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Original Research

Use of Autologous Skin Cell Suspension for the Treatment of Hand Burns: A Pilot Study

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Purpose: Autologous skin cell suspension (ASCS) is a valid alternative and adjunct to split-thickness skin grafting (STSG) for treating burns. Limited data exists regarding the use of ASCS for hand burns. We hypothesized that using ASCS in hand burns shortens healing time with no difference in complications and less donor site morbidity.
Methods: This was a retrospective chart review of second- and third-degree hand burns treated at a level 1 Trauma and Burn Center from 2017 to 2019. Study groups included patients with hand burns treated with ASCS in combination with STSG and those treated with STSG alone. Outcomes included time to re-epithelialization, return to work, length of hospital stay, and complications including reoperation, graft failure, and infection.
Results: Fifty-nine patients aged 14 to 85 years (mean age 39 ± 15 years) met inclusion criteria. The ASCS treatment group comprised 37 patients; STSG comprised 22 patients. Mean follow-up time was 14 ± 7 months. The ASCS treatment group had a larger mean percent total body surface area (TBSA) (22% ± 14% vs 6% ± 8%; $P < .05$). There was no difference in time to wound re-epithelialization between both groups (ASCS, 11 ± 4 days vs STSG, 11 ± 5 days). Mean length-of-stay was 23 ± 13 days compared to 10 ± 13 days ($P < .05$) between the ASCS and STSG groups, respectively. No patients in the ASCS group required reoperation, whereas 2 patients in the STSG group required such for an infection-related graft loss and a web space contracture release. On multivariable analysis adjusting for TBSA, ASCS was associated with an earlier return to work ($P < .05$).
Conclusions: ASCS is safe and effective in treating hand burns. ASCS was associated with similar rates of re-epithelialization, earlier return to work, and no difference in complications compared with STSG.
Type of study/level of evidence: Therapeutic IV.

Deep dermal injuries involving the hand are potentially debilitating and benefit from tangential excision and skin grafting methods for hand reconstruction.[1] Early excision of burn wounds and prompt closure with autologous split-thickness skin grafts are the current standard of care.[2,3] Severe hand burns requiring skin grafting present unique challenges. To achieve a functional and aesthetic outcome, healing by secondary intention and scar formation should be minimized.[4] Delayed wound healing can result in scar contracture throughout the hand leading to a restricted range of motion, decreased functional strength, impaired work and daily activity performance, and the need for further surgery.[5] Inherent limitations of split-thickness skin grafting (STSG) include the risk of donor site morbidity and availability of noninvolved donor skin. Moreover, this treatment strategy is associated with pain, pruritis, infection, dyschromia, dyspigmentation, delayed healing, and hypertrophic scarring.[6–8]

Autologous skin cell suspension (ASCS) has been implemented as a valid alternative and adjunct to STSG for treating burns as less

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donor skin is used to cover large burn areas.[2,8] ASCS is generated from immediate point-of-care processing of a small split-thickness skin sample that can be applied with a ratio of 1:80 (1 cm^2 of biopsy to cover up to 80 cm^2 of damaged area).[9,10] Coupled with STSG, this method achieves rapid burn wound closure with acceptable long-term scar and satisfaction outcomes without safety concerns.[11–13]

However, data regarding the use of ASCS for hand burns are limited. Thus, this study aimed to determine the effectiveness of ASCS in treating hand burns and compare outcomes with traditional skin graft techniques. We hypothesized that using ASCS in hand burns shortens the healing time with fewer complications and less donor site morbidity.

Materials and Methods

Study design

We conducted a single-center, retrospective review of patients treated for second- and third-degree hand burns. Two study groups included patients with hand burns treated with ASCS in combination with STSG and those treated with STSG alone (standard of care). This study received institutional review board approval (IRB# 19-1109-UMC-NO).

