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Original Article

Soft-tissue expansion versus composite skin grafting for plastic and reconstructive surgery in burn patients

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Abstract: Objective: To compare and analyze the effects of soft-tissue expansion and composite skin grafting for plastic and reconstructive surgery in burn patients. Methods: Burn patients (n=116) who were admitted to Tangshan Gongren Hospital for plastic and reconstructive surgery from March 2017 to March 2019 were recruited in this study. The patients were assigned to the composite skin graft group or the soft-tissue expansion group according to a random number table, with each group having 58 patients. Patients in the composite skin graft group underwent composite skin grafting, while those patients in the soft-tissue expansion group were treated with soft-tissue expansion. After surgery, the time to wound healing and time to blood circulation recovery were analyzed in patients of the two groups. The levels of ACTH (adrenocorticotropic hormone), cortisol (Cor) and endothelin-1 (ET-1) in serum were measured using the turbidimetric immunoassay. The levels of interleukin-8 (IL-8), interleukin-17 (IL-17) and hypersensitive C-reactive protein (hs-CRP) were tested by enzyme linked immunosorbent assay. Additionally, patients in both groups were compared in the therapeutic effects and occurrence of complications. Results: After surgery, the time to wound healing and time to blood circulation recovery were shorter in the soft-tissue expansion group than in the composite skin graft group (both $P<0.05$). Lower levels of ACTH, Cor, ET-1, IL-8, IL-17 and hs-CRP were observed in the soft-tissue expansion group than in the composite skin graft group, and the soft-tissue expansion group also had more effective treatment and a lower rate of complications (all $P<0.05$). Conclusion: The use of soft-tissue expansion for plastic and constructive surgery in burn patients accelerated wound healing, recovery of blood circulation and resulted in weaker surgery-induced stress response and inflammatory response. The soft-tissue expansion treatment was more effective and safer. Therefore, this surgical technique is useful in clinical practice.

Keywords: Soft-tissue expansion, composite skin grafting, plastic and reconstructive surgery for burns, surgery-induced stress response

Introduction

In clinical medicine, the symptoms of thermal injuries in skin tissue, mucosal tissue, subcutaneous and submucous tissue caused by action of external high temperature and heat have been collectively referred to as burn injuries which include composite injury and critical burn injury [1, 2]. The epidemiological data reveal the incidence of burn injury remains high and shows a rising trend in China in recent years. Previous studies have indicated that the result of being burned has a bad impact on the appearance of patients, and also poses a severe threat to their physical and mental health. Therefore, it is of great significance to develop effective therapies for treatment of burn injuries [3, 4].

Soft-tissue expansion mainly refers to a technique used by a plastic surgeon to transplant a patient's own normal skin tissue to the burn wounds. Specifically, a plastic surgeon expands the size of a patient's normal skin tissue with an artificial expander, and transplants the expanded normal skin tissue to the burn wounds, realizing the purpose of repair and reconstruction of the defects [5]. When soft-tissue expansion is applied to treat burned patients, the expanded skin created from the normal skin tissue show no significant difference in thickness, color and texture from the normal skin tissue. Hence, treatment of the burn wounds effectively avoids new cicatrix generation and has an ideal effect in clinical practice [6]. Composite skin grafting is a technique by which acellular allogenic dermal matrix

(ADM) is transplanted to the burn wounds and mixed with split thickness skin autografts of a patient to create composite grafts for repairing and reconstructing the defects. The technique significantly improves the appearance of scar tissue in the burn patients, with a high survival rate of skin grafts [7-10]. The result of a study demonstrated that composite skin grafting in which composite skin grafts were used as skin substitutes, had the advantages of no antigenicity and folds, close adsorption with the wound surface and simple procedures, so it could effectively reconstruct the burnt tissue [11]. Clinically, soft tissue expansion is currently more widely used than composite skin grafting. Therefore, we hypothesized that soft tissue expansion would result in an ideal effect for the treatment of burn injuries. In this study, patients with burn injuries underwent soft tissue expansion or composite skin grafting, and then the therapeutic effects of the two surgical techniques were observed.

