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The Metabolic Impact of Biodegradable Temporizing Matrix in Burn Patients: A Retrospective Analysis of Resting Energy Expenditure and Inflammation

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Abstract

Severe burn injuries induce a hypermetabolic state, significantly increasing resting energy expenditure (REE) and systemic inflammation, which can impact wound healing and patient recovery. Biodegradable temporizing matrix (BTM), a synthetic polyurethane dermal substitute, has been increasingly used for large TBSA burns, yet its metabolic effects remain unclear. This retrospective cohort study analyzed burn patients from 2013 to 2022 who underwent metabolic cart measurements following excision and wound coverage with autograft, allograft, or BTM. Mixed-effects linear regression modeling was performed to assess the impact of wound coverage type on REE and C-reactive protein (CRP) levels over time. Among 226 patients, those receiving BTM had significantly higher REE (+403.5 kcal, $P < .05$) compared to allograft when considering all-time points. However, when restricting analysis to 2-8 weeks post-excision, REE differences were not significant, while CRP levels were significantly lower in the BTM (−3.07 mg/dL, $P = .0388$) and autograft (−3.32 mg/dL, $P = .0107$) groups relative to allograft. These findings suggest that BTM use is associated with increased metabolic activity but a reduced inflammatory response over time. The observed differences in metabolic and inflammatory profiles provide insight into the biologic impact of BTM and support further investigation into its role in optimizing burn wound management and recovery.

Key words: burns; hypermetabolism; resting energy expenditure; biodegradable temporizing matrix; C-reactive protein.

INTRODUCTION

Burn injuries impose substantial physiological stress, triggering hypermetabolic responses as the body attempts to recover from trauma. Following significant burn trauma, patients exhibit a marked increase in resting energy expenditure (REE), with caloric needs escalating between 20% and 100%, depending on the severity of the burn.[1] This hypermetabolic state is linked to elevated energy losses, malnutrition, and delayed wound healing.[2] As such, appropriate interventions to modulate this metabolic response are crucial. One such intervention involves the use of a metabolic cart, a device designed to measure REE, which allows clinicians to better understand the patient's metabolic status and adjust nutritional and therapeutic strategies accordingly. Resting energy expenditure has been shown to be increased in larger TBSA burns, males, and nonsurvivors.[1] Another variable that provides insight into burns' impact is C-reactive protein (CRP), a biomarker of inflammation that has been shown to correlate with the size of burns,[3] mortality[4] and is positively associated with increased metabolism in burn patients and the critically ill.[2,5]

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Biodegradable temporizing matrix (BTM), a synthetic polyurethane matrix, has emerged as a novel tool for temporarily covering large TBSA burns. Its role in modulating the metabolic impact of burns, specifically in comparison to traditional autografting techniques, is unknown. While BTM provides an essential physical barrier for wound management, there is anecdotal evidence and some scientific evidence of patients receiving BTM having a different trajectory with improved mobility, quicker progression with therapies, improved mental status, improved wound bed stabilization in a single case report,[6] reduced infections,[7] improved skin graft take, and it has also been shown to be an excellent wound bed for cultured epithelial autografts when combined with widely meshed autograft.[8] While there is a lack of rigorous evidence to support these claims, our group is consistently using BTM for large TBSA burns, frail patients who need staged procedures, and more complicated wounds with exposed structures such as tendon, bone, or cartilage with reasonable outcomes.

Despite these encouraging outcomes from our single institution's anecdotal experience, the biologic underpinnings of why patients treated with BTM appear to recover their physiology faster and have improved clinical parameters than those without it remain a mystery. Clinical observations suggest that patients treated with BTM demonstrate improved recovery and expedited mobilization[9]; however, there is a lack of robust evidence to substantiate these claims. Understanding these mechanisms could pave the way for better burn care and improved patient outcomes, especially in massive TBSA burns. Thus, the aim of this study is to assess the impact of BTM on resting energy expenditure and determine whether there is a significant difference in metabolic rates between patients receiving BTM versus those treated with autografts or allografts following their initial excision procedure.

METHODS

After local institutional board approval, a retrospective cohort study was performed on adult burn patients admitted from December 2013 to November 2022 who had a metabolic cart performed and were admitted to the burn service. Metabolic carts are typically ordered on all burns greater than 20% TBSA. Metabolic carts are started at least 3 days after their burn injury and are repeated weekly as staffing, equipment, and acuity of the patient allows. Patients were excluded from analysis if they did not have a thermal cutaneous injury, did not have a complete REE performed, or did not undergo any excision/-grafting (Figure 1). Data collected included demographics, injury characteristics, burn size/depth, surgical data, REEs, CRP levels, and outcome data. CRP levels were collected weekly during this period for an unrelated quality improvement project. Predicted REE was calculated using the Harris–Benedict equation using preinjury weight if documented or admission weight if preinjury weight was not documented. Surgical data collected included days from admission for each procedure, percentage of TBSA that was excised, and percentage of TBSA that was covered with autograft, allograft, BTM, or other skin substitute. Other skin substitutes such as xenograft and primatrix which were excluded from analysis. Common surgical practice at our institution is to perform a near-total excision of all nonviable tissue, followed by primary autografting of high functional areas until donor sites are exhausted. While it is individual surgeon preference, which is based on our anecdotal experience of positive outcomes, the remaining excised wounds are routinely placed in BTM unless wound bed quality supports allografting. Biodegradable temporizing matrix was introduced in 2017 to our institution. As it was common practice to use multiple coverage modalities in massive burn injuries during their first excision and grafting operation, it was not possible to categorize patients being exclusively covered with autograft, allograft, or BTM. Patients' wound coverage was categorized as either autograft, allograft, or BTM depending on which was the largest percentage of TBSA covered by autograft, allograft, or BTM during their first excisional operation only. If there was no dominant coverage category, they were considered mixed coverage and excluded from analysis.