Eligibility and exclusion criteria

All patients with second- and third-degree hand burns presenting to a level 1 Trauma and Burn Center from 2017 to 2019 were considered (n = 69). Subjects must have been treated with ASCS and widely meshed STSG or STSG alone. Patients with underlying wrist or hand osseous pathology or neurovascular insult were excluded. Additional exclusion criteria included burns caused by chemicals, electricity, and/or radioactive substances (n = 7); the inability of the patient to follow outlined treatment protocols (n = 1); known hypersensitivity to trypsin or compound sodium lactate (Hartmann's) solution (n = 1); and a life expectancy of <1 year based on age, inhalation injury, percent total body surface area (TBSA), and comorbidities (n = 2). Treatment protocols include postoperative mobility guidelines, which are specific to the region burned. All protocols specify timing for therapy of unburned areas as well as timing/duration of functional splinting and physical therapy/occupational therapy for burned extremities.

Treatment

The burn injuries were excised to remove all nonviable tissue and create a sterile wound bed. Hemostasis was achieved with epinephrine-soaked Telfa (Covidien) and monopolar electrocautery to facilitate graft healing and prevent hematoma formation underneath the STSG. Wound areas were measured and documented.

Three different meshing ratios were incorporated in the study based on the extent of the injury and available donor sites. The ratios included 1:1, 2:1, and 3:1 with larger ratios used for larger burns. For both ASCS and STSG, donor skin was harvested at 0.008 inches or 0.010 inches and meshed as necessary. The ASCS preparation using the RECELL system (Avita Medical) was either harvested separately or trimmed from skin harvested for the meshed STSG. The total area of donor sites for the initial STSG was measured and documented. For both treatment groups, the meshed STSG was maintained in saline-moistened gauze until placement on the excised wound bed. STSG was secured in place to the wound bed with either staples or sutures at the surgeon's discretion.

The RECELL system is a device that enables surgeons to produce a suspension of Spray-On Skin Cells (Avita Medical) using a small sample of the patient's skin. This suspension contains the cells necessary to regenerate the epidermis and is prepared and applied at the point-of-care. The kit available in the United States allows up to 1920 cm^2 of expansion. The cost of the RECELL kit varies upon device utilization between $6,000 and $7,000.

The RECELL system was used per the manufacturer's instructions in the ASCS treatment group. A skin sample (1 cm^2 per 80 cm^2 of intended treatment area) was incubated for 15 to 20 minutes in a warmed proprietary enzyme solution to break down cell adhesions and extracellular matrix. After removal from the enzyme solution and placement on the device's sterile tray, a buffer solution was used to rinse the skin sample. The skin sample was then completely disaggregated by vigorously scraping both the dermal and epidermal layers. The disaggregated skin cells were suspended in a buffer solution, filtered, drawn into the application syringe, and applied over the more widely meshed STSG on the wound areas (Fig. 1). Telfa Clear Wound Dressing was applied to the inferior margin of the wound before proceeding with ASCS application. The cell suspension was sprayed on the wound from the most elevated part to the least elevated part so that the run-off waste was minimized. One ASCS application was delivered to the entire surface of the wound. Finally, the Telfa Clear Wound Dressing was wrapped over the treated site and secured in place.[11]

The STSG-only treated areas received a primary dressing of Assist Silver (Milliken) or CONFORMANT 2 (Smith & Nephew) and a wound vacuum-assisted closure per surgeon preference. For recipient sites not covered with a wound vacuum-assisted closure, a secondary dressing of Xeroform Occlusive Petrolatum Gauze Dressing (Covidien) was placed over the primary dressing, and additional padding of gauze and a crepe bandage were used at the surgeon's discretion for exudate absorption and protection. For the initial 48 hours after treatment, secondary dressings were changed every other day for a review of the treated areas and were replaced as appropriate. The Telfa Clear primary dressing remained in place for a minimum of 6 to 8 days and was not manipulated unless medically necessary. Following re-epithelialization, the treated areas were protected for a minimum of 2 weeks using light hydrophobic compression garments/sleeves or dry gauze and elastic bandaging along with the continued use of Xeroform dressings as needed. Vigorous cleansing or excessive application of topical creams was avoided to prevent damaging the newly formed skin.[11]