Materials and methods

Materials

Study subjects: One hundred and sixteen burn patients who were admitted to Tangshan Gongren Hospital for reconstructive plastic surgery between March 2017 and March 2019 were enrolled in this study and assigned to receive either composite skin grafting (n=58, composite skin graft group) or soft-tissue expansion (n=58, soft-tissue expansion group) based on a random number table. The composite skin graft group included 47 male patients and 11 female patients, and the patients ranged from 23 to 49 years of age (mean, 36.5±6.2 years) and had soft-tissue defects of 3.5×4.9 to 8.6×15.3 cm^2. In the soft-tissue expansion group, there were 46 male and 12 female patients; the patients were aged between 23 and 50 years (mean, 36.9±6.5 years), and the soft-tissue defects varied from 3.5×4.9 to 8.6×15.4 cm^2 in size. The differences between the two groups in sex, age, and size of soft tissue defects were insignificant, so the groups were comparable.

Inclusion criteria: Patients were included in this study if they were diagnosed as having Grade III burns in Tangshan Gongren Hospital in accordance with the diagnostic criteria for Grade III burns developed by Chinese Society of Burns, Chinese Medical Association [11]. In addition, the patients' complete medical records were available and they had received no prior relevant treatment. All patients and their families in both groups were informed and provided written consent. This study was approved by the Ethics Committee of Tangshan Gongren Hospital.

Exclusion criteria: Patients were excluded from this study if they had skin cancer, coagulation dysfunction, cardiac, hepatic or renal impairment, or poor communication ability.

Methods

Surgical techniques: All the patients who had Grade III burns first had their scar tissue removed, then they were treated with composite skin grafting or soft-tissue expansion.

Composite skin grafting: With the patient under general anesthesia, the scar tissue was excised and deformities were corrected. After hemostasis, the incision was cleansed and dressed with antibiotic solution. After being washed in normal saline, the acellular allogeneic dermal tissue was grafted and the burn wounds were resurfaced, and closed and sutured tightly. Skin autografts were taken and attached to the membrane of acellular allogeneic dermal matrix, followed by fixation and dressing of the grafts.

Soft-tissue expansion: Each patient was measured for the shape and size of the burn wounds, then an well-sized expander was selected. According to the burn wound and the surrounding expansion area, the skin expansion region was designed and marked out. An incision was made in the boundary region between the burn wound and the surrounding expansion area, advanced from the incision site to the muscle layer, and bluntly dissected. After that, the expander was inserted under the soft tissue, followed by hemostasis, drainage tube placement and negative pressure drainage. Then, the incision was sutured. Seven days after the surgery, 20-25 mL of normal saline was infused twice a week into the balloon of the expander for 7 to 8 weeks. Normal skin tissue was expanded to meet the requirements of the operation, the infused normal saline was extracted, and the expander was removed. The flaps were pushed to cover and reconstruct the burn wound, and then suturing and pressure dressings were applied.

Outcome measures: Primary outcome: The primary outcome was the recovery of the burn wound. The time to wound healing and time to blood circulation recovery were statistically compared between the two groups. Response evaluation was performed as follows. The clinical therapeutic effects were classified into markedly effective, effective and ineffective. The treatment was markedly effective if a patient's wound was completely healed, the blood circulation returned to normal, and the grafted skin was insignificantly different from normal skin tissue in thickness, texture and color. The treatment was effective if the wound was significantly improved, the blood circulation was good, but there were some differences between the grafted skin and normal skin tissue in thickness, texture and color. The treatment was ineffective if the wound healing and blood circulation were poor, and the grafted skin was significantly different from normal skin tissue in thickness, texture and color. The overall response rate was calculated in the following formula: Overall response rate = (Markedly effective cases + Effective cases)/ Total cases * 100%.