Univariate analyses were performed using student *t*-tests for continuous variables and chi-squared for categorical variables. Mixed-effects linear modeling was performed for repeated REE measures and CRP measures using a random intercept to account for inter-individual variability with a random effect of subject number to also account for within-subject correlation of sequential REE and CRP measurements. To adjust for the fact that REE and CRP values were obtained at different time points relative to each patient's first excision, "days from first excision" was included as a covariate in the model. This approach allowed for adjustment rather than direct matching of measurement intervals across subjects. Two different mixed-effects models were created for both REE and CRP with the first model including all measurements during the subject's entire admission and a second subset model only incorporating measurements between 2 and 8 weeks after initial excision and wound coverage operation. The second model was created starting at 2 weeks to account for any potential metabolic benefits of BTM, which may only manifest after its 2-week integration period. The stopping point of 8 weeks was chosen to eliminate any potential effect of small sample sizes at later dates where there was significant drop out of subjects with data passed 60 days from initial operation (22% of patients had REE beyond a mean of 61 days and 32% had CRP data beyond a mean of 54 days from initial operation). Model selection was performed in a stepwise fashion, and the best model was chosen based on the lowest Akaike information criteria. All statistics were performed using R software, version 4.1.1 (www.r-project.org).

RESULTS

There were 226 patients included in the study. Nearly two-thirds or 154 patients (68%) had primarily autograft after their first excision operation with BTM (N = 39) and allograft (N = 33) encompassing the remaining 32% almost equally (Table 1). The average age for the entire study population was 46 years, which was similar among all the wound coverage groups. Most patients (76.5%) were male with similar distributions across all groups. Flame burns were the most common mechanism of injury in all groups. Total burn size was different between the groups with allograft having the highest TBSA at 58%, followed by 45% in the BTM group and 38.5% in the autograft group. Length of stay followed

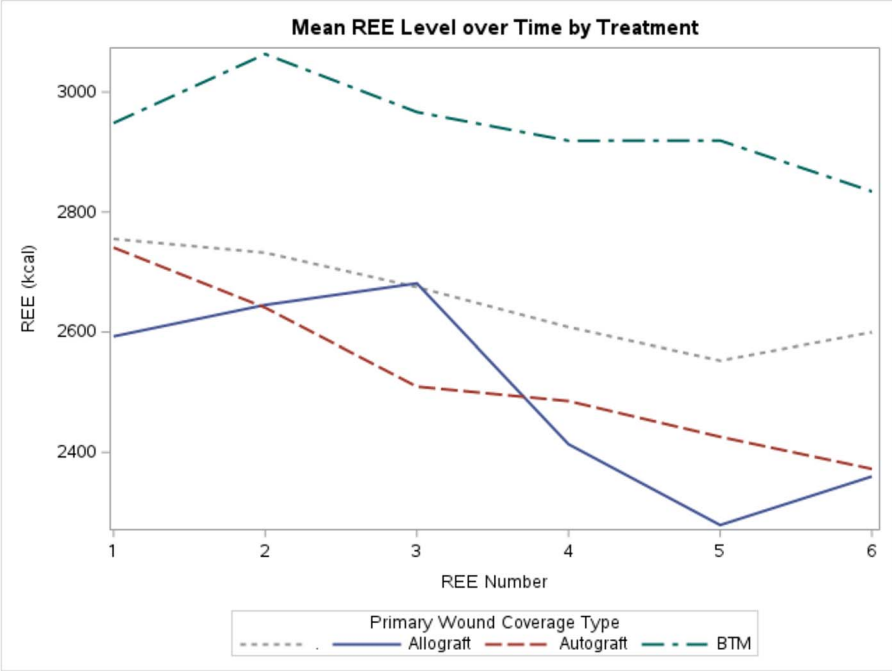

Figure 1. Consort Diagram of Inclusions and Exclusions

a similar trend with allograft patients staying the longest at 91 days on average, followed by 84 days in the BTM group and 58 days in the autograft group. About three-quarters of all patients were male, which was consistent between the groups. The BTM group had the most inhalation injuries at 38.5%, followed by 28.5% and 27% in the autograft and allograft groups, respectively. Mortality was highest in the allograft group at 30%, followed by 15% in the BTM group and 8.5% in the autograft group. The average percentage exercised in each patient's first operation was 30%. The percentage of TBSA excised for allograft was the highest at 43% followed by 36.5% in the BTM group and 25% in the autograft group. The percentage of TBSA covered by autograft, allograft, or BTM after their initial excision is shown in Table 1.

Resting energy expenditure for all patients and each coverage group is shown in Table 2. The average REE across all-time points was the highest in the BTM group when evaluating sequential REE measurements (Figure 2 and Table 2). The metabolic carts were not performed at equal time intervals in all patients which is shown in the days from excision to each REE in Table 2 and illustrated in Figure 3. The time from initial excision and coverage to first measured REE was the longest in the allograft group (15.8 days) compared to 8-9 days in the BTM and autograft groups. This trend continued for the second measured REE and became even more divergent after REE 5 when patient dropout started to affect the time more dramatically. The percentage of measured first REE after excision to predicted REE based on the Harris–Benedict equation ranged from 50% to 287%. The mean for all patients was 154.9 ± 37.97%. The percent of predicted REE was 146.55 ± 35.1% in the allograft group, 152.5 ± 37.6% in the autograft group and 171.3 ± 38.2 in the BTM group on their first REE after initial excision.

