Treatment of Stage 4 Pressure Injuries with Autologous Heterogenous Skin Construct
A Single Center Retrospective Study

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Introduction

Pressure injuries (PI) are a challenging problem in healthcare, affecting 2.5 million people per year in the United States, with 60,000 deaths directly attributed to pressure injuries annually. Surgical closure is the treatment of choice for stage 3 and 4 PI, but with complication rates of 59-73%, less invasive and more effective treatments are needed.

Autologous heterogeneous skin construct (AHSC) is a novel autograft, made from a small, full-thickness harvest of healthy skin. This single-center retrospective cohort study sought to determine the effectiveness of AHSC in the treatment of recalcitrant stage 4 pressure injuries.

Materials and Methods

Institutional review board (IRB) approval (IRB 1731663-2) was obtained for this retrospective cohort study, which meets the waiver criteria, as described in the 45 Code of Federal Regulations (CFR) 164.512 (i) (2) (ii). All patients treated with an autologous heterogeneous skin construct (AHSC) for pressure injuries between January 2020 and May 2021 at a single center were included. The only exclusion criterion was the absence of at least 2-months of follow-up data. There were no other exclusion criteria, including no restrictions on age, PI etiology, location, duration, or prior treatment. Patient demographics, wound characteristics, and ASHC treatment details of all patients were retrospectively collected directly from the electronic health record. The primary efficacy outcome was complete wound closure. Secondary efficacy outcomes included percent area reduction, percent volume reduction, and coverage of exposed structures. Analysis included donor site and wound complications, the need for reoperation, and wound recurrence. Data on the number of hospitalizations, number of days spent in the hospital, and operations related to the index wound were collected from the first appearance of the wound.

All wounds were surgically debrided to viable intact tissue. Negative pressure wound therapy (NPWT) was applied to open wounds between procedures. Donor tissue harvesting and AHSC deployment were performed under aseptic conditions. Donor tissue was obtained from an area of healthy skin, typically the trunk or abdomen. A small, full-thickness ellipse of the skin, including a layer of hypodermis, was excised using a sharp surgical scalpel. Hemostasis was ensured and the donor sites were closed primarily under minimal tension.

The donor tissue was processed into AHSC and returned within 2-4 days in the consistency of a paste. AHSC is spreadable and able to cover an area much larger than the size of the donor tissue. Donor tissue is not cultured or grown ex-vivo.

Each patient's individualized AHSC was dispensed and spread evenly over all surfaces of their prepared wound bed, including undermined and tunneled areas. A non-absorbent silicone sheet, fenestrated to allow for fluid egress, was placed in the central, open portion of the wound, held against the wound surface with the negative pressure foam and secured directly to the outer wound margins with staples or sutures. Hydrocolloid wafer was cut into strips and placed around the wound margin, to protect the peri-wound from moisture and help maintain the air-tight seal of the NPWT dressing.(Figure 1) NPWT was left in place for one week and subsequent dressings were determined, based on ongoing wound assessment.

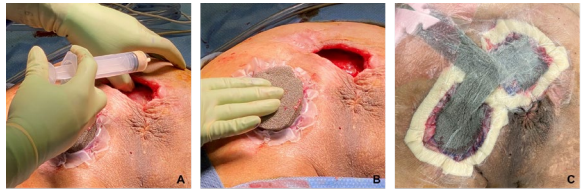

Figure 1a: applying AHSC1b: silicone with foam bolster 1c: completed NPWT dressing with hydrocolloid strips

Postoperative protocols varied depending on wound characteristics. However, in most cases NPWT was continued and changed weekly until the wound volume was restored. In all cases, a moist wound-healing environment was maintained with appropriate dressings until wound closure. Protection of the wound from pressure and other mechanical forces was stressed throughout the treatment period. Nutritional status, bacterial burden, and all other wound-related factors were monitored on an ongoing basis.

