allograft use when matching for demographics, comorbidities, and burn characteristics. Stratifying by ABSI-a validated predictor of burn survival-this finding was only consistent with more morbid burns. In those with ABSIs less than ten, there was no significant difference in inpatient mortality. While the overall model demonstrated a 3.2% increase in mortality, the higher ABSI group showed nearly a 9.2% increase in inpatient death. Prior research from Fletcher et al. likewise showed increased mortality associated with allograft use [3], even through their study lacked adjustment for patient demographic and burn characteristics and did not stratify by burn severity. For secondary outcomes, similar to Fletcher et al. study, this analysis showed a significantly longer inpatient stay, more operations, and more complications when allograft was used regardless of ABSI.

Table 3 – Standardized Mean Differences Before and After Matching.

Variable	Standardized mean differences		Absolute reduction
	Raw	Matched	
Age	0.16	0.02	0.13
Female	0.10	−0.03	0.13
TBSA			
20-29%	−0.21	−0.01	0.20
30-39%	−0.05	0.11	0.16
40-49%	0.33	0.02	0.32
Deepest depth			
Second degree	−0.37	−0.04	0.33
Third degree	0.30	0.02	0.28
Inhalation injury	0.04	0.01	0.03
Elixhauser comorbidity			
<1	−0.28	−0.03	0.25
2	0.14	0.02	0.12
3	0.15	0.03	0.11
>4	0.13	0.02	0.11
Race			
White	−0.01	−0.02	0.01
Black	0.03	−0.02	0.05
Hispanic	0.09	−0.09	0.18
Other	0.02	0.00	0.02
Missing	−0.10	0.05	0.15
Payer			
Medicare	0.18	−0.01	0.19
Medicaid	−0.03	−0.01	0.02
Private	−0.05	−0.08	0.03
Self-pay	−0.08	0.02	0.10
Other	−0.02	0.03	0.05
Missing	0.01	0.07	0.05
Income quartile			
1	−0.05	0.01	0.06
2	−0.13	0.07	0.20
3	0.09	−0.04	0.13
4	0.22	−0.04	0.25
Missing	-0.10	−0.08	0.02
Bed-size			
Small	−0.16	−0.02	0.14
Medium	0.26	−0.02	0.28
Large	−0.17	0.05	0.22
Census division			
Northeast	−0.17	−0.02	0.15
Midwest	−0.29	−0.07	0.21
South	−0.04	0.06	0.11
West	−0.04	0.00	0.04
Trauma center	0.14	0.04	0.10

TBSA, Total body surface area.

While there is no clear explanation for these results, we conceive two hypotheses that may explain the observed findings. For one, allograft is known to cause a hostile reaction from the recipient given the immunologic mismatch [30]. This could weaken immune defenses and make patients more susceptible to infections and subsequent death [11]. Given available data, we attempted to capture this with patient safety indicators, which were all higher with allograft use. The

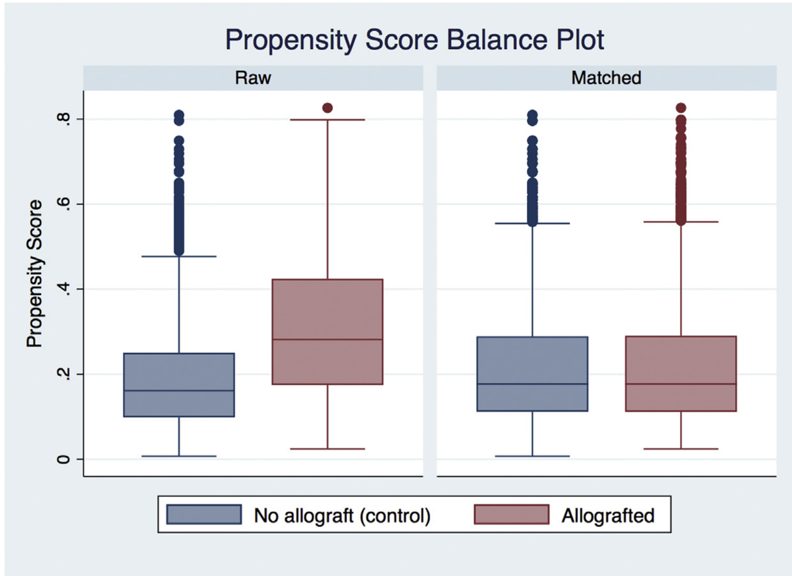

Fig. 4 – Propensity score balance plots before and after matching. Whiskers denote the 5th and 95th percentiles, boxes represent 25th and 75th percentiles, and dots reflect outliers. The horizontal inner lines are medians.