Mixed methods linear regression models were created to assess independent factors associated with increasing REE for the entire length of stay (Table 3a) as well as only for a period of 2-8 weeks after initial excision (Table 3b). In the entire length of stay model, mortality, total TBSA burned, and autografting contributed to model selection but were not significant in the model. Significant results showed that each day after initial excision, the REE decreased by 5.2 kcal. As age increased by 1 year the REE decreased by 8.65 kcal. Females' REEs were 462 kcal less compared to men. Biodegradable temporizing matrix was significantly associated with a 403.5 kcal increase in REE compared to the reference group allograft. In the model limited to a 2-8-week period after initial excision, total TBSA and both autograft and BTM were not significant. The remaining variables included showed a similar effect size to the entire length of stay model.

The analysis of CRP levels over time revealed distinct trends across the study population, with differences based on coverage type (allograft, autograft, and BTM). C-reactive protein levels initially peaked around the second or third CRP measurement (Figure 4), around 13-30 days post initial excision (Figure 5), and then gradually declined. There was a broad range and standard deviation for the time intervals relative to admission for the first several CRP measurements, including some measured prior to excision, which makes direct comparisons of CRP time points problematic (Table 4). Mixed methods linear regression models were created to account for these repeated measures and variable time intervals, which are shown in Tables 5a and 5b. When including all-time points and controlling for time from admission, age, sex, total TBSA, inhalation injury, and death, neither BTM nor autograft had significantly changed CRP levels relative to the allograft group (Table 5a). When only evaluating time points

Table 1. Demographics, Injury Characteristics, and Initial Excision Data

Variable	All Patients *N* = 226	Allograft *N* = 33	Autograft *N* = 154	BTM *N* = 39
Age	45.85 ± 15.95	43.06 ± 14.50	45.89 ± 15.58	48.08 ± 18.41
Total TBSA	42.32 ± 19.2	57.58 ± 22.09	38.46 ± 16.30	44.64 ± 20.86
Second degree TBSA	17.47 ± 18.10	17.41 ± 20.96	17.41 ± 16.54	17.77 ± 21.66
Third degree TBSA	25.59 ± 22.37	40.20 ± 32.07	21.05 ± 17.54	31.15 ± 23.60
Length of stay	67.50 ± 45.82	91.33 ± 57.78	58.16 ± 40.52	84.21 ± 43.30
Male sex	173 (76.5%)	26 (78.8%)	117 (75.98%)	30 (76.92%)
Inhalation injury	68 (30%)	9 (27%)	44 (28.57%)	15 (38.46%)
Death	29 (12.8%)	10 (30.3%)	13 (8.44%)	6 (15.38%)
Mechanism of injury				
Flame	210	30	145	35
Scald	5	0	3	2
Contact	3	0	2	1
Chemical	2	1	1	0
Electrical	6	2	3	1
Tracheostomy	130 (57.5%)	27 (81.8%)	75 (48.70%)	28 (71.79%)
TBSA % excised during first surgery	29.65 ± 15.32	43.24 ± 18.08	24.99 ± 11.93	36.55 ± 15.61
TBSA % autograft	16.97 ± 11.64	6.02 ± 8.58	22.18 ± 9.26	5.65 ± 7.05
TBSA % allograft	3.17 ± 9.33	15.94 ± 17.40	1.08 ± 4.67	0.52 ± 1.57
TBSA % BTM	5.79 ± 12.28	0	1.13 ± 3.63	29.08 ± 12.86

Continuous variables expressed as mean ± SD. Count variables are expressed as frequency (percentage). Abbreviations: BTM, biodegradable temporizing matrix; TBSA, total body surface area burned.

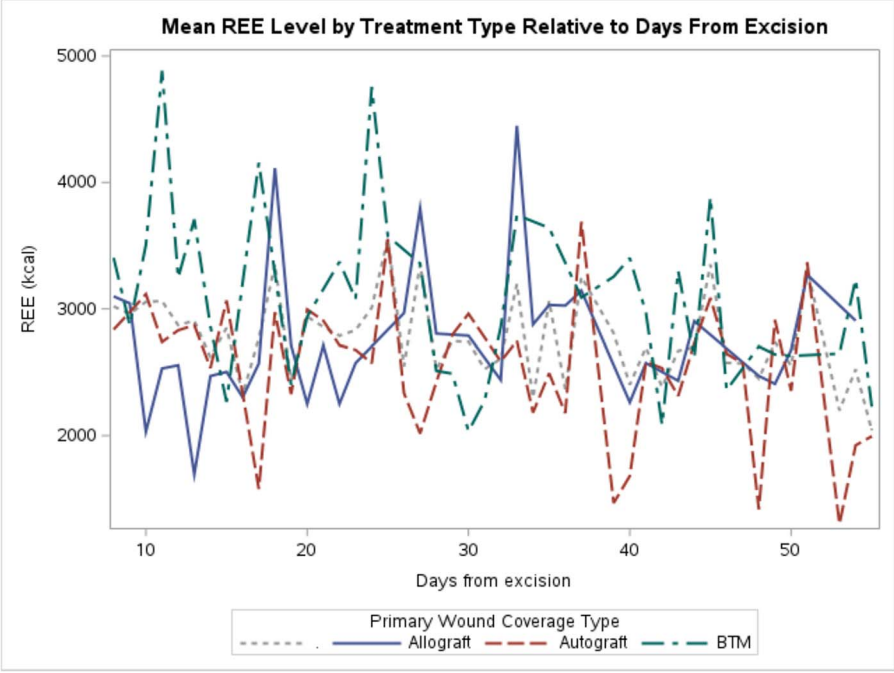

Figure 2. Mean REE in Kilocalories Over Time by Wound Coverage Type. REE number is the sequence of REE measurements over time. Abbreviations: BTM, biodegradable temporizing matrix; REE, resting energy expenditure.