Secondary outcomes: The secondary outcomes were the levels of serum markers. Venous blood (3 mL) was extracted from each patient before and after treatment, and centrifuged for 15 min. Subsequently, the serum was isolated and stored at -70°C for examination.

The levels of ACTH (adrenocorticotropic hormone), cortisol (Cor) and endothelin-1 (ET-1) in serum were detected with the use of turbidimetric immunoassay [12]. Three tubes were prepared and labeled as standard tube, test tube and blank tube, respectively. After buffer solution (350 μL) had been added into each of the three tubes, prepared standard solution of ACTH, Cor, ET-1 (20 μL) was added into the standard tube, serum (20 μL) into the test tube, and distilled water (20 μL) into the blank tube. Then the three tubes were shaken evenly and placed at room temperature for 5-10 min. A colorimetric assay was performed using a spectrophotometer (Shanghai Lab-Spectrum Instruments Co., Ltd, Model: Alpha-1900SPlus). At a wavelength of 500 nm, the blank tube was modulated to zero, the absorbance was recorded, and the levels of ACTH, Cor and ET-1 in serum were calculated.

The levels of interleukin-8 (IL-8), interleukin-17 (IL-17) and hypersensitive C-reactive protein (hs-CRP) were measured using the enzyme linked immunosorbent assay [13]. The antigen was diluted by addition of carbonate buffer solution (50 mm), and then added into the reaction pores of polystyrene. After being coverslipped, the mixture was placed at 4°C for 24 hours, washed 3 times the next day and dried. Prepared dilution (pH value of 7.4, 0.02 mol/L Tris-HCl buffer), diluted sample to be tested (0.1 mL), and positive and negative control samples were added into each well, and placed at 42°C for 60 min, followed by liquid removal, three-time washing and drying. The antibodies (0.1 mL) including IL-8, IL-17 and hs-CRP (IL-8 antibody: Shanghai XinYu Biotech Co., Ltd, Cat No: XY17038-1; IL-17 antibody: Shanghai Yu Bo Biotech Co., Ltd, Cat No: YB01378; hs-CRP antibody: Daqing MabCom, Inc., Cat No: TM011-1) were added into each well, then the previous procedures were repeated (60-min placement, liquid removal, three-time washing and drying). In addition, substrate solution (Na_2HPO_4 at 0.1 mol/L, citric acid at 0.05 mol/L) was added into each well and mixed evenly, to which o-phenylenediamine (0.1 mL) was added, and protected from light for 20 min. H_2SO_4 at 2 mol/L (0.05 mL) was added into each well and the reaction was stopped. The A450 values were detected by a microplate reader (Shandong Yuntang Intelligent Technology Co., Ltd., Model: YT-MB-96S), and the levels of IL-8, IL-17 and hs-CRP were analyzed.

The rates of complications were assessed in patients of the two groups. The number of cases with complications were counted and compared between the two groups. More than one complication occurring in the same case was recorded as 1 case. The complication rate was calculated as follows: Complication rate = Complication cases/Total cases * 100%.

Statistical analysis

In this study, data analyses were performed with the use of SPSS statistical software, version 20.0. Measurement data were described

Table 1. Comparison of patient general data

Group	n	Male-female distribution	Mean age	Size of soft tissue defects
Composite skin graft group	58	47/11	36.5±6.2	74.6±45.6
Soft-tissue expansion group	58	46/12	36.9±6.5	73.8±45.1
t/χ^2		0.054	0.339	0.095
P		0.816	0.735	0.924