Independent and dependent variables

Medical records were reviewed to identify demographic and clinical information including age, sex, race/ethnicity, language, insurance, hand dominance, hand involved, diabetes, smoking status, and percent TBSA. Primary outcomes were time to wound re-epithelialization, time to return to work, the length of hospital stay, and complications such as reoperation, graft failure, and infection. Time to wound re-epithelialization was established as the time point when the entire wound bed had developed a layer of epithelial skin. This was determined at various dressing change time points by an experienced burn surgeon (Figs. 2–4). Time to return to work was obtained from clinic notes during patient follow-up appointments. Length-of-stay was calculated from admission and discharge dates within the patient's electronic medical record. Complications were obtained from surgeon notes as well as preoperative indications for revision/reconstructive surgery.

Data analysis

Demographic and baseline characteristics were compared between the groups (ASCS vs STSG) using either χ^2 tests or Fisher exact

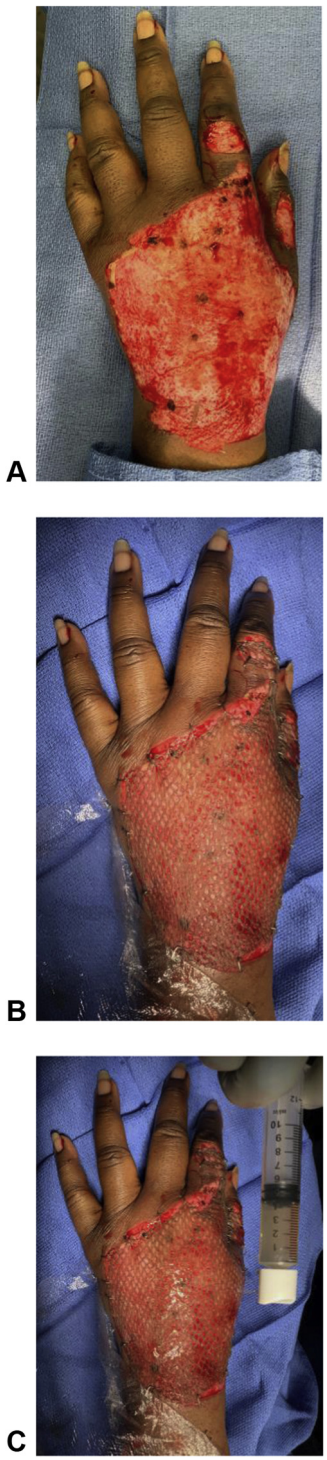

Figure 1. Technique for ASCS and STSG treatment of hand burn injury. **A** After tangential excision and obtaining hemostasis. **B** A 2:1 widely meshed STSG was harvested and placed. Permeable clear wound dressing was secured along the dependent margins of the field to minimize the loss of spray skin graft. **C** The wound was sprayed with ASCS evenly and covered with the permeable layer as the primary dressing.