between 2 and 8 weeks after excision and controlling for the same variables, both autograft (−3.32; P = .0107) and BTM (−3.07; P = .0388) had significantly lower CRP levels relative to allograft. In the all-time points model (Table 5a), there was also significance with days from admission to CRP level with 0.093 mg/dL (P = <.0001) decrease for each day, total TBSA with a 0.11 mg/dL (P = <.0001) increase for each percent TBSA burned, and death with 2.85 mg/dL

Table 2. Resting Energy Expenditure Over Time

Time point	Metric	All Patients *N* = 226	Allograft *N* = 33	Autograft *N* = 154	BTM *N* = 39
Predicted REE	Mean ± SD (kcal)	1795.0 ± 350.98	1776.4 ± 280.13	1815.61 ± 354.40	1729.6 ± 388.86
REE1	Mean ± SD (kcal)	2755.11 ± 760.25	2592.67 ± 704.01	2740.72 ± 737.90	2948.28 ± 864.80
	Patients *n* (%)	223 (98.7%)	33 (100%)	151 (98.7%)	39 (100%)
	Days from excision to time point (mean ± SD)	9.56 ± 12.38	15.82 ± 21.06	8.70 ± 9.39	8.13 ± 11.60
REE2	Mean ± SD (kcal)	2732.18 ± 774.38	2645.17 ± 597.62	2640.56 ± 749.52	3063.24 ± 898.18
	Patients *n* (%)	136 (60.2%)	24 (72.7%)	83 (53.9%)	29 (74.4%)
	Days from excision to time point (mean ± SD)	27.71 ± 15.54	32.08 ± 18.74	27.10 ± 15.33	25.85 ± 12.92
REE3	Mean ± SD (kcal)	2674.82 ± 784.08	2681.12 ± 748.85	2509.49 ± 778.47	2966.58 ± 762.78
	Patients *n* (%)	84 (37.2%)	17 (51.5%)	43 (27.9%)	24 (61.5%)
	Days from excision to time point (mean ± SD)	42.65 ± 19.91	44.06 ± 16.30	42.79 ± 18.75	41.42 ± 18.10
REE4	Mean ± SD (kcal)	2608.26 ± 763.33	2413.45 ± 568.43	2485.39 ± 918.07	2918.81 ± 545.85
	Patients *n* (%)	50 (22.1%)	11 (33.3%)	23 (14.9%)	16 (41%)
	Days from excision to time point (mean ± SD)	61.1 ± 21.90	60.36 ± 19	62.83 ± 25.18	58.13 ± 19.69
REE5	Mean ± SD (kcal)	2552.61 ± 729.42	2278.71 ± 490.08	2425.75 ± 865.45	2919.13 ± 685.82
	Patients *n* (%)	22 (9.7%)	6 (18.2%)	8 (5.2%)	8 (20.5%)
	Days from excision to time point (mean ± SD)	86.23 ± 33.68	92.5 ± 14.98	83.75 ± 43.51	84 ± 36.12
REE6	Mean ± SD (kcal)	2599.79 ± 793.87	2359.75 ± 363.52	2372.33 ± 831.88	2834.43 ± 969.85
	Patients *n* (%)	14 (6.2%)	4 (12.1%)	3 (1.9%)	7 (17.9%)
	Days from excision to time point (mean ± SD)	98.5 ± 38.02	125.75 ± 10.11	58.67 ± 18.01	100 ± 41.01
REE7	Mean ± SD (kcal)	2298.6 ± 369.64	2079 ± 155.91	–	2628 ± 369.11
	Patients *n* (%)	5 (2.2%)	3 (9.1%)	–	2 (5.1%)
	Days from excision to time point (mean ± SD)	136.6 ± 27.84	152.67 ± 19.43	–	111 ± 12.73
REE8	Mean ± SD (kcal)	2755 ± 780.65	2203	–	3307
	Patients *n* (%)	2 (1.6%)	1 (3.0%)	–	1 (2.6%)
	Days from excision to time point (mean ± SD)	184 ± 6.47	231	–	137
REE9	Mean ± SD (kcal)	2103	2103	–	–
	Patients *n* (%)	1 (0.8%)	1 (3%)	–	–
	Days from excision to time point (mean ± SD)	265	265	–	–

Abbreviations: BTM, biodegradable temporizing matrix; REE, resting energy expenditure.

Table 3a. Mixed Methods Regression Model for Resting Energy Expenditure Including Patients' Entire Length of Stay

Variable	Estimate	Standard error	DF	*t*-value	*Pr* > |*t*|
Intercept	2894.50	248.83	215	11.63	<.0001
Days from admission to REE	−5.19	0.78	308	−6.61	<.0001
Age	−8.65	2.98	308	−2.91	.0039
Female sex	−462.23	96.78	308	−4.78	<.0001
Total TBSA	4.57	2.54	308	1.80	.0726
Inhalation injury	181.36	88.44	308	2.05	.0411
Death	−63.43	131.48	308	−0.48	.6298
Autograft	137.55	123.43	308	1.11	.2660
BTM	403.53	142.11	308	2.84	.0048

Male sex and allograft were reference variables. Abbreviations: BTM, biodegradable temporizing matrix; REE, resting energy expenditure; TBSA, total body surface area burned.