Table 4 – Treatment effects of allograft in major burns.

Outcome	ATE (95% Confidence interval)	p-value	ATET (95% Confidence interval)	p-value
Inpatient mortality (%)	2.8% (0.2–5.3%)	0.041	3.7% (0.1–7.0%)	0.022
Length of stay (days)	8.4 (6.1–10.7)	<0.001	9.3 (6.06–12.5)	<0.001
Total burn operations	1.6 (1.4–1.9)	<0.001	1.7 (1.4–1.9)	<0.001
Charges (U.S. dollars)	$139,476 (100,716–178,236)	<0.001	$135,960 (90,127–181,793)	<0.001
Composite PSI	0.13 (0.07–0.20)	0.001	0.16 (0.08–0.24)	0.001

ATE, Average treatment effects; ATET, Average treatment effects on treated; PSI, Patient safety indicator. Outcomes between the allografted and non-allografted cohorts were compared using average treatment effects (ATE). ATEs are the estimated effect of the entire untreated population receiving a treatment. Any outcome variable can be modeled using ATEs; thus, ATEs assume the unit of the outcome of interest. While ATEs yield a result generalizing to the entire burn population, the average treatment effect on the treated (ATET) models the treatment effect only on the patients within the study. We report both ATE and ATET to offer results for the general burn population and comparisons to the patients contained within the NIS database.

reason why mortality was not significantly increased in the lower ABSI cohort could possibly be explained by the overall lower mortality risk, and smaller surface area of allograft burden in this group. Additional research is needed to evaluate this finding.

We also hypothesize an indirect cause of increased mortality from allograft use. Given that allograft plays an intermediary role between burn excision and definitive coverage, the association between allograft use and prolonged inpatient stay and more operations is logical. This increased time in the hospital translates into more costly care and more frequent returns to the operating room. While some mention [3] allograft use as a means of avoiding re-grafting and potentially decreasing the need for repeated surgery, this study showed actually less total burn operations when avoiding allograft use. The increase in PSI composite with allograft use could result from by increased exposure to complications from prolonged inpatient stay and more returns to the OR. While this study cannot ascertain why surgeons chose allograft for any particular patient, it does suggest that abstaining from allograft when feasible may decrease complications and decrease health resource utilization—without impacting inpatient mortality.

The regional variation across the U.S.–even when controlling for other factors–suggests that allograft use is preference sensitive [31], i.e. surgeon choice dictates use more than patient indicators. Even in large burns which were excluded from this study, survey data suggest that excision and immediate autografting is the most common strategy for burns >20% TBSA, with 34.9% of centers using this approach compared to 22.9% preferring allograft placement as an intermediary surgery [8]. The differences in allograft use across the country could be explained by variability in surgeon comfort on autograft timing. For intermediate sized burns (20–50% TBSA) burn depth uncertainty is the most frequent reason cited for allograft use [3], which is not surprising given inter-rater diagnostic agreement among burn surgeons ranges from 64–76% [32]. While no burn surgeon should err on over-

Table 5 – Treatment effects of allograft stratified by abbreviated burn severity index.

Outcome	ATE (95% Confidence interval)	p-value
ABSI ≤ 5		
Inpatient mortality (%)	−1.3% (−2.8–0.1%)	0.785
Length of stay (days)	9.5 (7.4–11.6)	<0.001
Total burn operations	1.6 (1.4–1.8)	<0.001
Charges (U.S. dollars)	$125,330 (88,873–161,787)	<0.001
Composite PSI	0.10 (0.01–0.20)	0.037
ABSI 6–9		
Inpatient mortality (%)	0.7% (−1.8–3.3%)	0.541
Length of stay (days)	11.6 (8.9–14.3)	<0.001
Total burn operations	1.6 (1.4–1.8)	<0.001
Charges (U.S. dollars)	$173,361 (135,125–211,597)	<0.001
Composite PSI	0.19 (0.11–0.28)	0.001
ABSI ≥ 10		
Inpatient mortality (%)	9.2% (1.0–17.3%)	0.028
Length of stay (days)	9.6 (4.5–14.7)	<0.001
Total burn operations	2.0 (1.6–2.4)	<0.001
Charges (U.S. dollars)	$151,514 (88,057–214,973)	<0.001
Composite PSI	0.16 (.01–0.33)	0.042