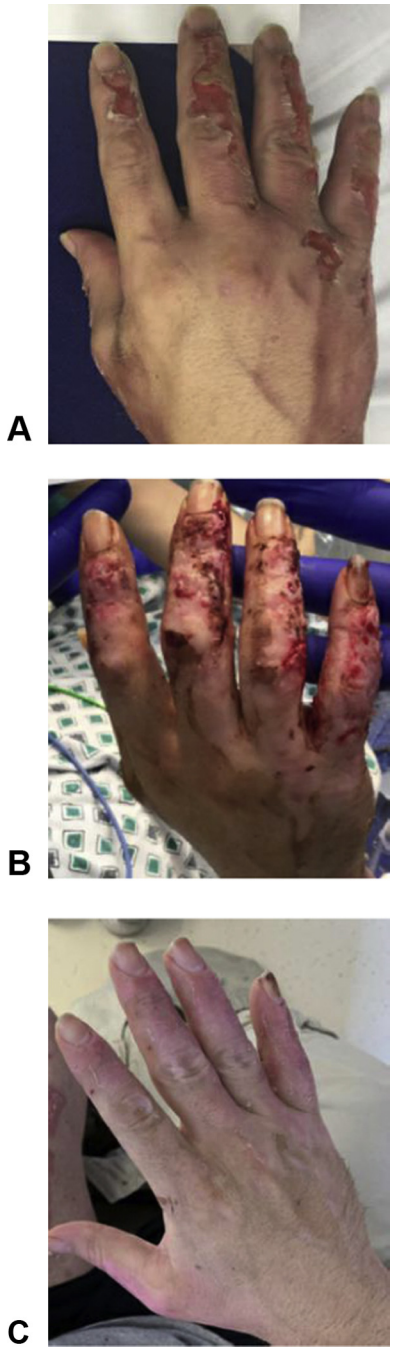

Figure 2. **A** A 33-year-old man sustaining a right-hand and torso burn injury with partial- and full-thickness burns involving 9% TBSA. Wound healing at **B** 9 days and **C** 20 days following ASCS and STSG treatment.

tests for categorical variables and Student t tests and Wilcoxon rank-sum tests for continuous variables. To identify predictors of re-epithelialization, time to return to work, and length-of-stay, analyses were performed using analysis of variance and linear regression models. Covariates were based on clinical significance and statistical significance in bivariate analyses. The significance level for inclusion in the final models was set at <0.1. Statistical analyses were conducted using Statistical Analysis Software software, version 9.4, for Windows (SAS Institute). All tests were two-sided with statistical significance set at a probability value of $P < .05$.

Results

Patient and clinical characteristics

Fifty-nine patients aged 14 to 85 years (mean age, 39 ± 15 years) met inclusion criteria. The ASCS treatment group comprised 37 patients; the STSG group comprised 22 patients (Table 1). There were no