(*P* = .0053) increase in CRP levels for patients that died. In the model, restriction to 2-8 weeks (Table 5b) after initial excision days to CRP measurement decreased 0.200 mg/dL (*P* = <.0001) for each day after, increased for every percent TBSA by 0.13 mg/dL (*P* = <.0001).

DISCUSSION

Burn injuries induce a hypermetabolic state characterized by significant physiological and metabolic stress, particularly evident in the escalation of REE. The increased metabolic

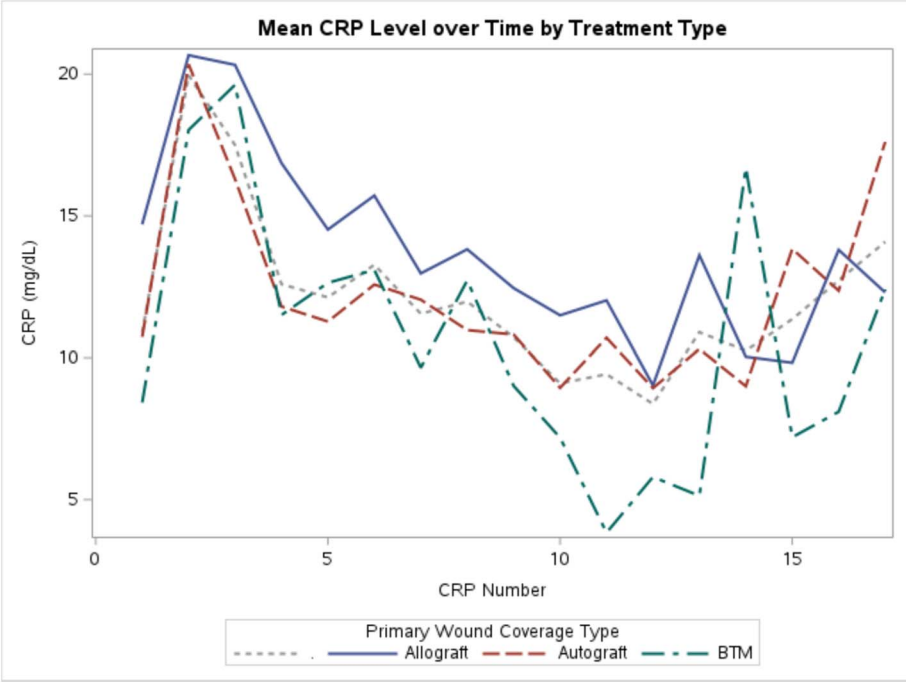

Figure 3. Mean REE in Kilocalories by Wound Coverage Type Relative to Days from Initial Excision. Abbreviations: BTM, biodegradable temporizing matrix; REE, resting energy expenditure.

Table 3b. Mixed Methods Regression Model for Resting Energy Expenditure Including only 2-8 Weeks After Initial Excision

Variable	Estimate	Standard error	DF	*t*-value	*Pr* > |*t*|
Intercept	3267.09	334.10	139	9.78	<.0001
Days from admission to REE	−11.16	3.03	91	−3.68	.0004
Age	−8.08	3.91	91	−2.07	.0416
Female sex	−360.30	120.65	91	−2.99	.0036
Total TBSA	3.40	3.25	91	1.05	.2981
Inhalation injury	315.95	106.89	91	2.96	.0040
Death	−285.76	180.50	91	−1.58	.1169
Autograft	−114.57	151.95	91	−0.75	.4528
BTM	153.84	168.99	91	0.91	.3651

Male sex and allograft were reference variables. Abbreviations: BTM, biodegradable temporizing matrix; REE, resting energy expenditure; TBSA, total body surface area burned.

demand, ranging from 20% to 100% above baseline, reflects the body's efforts to meet the energetic requirements of tissue repair, immune activation, and systemic inflammatory responses. This hypermetabolic state, if not managed adequately, can lead to profound energy deficits, delayed wound healing, and poor outcomes.[10] Our findings underscore the metabolic impact of different wound coverage techniques, including allografts, autografts, and BTM on REE and CRP. In this study, using mixed models linear regression modeling we showed that when using REE measurements during their entire hospital stay, patients who had a majority of their excised wounds placed in BTM had significantly increased REE by about 400 kcal relative to allograft. Using the same methods but restricting to only 2-8 weeks after their initial excision, patients placed in mostly BTM and autograft had significantly lower CRP measurements by about 3 mg/dL relative to allograft. While no causal relationship can be drawn from the study design employed in the current study, these findings warrant further discussion. What surgeons choose to cover excised burn wounds with affects the patients' clinical course, and the findings of this study may at least partially explain the anecdotal evidence we are seeing with improved clinical parameters seen in patients who receive BTM compared to allograft to temporize their excised wounds.

Patients receiving BTM demonstrated consistently elevated REE levels compared to those treated with autografts or allografts, persisting throughout the study period, which remained