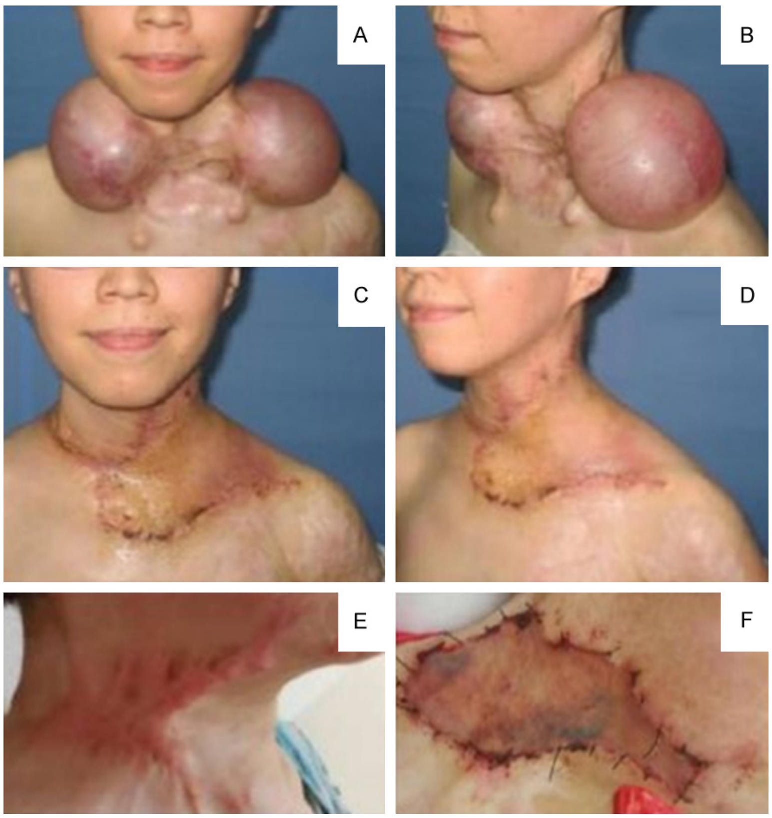

Figure 1. Images for patients undergoing soft tissue expansion or composite skin grafting. A: An expander is placed into a patient during soft-tissue expansion; B: An expander is placed into a patient during soft-tissue expansion; C: After the patient completed soft tissue expansion; D: After the patient completed soft tissue expansion; E: Before the patient received grafts during composite skin grafting; F: After the patient received grafts during composite skin grafting.

Table 2. Comparison of patient wound recovery ($\bar{x}$ ± sd)

Group	n	Wound healing	Blood circulation recovery
Composite skin graft group	58	17.7±2.6	20.7±3.2
Soft-tissue expansion group	58	13.6±2.3	17.2±2.9
t		8.995	6.172
P		0.001	0.001

as mean ± standard deviation ($\bar{x}$ ± sd). Inter-group comparisons were made using one-way ANOVA, while between-group comparisons were conducted by the LSD-t test. A *p* value of less than 0.05 indicated statistical significance.

Results

Patient general data

Table 1 shows that there were no significant differences between the soft-tissue expansion group and the composite skin graft group in male-female distribution, mean age, or size of soft tissue defects (all P>0.05).

Surgical images

The images for patients undergoing soft tissue expansion or composite skin grafting were shown in **Figure 1**.

Comparison of patient wound recovery

The wound healing and blood circulation recovery were faster in the soft-tissue expansion group than in the composite skin graft group, and the differences were significant (P<0.05, **Table 2**).

Comparison of ACTH, Cor and ET-1 levels in serum before and after surgery

The levels of ACTH, Cor and ET-1 differed insignificantly between the two groups before surgery (all P>0.05). After treatment, elevated levels of ACTH, Cor and ET-1 were seen in both groups, and the levels of ACTH, Cor and ET-1 in serum were significantly lower in the soft-tissue expansion group (all P<0.05, **Figure 2**).