Table 1: Patient Demographics

Total no. patients N (%)	17
No. patients with one PI	12 (70.5%)
No. patients with two PIs	5 (29.5%)
Mean age in years (range)	56.9 (29.3-78.5)
Female N (%)	6 (35%)
Male N (%)	11 (65%)
Race N (%)	
Black	2 (12%)
Hispanic	2 (12%)
Non-Hispanic White	13 (76.5%)
Mean BMI (range)	28.8 (17-46)
Co-Morbidities N (%)	
DM	10 (59%)
Malnourishment	17 (100%)
Renal disease	2 (12%)
Paralysis	14 (82%)
C5	1 (6%)
T4-5	5 (29%)
T10-S1	8 (47%)
Cardiovascular disease	7 (41%)
Autoimmune Disease	3 (18%)
History of Wound Infection	17 (100%)
Drug resistant infection	11 (65%)
Osteomyelitis	3 (18%)
History of Sepsis	3 (18%)
Above knee amputation	1 (6%)
Bilateral Above Knee Amputations	1 (6%)
Hospital admission during treatment N (%)	17 (100%)
LTC or SNF during treatment N (%)	8 (47%)
Primary ambulatory method N (%)	
Cane/crutches/walker	3 (18%)
Wheelchair	11 (65%)
Stretcher	1 (6%)
Mean wounds/patient, of any type, during treatment (range)	3.4 (1-11)
Number of patients with no additional wounds (%)	4 (24%)
Number of patients with 1-2 additional wounds	7 (41%)
Number of patients with 3-4 additional wounds	3 (18%)
Number of patients with 5-6 additional wounds	2 (12%)
Number of patients with 10 additional wounds	1 (6%)

Table 2: Wound Characteristics

Total number of treated wounds	22
Pressure Injury Location N (%)	
Sacrum	7 (31%)
Ischium	13 (59%)
Other	2 (9%)
Stage IV pressure injury N (%)	22 (100%)
Exposed bone	21 (95%)
Wounds with history of failed flap N (%)	13 (59%)
1 failed flap	7 (32%)
2 failed flaps	4 (18%)
3 failed flaps	1 (5%)
4 failed flaps	1 (5%)
Mean wound age in months	29.7 (±28.4)
Mean wound area in cm^2	29.4 (±15.6)
Mean wound volume in cm^3	106.1 (±112.8)

Table 3: Outcomes

Total number of wounds N	22
Wounds with coverage of deep structures N (%)	21 (95%)
Mean days to coverage (SD)	33 (±19)
Median days to coverage (range)	31 (3-73)
Wounds achieving 95% volume reduction N (%)	15 (68%)
Mean days to 95% reduction (SD)	106 (±83)
Median days to 95% reduction (range)	59 (18-283)
Wounds achieving full closure N (%)	11 (50%)
Mean days to closure (SD)	146 (±93)
Median days to closure (range)	118 (41-302)
Wound recurrence in wounds that healed N (%)	2 (18%)
Mean days to recurrence	243
Mean percent area reduction	69%
Mean percent volume reduction	81%
Wounds receiving a second AHSC application N (%)	6 (30%)
Donor site complication N (%)	0 (0%)
Mean follow up weeks (SD)	39 (±16)
Median follow up weeks (range)	32 (12-72)
Mean AHSC dose µL/cm2 (SD)	424.4 (±324.3)
Median AHSC dose µL/cm2 (range)	309 (128.5-1700)

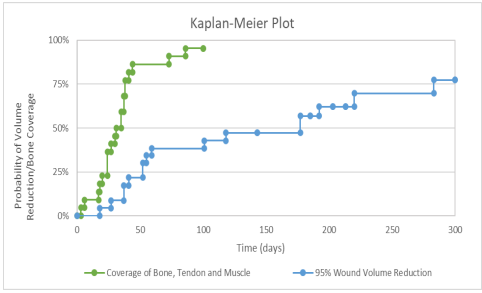

Figure 2. time to volume restoration and coverage of exposed bone in stage IV pressure injuries