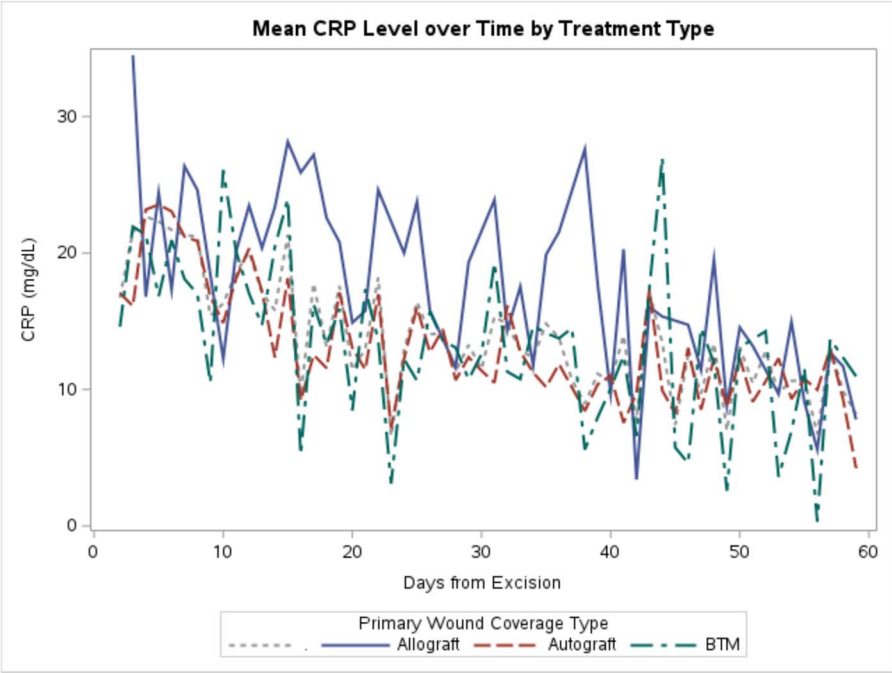

Figure 4. Mean C-Reactive Protein Level in mg/dL Over Time by Wound Coverage Type for the First 15 Measured CRP Levels. CRP number is the sequence of CRP measurements over time, which varies from patient to patient. Abbreviations: BTM, biodegradable temporizing matrix; CRP, C-reactive protein.

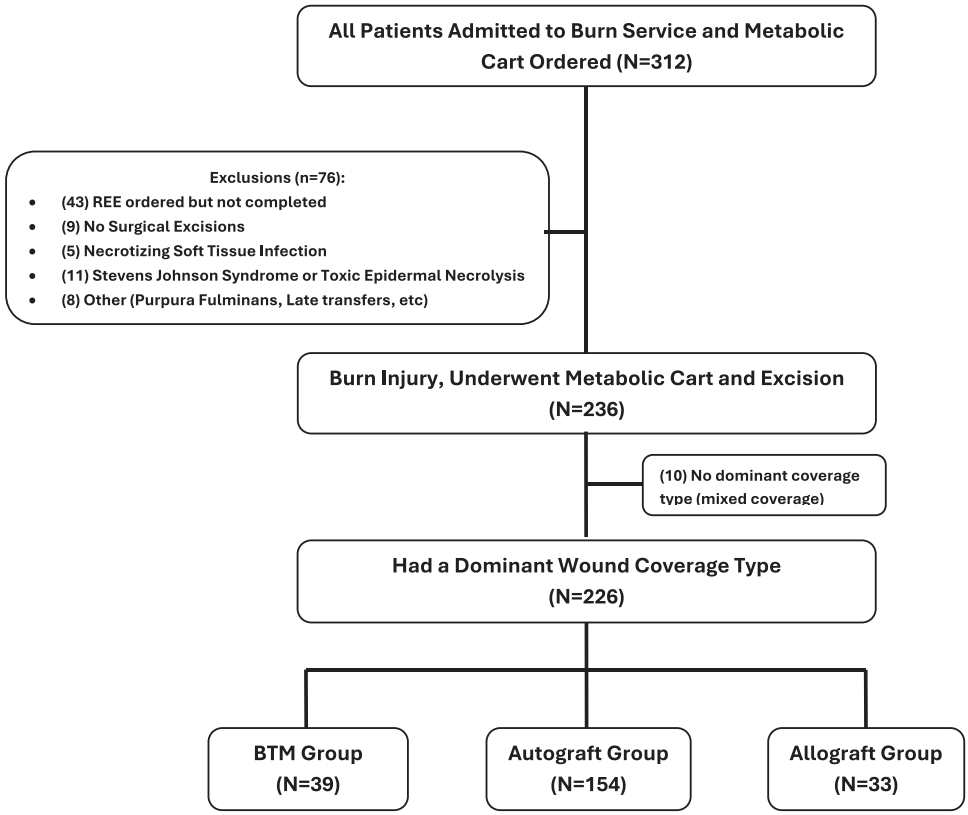

Figure 5. Mean C-Reactive Protein Level in mg/dL Over Time by Wound Coverage Type for the First 60 Days After Initial Excision. Abbreviations: BTM, biodegradable temporizing matrix; CRP, C-reactive protein.