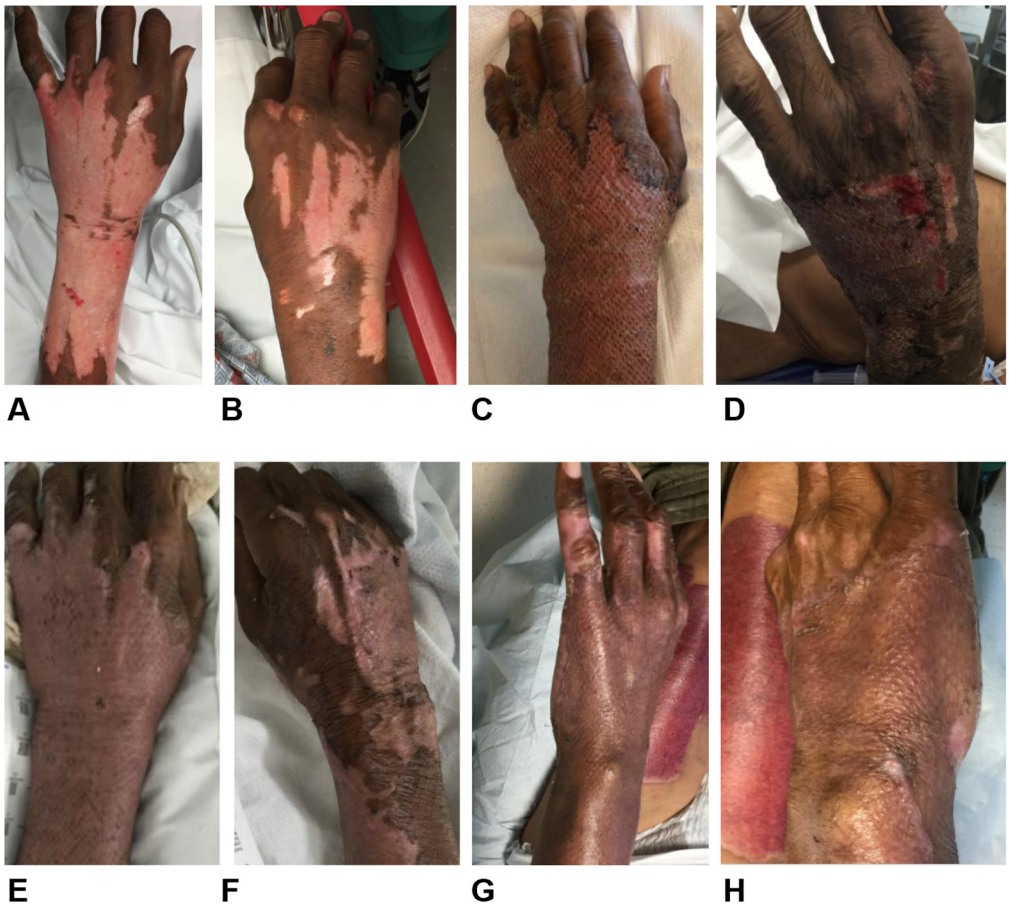

Figure 3. A, B An 87-year-old man sustaining bilateral hand and torso partial- and full-thickness burns involving 9% TBSA. Wound healing at **C, D** 9 days, **E, F** 14 days, **G, H** and 28 days following ASCS and STSG treatment.

significant differences in patient age between the ASCS and STSG groups (mean, 41 ± 17 vs 37 ± 12 years, respectively; $P = .26$). Percent TBSA was higher in the ASCS group than that in the STSG group with a mean of 22% versus 6%, respectively ($P < .05$). The prevalence of diabetes ($P = .11$) and smoking ($P = .66$) were similar between both groups.

A higher percentage of hand burn injuries involved the patient's dominant hand in the ASCS group compared with that in the STSG group (86% vs 55%, respectively; $P < .05$).

Unadjusted outcomes

There was no difference in time to wound re-epithelialization between ASCS (11 ± 4 days) and STSG (11 ± 5 days) treatment groups ($P = .99$) (Table 2). The mean time to return to work for the ASCS group (48 ± 22 days) was not significantly different from that of the STSG group (73 ± 88 days; $P = .20$). The mean length-of-stay was 23 ± 13 days compared with 10 ± 13 days ($P < .05$) for the ASCS and STSG groups, respectively. No patients in the ASCS group required reoperation, whereas 2 patients in the STSG group required reoperation.

The independent variables associated with increased length-of-stay were percent TBSA ($P < .05$) and involvement of the dominant hand ($P < .05$; Appendix A is available on the Journal's Web site at www.jhsgo.org).

Adjusted outcomes

In the multivariable analysis, the higher percent TBSA was associated with longer time for re-epithelialization ($P < .05$) and length-of-stay ($P < .05$). ASCS was associated with a shorter time for return to work ($P = .05$) (Table 3).

Complications

No patients in the ASCS group required reoperation, whereas 2 patients in the STSG group required reoperation. One was for infection-related graft loss and the other for web space contracture release (Table 4). Given the small number of complications, no adjusted analyses were performed.

Discussion

Treatment goals for hand burns include retaining maximal function and aesthetics without increased risk of complications. Currently, no studies address the efficacy and safety of ASCS for the treatment of hand burns.