ATE, Average treatment effects; PSI, Patient safety indicator.

excision, there is a delicate balance in becoming too comfortable with deferring autografting at the cost of prolonging inpatient stay, increasing the risk of complications, and subjecting patients to additional general anesthesia and surgery—not to mention the increased costs and utilization of healthcare resources. For larger burns where no donor skin is available, the use of allograft is less controversial, and additional studies could evaluate the comparative effectiveness of different strategies in burn treatment,

The study is limited by its retrospective nature and use of a national database. The accuracy of data is limited by the NIS methodology including facility-level diagnosis and procedure coding. Missing data varies and can be statistically problematic with large databases such as the NIS [33]. This problem was alleviated by including a missing data value for all covariates and including it in the regression analysis and propensity score models. This study evaluated national data, and thus reflects the entire U.S. population treated for burns as opposed to only ABA verified burn centers. Given that nearly 40% of burn patients are not treated at verified burn centers [34], evaluating both verified and non-verified centers gives a more accurate assessment of U.S. burn care. Conclusions should be considered in this context.

Regarding comparisons in regional variation, as a sampled database, HCUP recommends cautious analysis, and dissuades state level comparisons altogether [35]. However, at the level of U.S. Census Divisions, HCUP explains that their sampling methods are sufficient to inform analysis when weighted properly [36]. Burn care uniquely aggregates into specialized centers, which may or may not be represented equally in the NIS. Attempts at hospital identification are prohibited by HCUP, precluding the ability to ascertain whether sampling biases effect the representation of regional burn centers by U.S. Census Divisions. Therefore, our regional analysis should be interpreted with this limitation.

Allograft is certainly not the only intermediate in covering excised burns. Xenograft (ICD-9 86.65) and artificial dermal matrices (ICD-9 86.67) such as Integra may be used as temporary wound coverage. Our data revealed relatively low use of both, and thus were not included in the analysis. A randomized controlled trial would offer the greatest detail in answering the question of allograft effectiveness in burn survival. However multiple barriers including limited funding make this unlikely. Prospective comparative effectiveness research, directly comparing allograft to other strategies could further elucidate the best means of acute burn surgical treatment. The results of this study do not support abstaining from allograft use altogether. Instead, burn surgeons should be aware of the treatment effects of allograft including its association with mortality, complications and increase health services utilization.

5. Conclusion

After adjustment, allograft use in major burns 20–50% TBSA varied widely across the U.S. and was associated with an increase in inpatient mortality, which was significant in those patients with ABSI scores >10. There was also a notable correlation with increased inpatient complications, longer length of stay, more burn operations, and greater total charges regardless of ABSI score. This analysis suggests that better studies are needed to justify the use of this costly and limited resource in the intermediate sized major burn population.

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Appendix A.

- ICD-9 codes for burns.
  - 940*
  - 941*
  - 942*
  - 943*
  - 944*
  - 945*
  - 946*
  - 948*
  - 949*
- Burn surgical codes.
  - 86.22: Excisional debridement of burn.
  - 86.6: Generic skin graft.
  - 86.60: Skin graft NOS.
  - 86.61: FTSG to hand.

- 86.62: Other skin graft to hand.
- 86.63: FTSG to other.
- 86.65: Xenograft.
- 86.67: Dermal regenerative graft.
- 86.69: Other skin graft.
- 86.91: Excision of skin for graft.

- ICD-9 codes for Patient Safety Indicator composite.
  - Thromboembolic disease (PSI 12).
    - 453.4, 453.40, 453.41, 453.42, 453.8, 453.9.
  - Pneumonia related to hospitalization (PSI 4).
    - 482.0, 482.1, 482.2, 482.3, 482.30, 482.31, 482.32, 482.39, 482.4, 482.40, 482.41, 482.42, 482.49, 482.8, 482.81, 482.82, 482.83, 482.84, 482.89, 482.9, 485, 486, 507.0.
  - Sepsis (PSI 13).
    - 038.0, 038.1, 038.10, 038.11, 038.12, 038.19, 038.2, 038.3, 038.40, 038.41, 038.42, 038.43, 038.44, 038.49, 038.8, 038.9, 785.52, 995.91, 995.92.
  - Postop bleeding (PSI 9).
    - 998.12, 998.11, 998.1.
  - Wound complications (PSI 14).
    - 996.55, 998.3, 998.30, 998.32, 998.33, 998.5, 998.51, 996.59, 998.83, 998.9.

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