Table 4. C-reactive Protein Levels for All Patients and by Coverage Group

Time point	Metric	All patients *N* = 226	Allograft *N* = 33	Autograft *N* = 154	BTM *N* = 39
CRP 1	Mean ± SD (mg/dL)	10.88 ± 9.85	14.70 ± 10.43	10.73 ± 10.18	8.42 ± 7.15
	Patients *n* (%)	199 (88.0%)	29 (87.9%)	133 (86.4%)	37 (94.9%)
	Days from excision to time point (mean ± SD)	5.9 ± 23.9	16.14 ± 34.50	4.08 ± 20.29	4.51 ± 24.87
CRP 2	Mean ± SD (mg/dL)	19.96 ± 9.15	20.67 ± 8.15	20.35 ± 9.29	18.03 ± 9.37
	Patients *n* (%)	187 (82.7%)	28 (84.8%)	124 (80.5%)	35 (89.7%)
	Days from excision to time point (mean ± SD)	13.40 ± 24.34	24.89 ± 33.66	10.94 ± 18.59	12.91 ± 30.98
CRP 3	Mean ± SD (mg/dL)	17.49 ± 9.53	20.33 ± 8.72	16.30 ± 9.46	19.62 ± 9.85
	Patients *n* (%)	174 (77.0%)	27 (81.8%)	117 (76.0%)	30 (76.9%)
	Days from excision to time point (mean ± SD)	17.01 ± 35.85	31.04 ± 33.90	14.76 ± 39.11	13.13 ± 17.28
CRP 4	Mean ± SD (mg/dL)	12.59 ± 8.35	16.86 ± 7.99	11.80 ± 8.70	11.50 ± 6.20
	Patients *n* (%)	156 (69.0%)	26 (78.8%)	101 (65.6%)	29 (74.4%)
	Days from excision to time point (mean ± SD)	26.80 ± 23.59	39.00 ± 34.75	25.57 ± 20.56	20.17 ± 17.57
CRP 5	Mean ± SD (mg/dL)	12.12 ± 8.03	14.52 ± 9.18	11.27 ± 7.99	12.64 ± 6.88
	Patients *n* (%)	138 (61.1%)	24 (72.7%)	85 (55.2%)	29 (74.4%)
	Days from excision to time point (mean ± SD)	35.09 ± 25.06	46.83 ± 35.95	34.48 ± 22.50	27.14 ± 17.57
CRP 6	Mean ± SD (mg/dL)	13.27 ± 7.87	15.72 ± 8.31	12.58 ± 8.47	13.09 ± 6.02
	Patients *n* (%)	107 (47.3%)	19 (57.6%)	59 (38.3%)	29 (74.4%)
	Days from excision to time point (mean ± SD)	34.93 ± 14.51	38.89 ± 8.95	34.08 ± 14.28	34.03 ± 17.60
CRP 7	Mean ± SD (mg/dL)	11.55 ± 7.67	12.97 ± 7.41	12.04 ± 8.73	9.65 ± 5.22
	Patients *n* (%)	89 (39.4%)	17 (51.5%)	47 (30.5%)	25 (64.1%)
	Days from excision to time point (mean ± SD)	41.54 ± 15.11	46.18 ± 9.59	40.00 ± 14.37	41.28 ± 18.97
CRP 8	Mean ± SD (mg/dL)	11.97 ± 6.89	13.82 ± 5.46	10.97 ± 6.70	12.72 ± 8.22
	Patients *n* (%)	74 (32.7%)	15 (45.4%)	41 (26.6%)	18 (46.2%)
	Days from excision to time point (mean ± SD)	47.19 ± 12.84	51.20 ± 10.33	47.14 ± 15.20	43.94 ± 6.89
CRP 9	Mean ± SD (mg/dL)	10.72 ± 7.42	12.45 ± 6.54	10.82 ± 8.45	9.01 ± 5.68
	Patients *n* (%)	63 (27.9%)	14 (42.4%)	33 (21.4%)	16 (41.0%)
	Days from excision to time point (mean ± SD)	54.14 ± 14.27	57.86 ± 11.30	53.42 ± 17.64	52.38 ± 7.08
CRP 10	Mean ± SD (mg/dL)	9.10 ± 7.63	11.49 ± 6.55	8.94 ± 8.85	7.19 ± 5.60
	Patients *n* (%)	54 (23.9%)	13 (39.4%)	27 (17.5%)	14 (35.9%)
	Days from excision to time point (mean ± SD)	63.15 ± 16.43	64.38 ± 12.72	62.74 ± 18.95	62.79 ± 15.22
CRP 11	Mean ± SD (mg/dL)	9.42 ± 7.14	12.02 ± 6.83	10.70 ± 7.48	3.83 ± 3.32
	Patients *n* (%)	37 (16.4%)	11 (33.3%)	17 (11.0%)	9 (23.1%)
	Days from excision to time point (mean ± SD)	73.73 ± 31.68	70.09 ± 14.12	68.00 ± 23.11	89.00 ± 53.36
CRP 12	Mean ± SD (mg/dL)	8.38 ± 6.95	9.03 ± 5.61	8.93 ± 8.54	5.80 ± 4.78
	Patients *n* (%)	32 (14.2%)	11 (33.3%)	15 (9.7%)	6 (15.4%)
	Days from excision to time point (mean ± SD)	76.69 ± 21.31	77.09 ± 13.80	74.33 ± 25.95	81.83 ± 22.35
CRP 13	Mean ± SD (mg/dL)	10.90 ± 8.08	13.61 ± 8.89	10.31 ± 7.58	5.13 ± 5.84
	Patients *n* (%)	24 (10.6%)	9 (27.3%)	12 (7.8%)	3 (7.7%)
	Days from excision to time point (mean ± SD)	79.46 ± 16.58	83.44 ± 16.52	75.83 ± 18.61	82.00 ± 2.00
CRP 14	Mean ± SD (mg/dL)	10.25 ± 8.08	10.04 ± 8.58	9.00 ± 8.19	16.70 ± 4.95
	Patients *n* (%)	19 (8.4%)	8 (24.2%)	9 (5.8%)	2 (5.1%)
	Days from excision to time point (mean ± SD)	84.53 ± 19.89	88.88 ± 18.29	79.67 ± 23.38	89.00 ± 1.41
CRP 15	Mean ± SD (mg/dL)	11.36 ± 8.60	9.83 ± 7.74	13.83 ± 10.30	7.20
	Patients *n* (%)	14 (6.2%)	7 (21.2%)	6 (3.9%)	1 (2.6%)
	Days from excision to time point (mean ± SD)	88.0 ± 24.38	94.86 ± 20.80	78.83 ± 29.16	95.00

Only the first 15 measured levels are represented. Fewer than 10 patients had measurements beyond 16 CRP levels. Abbreviations: BTM, biodegradable temporizing matrix; CRP, C-reactive protein.

true on mixed methods linear regression modeling but only when all-time points were included and not when only looking at 2-8 weeks post initial excision and majority BTM placement. While we hypothesized the REE may be lower in patients covered with BTM, which may account for improved clinical parameters seen anecdotally but we found the opposite. However, this could theoretically be explained by the double-edged sword nature of hypermetabolism. The elevated REE could be beneficial and elevated as a marker of increased systemic healing activities or heightened tissue remodeling and regeneration highlighting its potential influence on metabolic recovery dynamics.