Although we are not aware of any previous work evaluating the use of ASCS with STSG in hand burns, several authors have evaluated a similar concept in using ASCS for deep partial-thickness (DPT) facial burns. Like hand burns, facial burns present challenges in burn care including hypertrophic scarring and dyspigmentation that may impact form and function. Recently, Molnar et al[14] compared ASCS with STSG for the treatment of DPT facial burns. This prospective observational study of 5 patients showed no major complications and 1 superficial hematoma that did not result in a poor outcome. Healing and cosmetic outcomes were equivalent if not better than outcomes typical of STSG. They concluded that the treatment of DPT facial burns with

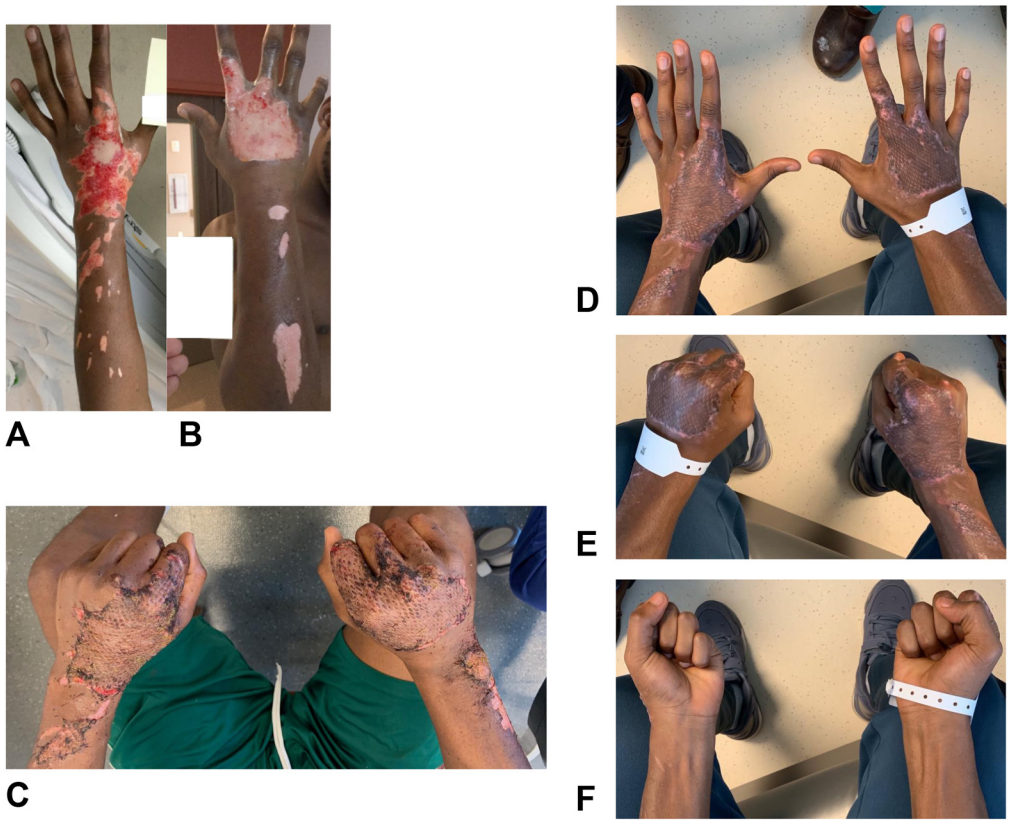

Figure 4. **A, B** A 22-year-old man sustaining bilateral hand burn injuries with partial- and full-thickness burns involving 3% TBSA. **C** Wound healing at 10 days and **D** repigmentation and active range of motion at 35 days following ASCS and STSG treatment.

Table 1
Patient Demographic Characteristics in Autologous Skin Cell Suspension and Split-Thickness Skin Graft Patient Populations

Characteristic	ASCS (n = 37)	STSG (n = 22)	*P* Value
	——— Mean (SD) ———		
Age	41 (17)	37 (12)	.26
Range	14–85	17–63	
% TBSA	22 (14)	6 (8)	<.05
Range	3–72	1–36	<.05
Follow-up (days)	524 (206)	670 (177)	
	——— % ———		
Sex			.56
Male	70	77	
Race			.87
Caucasian	59	55	
African American	30	36	
Hispanic	11	9	
Diabetes	11	0	.11
Smoking	51	45	.66
Insurance			
Private	57	45	.73
Medicare/Medicaid	24	23	
Self-pay	11	18	
Worker's comp	8	14	
Dominant hand	86	55	<.05