Table 4: Wound Related Morbidity**

Mean amount/year*	Pre AHSC	Post AHSC	Difference	Z value	P value
Hospital admissions	2.4 (±1.29)	0.74 (±0.85)	1.65	-3.290	0.001
Days in hospital	24.02 (±16.8)	3.1 (±4.25)	20.92	-3.361	<0.001
Operative procedures	2.87 (±1.64)	0.51 (±0.75)	2.36	-3.574	<0.001

Results

Patient demographics are shown in Table 1. Seventeen patients (22 wounds) were treated with AHSC. Of the patients, 70.5% (12) had one PI and 29.5% (5) had two PIs. The mean patient age was 56.9 years (range 29.3-78.5); six (35%) were female and 11 (65%) were male; two (12%) were black, two (12%) were Hispanic, and 13 (76.5%) were non-Hispanic white. All patients had a history of infection (drug-resistant infection, 65%; osteomyelitis, 18%; sepsis, 18%), malnutrition, and hospital admission during treatment. More than half (59%) of the patients had diabetes mellitus. One patient had a history of single below-knee amputation (BKA) and one patient had recent bilateral BKA. Most patients had paralysis (82%), 70% were non-ambulatory, all used some form of assistive device for locomotion, and 47% required skilled nursing facility placement. During the treatment period, the mean number of wounds (of any type), per patient, was 3.4 (range 1-11).

Wound characteristics are presented in Table 2. Notably, the mean wound age for the cohort was 29.7 months (±28.4), 59% (13) of the wounds had failed at least one attempt at flap reconstruction (range 1-4), and 95% (21) had exposed bone in their index ulcer at the onset of treatment. The mean initial wound area and volume were 29.4 cm2 (±15.6) and 106.1 cm3 (±112.8), respectively.

Outcomes are shown in Table 3. Complete closure was achieved in 50% of patients in a mean time of 146 days (±93). Mean percent area and volume reductions were 69% and 81%, respectively, with a mean follow-up duration of 39 weeks (±16). A 95% volume reduction was achieved in 68.2% of patients in a mean time of 106 days (±83), and critical structures, such as bone and tendon were fully covered in 95% of patients in a mean time of 33 days (±19). Both are highlighted in the Kaplan–Meier graph in Figure 2. Progression of AHSC in one patient with a 14-year-old ischial PI is shown in Figure 3.

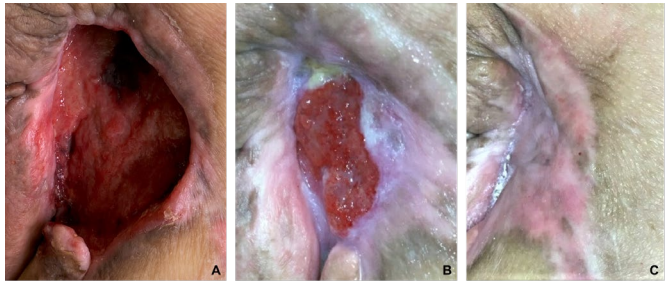

Figure 3a: prior to AHSC application; 3b: day 55 post AHSC application; 3c: day 118 post AHSC application

Wound-related morbidity results are shown in Table 4. Data on the number of hospitalizations, days spent in the hospital, and operations related to the index wound were collected from the first appearance of the wound. Data was analyzed using a Wilcoxon signed-rank test. Hospitalizations were found to have a mean annualized decrease of 1.65 per year (p=0.001), days spent in the hospital were found to have a mean decrease of 20.92 days per year (p<0.001) and number of operative visits was also found to be significant with a mean decrease of 2.36 per year (p<0.001).

Conclusions

In this retrospective case series, AHSC demonstrated the ability to cover exposed structures and achieve wound volume restoration, area reduction, and durable wound closure in chronic refractory stage 4 pressure injuries. The statistically significant decreases in hospital admissions, days spent in the hospital, and operative procedures noted with AHSC treatment are suggestive of an improvement in overall patient health and may have benefit in reducing the significant socioeconomic burden associated with PIs. AHSC represents a minimally invasive alternative to reconstructive flap surgery that preserves future reconstructive options, while minimizing donor-site morbidity and promoting improved patient health.