Table 5a. Mixed Methods Regression Model for C-Reactive Protein Including Patients' Entire Length of Stay

Effect	Estimate	Standard error	DF	*t*-value	*Pr* > |*t*|
Intercept	14.3734	1.9431	191	7.40	<.0001
Days from admission to CRP	−0.09271	0.006706	1236	−13.82	<.0001
Age	−0.05557	0.02328	1236	−2.39	.0172
Female sex	1.1943	0.7332	1236	1.63	.1036
Total TBSA	0.1083	0.01993	1236	5.44	<.0001
Inhalation injury	−0.6909	0.7110	1236	−0.97	.3314
Death	2.8482	1.0196	1236	2.79	.0053
Autograft	−1.2615	0.9413	1236	−1.34	.1804
BTM	−1.9882	1.0886	1236	−1.83	.0680

Male sex and allograft were reference variables. Abbreviations: BTM, biodegradable temporizing matrix; CRP, C-reactive protein; TBSA, total body surface area burned.

Table 5b. Mixed Methods Regression Model for C-Reactive Protein Including Only 2-8 Weeks After Initial Excision

Effect	Estimate	Standard error	DF	*t*-value	*Pr* > |*t*|
Intercept	15.8233	2.7843	136	5.68	<.0001
Days from admission to CRP	−0.2003	0.02083	471	−9.61	<.0001
Age	−0.01842	0.03264	471	−0.56	.5727
Female sex	2.0582	1.0008	471	2.06	.1033
Total TBSA	0.1303	0.02840	471	4.59	<.0001
Inhalation injury	−0.7410	1.0081	471	−0.74	.3325
Death	2.0544	1.4342	471	1.43	.1527
Autograft	−3.3161	1.2946	471	−2.56	.0107
BTM	−3.0723	1.4824	471	−2.07	.0388

Male sex and allograft were reference variables. Abbreviations: BTM, biodegradable temporizing matrix; CRP, C-reactive protein; TBSA, total body surface area burned.

However, hypermetabolism comes with the costs of catabolism, muscle wasting, and cardiovascular strain.[11,12] As long as the increased metabolism is not associated with disproportionate inflammation or hypermetabolic response without corresponding improvement in wound healing, then the increased REE, if related to BTM, can be a positive finding. The metabolic implications of such a finding warrant further investigation to elucidate the biologic underpinnings driving these observations.

One way to assess for inflammation is by checking CRP level. C-reactive protein levels in burn patients are known to be elevated, and trends are more helpful than isolated measurements.[13,14] C-reactive protein was used as the primary inflammatory marker because it was the only routinely available and consistently collected laboratory parameter in this retrospective cohort. The inflammatory trajectory, as assessed by CRP levels in the current study, also differed among treatment groups. Patients in the allograft group exhibited higher CRP levels and a more prolonged inflammatory response compared to those treated with autografts or BTM. This held true on mixed methods linear regression modeling but only for the 2-8 week time period and not the entire length of stay time period. This may indicate a more robust systemic inflammatory reaction or slower resolution of inflammation in the allograft group, potentially linked to the immunogenicity of allograft tissues.[15] Perhaps the finding of increased REE with decreased CRP supports a more beneficial balance of increased hypermetabolic response without increased systemic inflammation. This hypothesis is supported in preclinical studies demonstrating increased inflammatory cell infiltration in the early time period after BTM placement in a mouse model[16] and several other trials showing increased local wound inflammatory state but not necessarily systemic inflammatory response.[17,18]

The current study has many limitations but also many areas for future study. The retrospective study design, nonhomogenous groupings based on initial excision only, potential for wound coverage cross-over at later times, and exclusion of many other clinical factors that contribute to REE and CRP measurements do not allow for any causal inference. The number of CRP and REE measurements undertaken was not uniform, nor were the time intervals between them. We attempted to account for this using mixed methods modeling, but a more rigorous design with homogeneous coverage types and prescribed timing of measurements would allow for better evaluation. Additionally, there were very few patients that were completely covered with a single cover type and almost all of the patients had a mixture of cover types necessitating us to group based on the majority of each type. Furthermore, other clinical factors such as sepsis, other surgeries, mechanical ventilation, etc., were outside of the scope of this project and not incorporated into the models. These results should be interpreted with caution given these weaknesses that will be

difficult to overcome in future studies given the complexity of modern burn care.

CONCLUSIONS

In conclusion, while this study has limitations due to its retrospective nature and the variability in treatment practices, it provides valuable preliminary insights into the metabolic and inflammatory responses associated with different burn wound coverage techniques, particularly BTM. Although causal inferences cannot be drawn, our findings suggest that BTM may influence metabolic (increased REE) and inflammatory (decreased CRP) responses, potentially explaining the improved clinical outcomes seen anecdotally in patients with large TBSA burns. Given the complexities of burn care, including timing, treatment decisions, and clinical factors, this study represents a starting point for future, more controlled research to better understand the biological mechanisms behind these observations and refine strategies for optimizing recovery in burn patients.

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