Table 2
Unadjusted Analysis of Outcomes by Autologous Skin Cell Suspension Versus Split-Thickness Skin Grafting

Characteristic	ASCS (n = 37)	STSG (n = 22)	*P* Value
	——— Mean (SD) ———		
Re-epithelialization (days)	11 (4)	11 (5)	.99
Return to work (days)	48 (22)	73 (88)	.20
Length-of-stay (days)	23 (13)	10 (13)	<.05
Complications (n)	0	2	.14

ASCS may be an alternative to current treatments, especially in patients prone to dyspigmentation and/or scarring or with limited donor sites. Similarly, our study demonstrated comparable rates of wound re-epithelization for hand burns with no complications or return to the operating room for patients in the ASCS treatment group. Importantly, Molnar et al noted that donor site morbidity could be minimized by using ASCS and harvesting less skin per percent TBSA burn. We also use any excess ASCS to spray the donor sites with the intention of shortening healing time; however, this was not evaluated in this study.

Several studies have compared the rate of wound epithelialization in ASCS with that of STSG. Gardien et al[15] studied the time to wound closure of 40 adult patients with acute full-thickness burns managed with either ASCS or STSG. They found that wound epithelialization after 5 to 7 days was significantly better for the ASCS group (71%) than for the STSG group (67%). There were no adverse events between the 2 groups; however, the scar formation was reduced and skin elasticity was higher in the ASCS group. The effects of cultured epithelial autograft in suspension on epidermal healing and maturation compared with partial-thickness skin grafting were studied by Magnusson et al.[16] The authors used surface electrical capacitance as an indicator of transepidermal water loss to objectively determine epidermal maturation in 16 patients with burns treated with either ASCS (n = 8) or STSG with Dulbecco's Modified Eagle's Medium (n = 8). They found an

Table 3
Adjusted Analysis of Outcomes

Variable	Re-epithelialization			Return to Work			Length-of-Stay		
	β-Coefficient*	**95% CI**	***P* Value**	**β-Coefficient***	**95% CI**	***P* Value**	**β-Coefficient***	**95% CI**	***P* Value**
Intercept	11	8.8–12.9	<.05	22	-20 – 65	.29	3.2	-2.3–8.8	.25
ASCS	-1.7	-4.5–1.0	.22	-59	-102–-15	<.05	-2.4–3.0	-8.4–3.6	.42
% TBSA	0.10	0.01–0.2	<.05	1.7	-0.4–3.7	.11	0.8	0.6–1.0	<.05
DM	0.35	-4.1–4.7	.87	-27	-144–90	.64	1.6	-8–11	.74
Smoking	0.52	-1.6–2.7	.63	33	-5.6–72	.09	1.8	-2.9–6.4	.45
D hand				49	3.8–94	<.05	3.5	-2.3–9.2	.23
R-square	0.09			0.27			0.65		

D hand, dominant hand burn; DM, diabetes mellitus.
Reference comparisons were the use of ASCS, diagnosis of DM, and active smoking for re-epithelization; D hand was included in the return to work and length-of-stay models. All analyses are linear regression models.
* β-Coefficient in days.

Table 4
Complications in Autologous Skin Cell Suspension and Split-Thickness Skin Grafting Treatment Groups

Complication	ASCS (n = 37)	STSG (n = 22)
Contracture	0	1
Graft failure	0	0
Infection	0	1
Reoperation	0	2

increased rate of epithelialization and epidermal maturation in ASCS-treated burns compared with STSG-treated burns. In our cohort, time to re-epithelialization increased as percent TBSA increased, despite the use of ASCS. This suggests that percent TBSA is a primary factor in re-epithelialization. We hope to better control for this in future work by examining the use of ASCS in hand burns with <20% TBSA.

Few studies have evaluated the time to return to work following hand burns. Helm et al[17] reviewed time to return to work following hand burns in 70 patients. They found that 52 patients (74%) had returned to work at the 8-month assessment and that the best predictor of time to return to work was percent TBSA followed by use of STSG. The study did not include patients who had undergone ASCS treatment. Although not limited to hand burns, Quinn et al[18] reviewed 21 studies capturing 3134 patients with burn injuries and found that an average of 66% of patients returns to work following a burn injury. Lower percent TBSA was correlated with an earlier return to work. Time to return to work ranged from 4.7 weeks to 24 months with common barriers to return to work being burn severity, longer length-of-stay in the hospital, and the number of operative procedures. In our study, there was no significant difference in time to return to work between the ASCS (48 ± 22 days) and STSG (73 ± 88 days; $P = .20$) groups, despite the ASCS treatment group consisting of higher percent TBSA (22% ± 14% vs 6% ± 8%; $P < .05$). When adjusting for percent TBSA, ASCS was associated with an earlier return to work ($P < .05$). In addition, a greater percentage of patients in the ASCS group had their dominant hand affected by a burn injury (86%) compared with patients in the STSG groups (55%; $P < .05$), which was a significant variable for increased hospital length-of-stay ($P < .05$). Our study suggests that the use of ASCS may expedite return to work in patients with hand burns.

The effect of hospital length-of-stay on patient outcomes has been well documented in the trauma and burn patient populations. Mathew et al[19] studied the risk of developing complications because of excessive stay in the hospital in 416 trauma patients over a 4-year period. The longer hospital stay (>30 days) was independently associated with the development of complications and that each additional day in the hospital after the completion of medical care was associated with 5% higher odds of complications. We believe there are 2 primary reasons for this finding: increased severity of disease in burn and trauma patients that necessitates longer inpatient convalescence/rehabilitation and increased length-of-stay that lengthens the window to identify/diagnose comorbidities/diseases. Gojowy et al[20] performed a single-center cross-sectional study evaluating 42 long-term severe burn survivors with DPT burns >20% TBSA and found that both length-of-stay and hand function predicted physical summary scores and decreased health-related quality of life. Our study demonstrated an increased length-of-stay in the ASCS treatment group (23 ± 13 days) compared with the STSG treatment group (10 ± 13 days; $P < .05$). This finding is likely because of a higher percent TBSA burns being treated with ASCS as TBSA burned was the primary variable related to length-of-stay, wound re-epithelialization, and return to work.

Our study was limited by its retrospective nature. Patients were not randomized and data collection from the chart review was therefore limited to clinical documentation. Patients with larger burns tended to receive ASCS to their hands in addition to other burned areas. Measurements obtained for wound re-epithelialization were subjective despite being performed by various expert burn clinicians not necessarily involved in the surgical treatment of the patient. Another limitation is the small number of patients in this study. Despite the larger patient number compared with the previous literature, the study design reduces the generalizability of the results. Shorter follow-up for the ASCS group limits the time for the detection of complications in that group; however, most complications occur within 1 year of injury. Lastly, the study did not include patient-reported outcome data or functional measurements like grip strength or range of motion. A multicenter prospective study with treatment randomization and the inclusion of patient-reported outcomes and functional measurements would reduce the potential for bias.

In conclusion, this study demonstrates that ASCS is safe in treating hand burns compared with the current standard of STSG. Treatment with ASCS was associated with similar rates of re-epithelialization, decreased time to return to work, and no difference in complications compared with the STSG treatment alone. If cost is not prohibitive, these potential advantages warrant consideration of ASCS for hand burns. Given that the only kit available in the United States is best used for larger burns, we believe a smaller, less expensive kit limited to 300 cm^2 to 400 cm^2 of spray graft will be valuable in caring for patients with isolated hand burns.

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