Comparison of IL-8, IL-17 and hs-CRP levels

The levels of IL-8, IL-17 and hs-CRP were insignificantly different between the two groups before surgery (all P>0.05). After surgery, how-

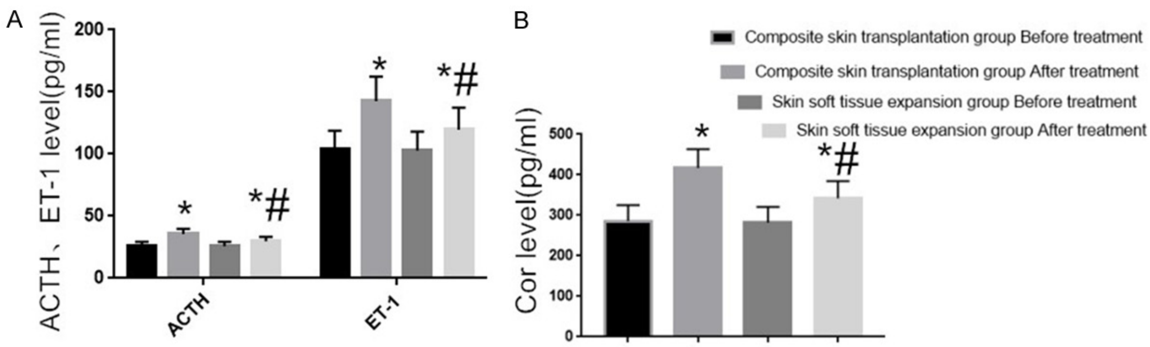

Figure 2. Comparison of ACTH, Cor and ET-1 levels. A: Levels of ACTH and ET-1; B: Level of Cor. Compared with the same group after treatment, *P<0.05; compared with the composite skin graft group, #P<0.05. ACTH: adrenocorticotropic hormone; Cor: cortisol; ET-1: endothelin-1.

ever, the levels of IL-8, IL-17 and hs-CRP in both groups were elevated, with significantly lower levels in the soft-tissue expansion group than in the composite skin graft group (all P<0.05, **Figure 3**).

Comparison of the treatment efficiency

The overall response rate of the soft-tissue expansion group was 91.38%, significantly higher than that (75.86%) of the composite skin graft group (P<0.05, **Table 3**).

Comparison of complications

The rate of complications was 20.69% in the soft-tissue expansion group, and it was significantly lower than that (37.93%) of the composite skin graft group (P<0.05, **Table 4**).

Discussion

A more commonly used method for burn treatment is plastic and reconstructive surgery. In recent years, with the continuous development of clinical medicine, and the non-stop advance in plastic surgery technology and reconstructive materials for burns, the reconstructive techniques for burn injuries have made great development and progress. The common surgical techniques for burn treatment include soft-tissue expansion and composite skin grafting [14, 15]. In this study, enrolled patients with burn injuries underwent soft-tissue expansion or composite skin grafting. The results showed that the time to wound healing and time to blood circulation recovery were shorter, and the treatment was more effective in patients with soft-tissue expansion than those patients with composite skin grafting, indicating that the application of soft-tissue expansion promoted wound healing of patients with burn injuries, and the clinical treatment was more significantly effective.

Multiple clinical studies have demonstrated that surgical treatment of a patient may stimulate the patients to a certain extent, resulting in surgery-induced stress response. It has some impact on the patient's wound healing and disease recovery. ACTH, Cor and ET-1 are the most frequently-used markers for evaluating the severity of surgery-induced stress response in clinical practice.

ACTH, a micro polypeptide hormone, is mainly generated by secretion of adenohypophysis. The changes in ACTH levels are closely associated with the severity of stress response, so ACTH level is often used in clinical judgment of the stress response [16]. Cor is primarily generated by the adrenal glands, and the expression level of Cor may be elevated abnormally with external stimulation. The changes in Cor levels are closely related to the severity of stress responses in the body [17]. ET-1, a bioactive peptide, inhibits renin secretion in the body, and the changes in ET-1 levels are closely associated with the stress response of the body [18]. A finding of this indicated that the levels of ACTH, Cor and ET-1 were less elevated in burn patients undergoing soft-tissue expansion, suggesting that the patients with soft-tissue expansion had a smaller surgery-induced stress response and higher safety.

According to some scholars, surgery is an invasive method for diagnosis and treatment. As a

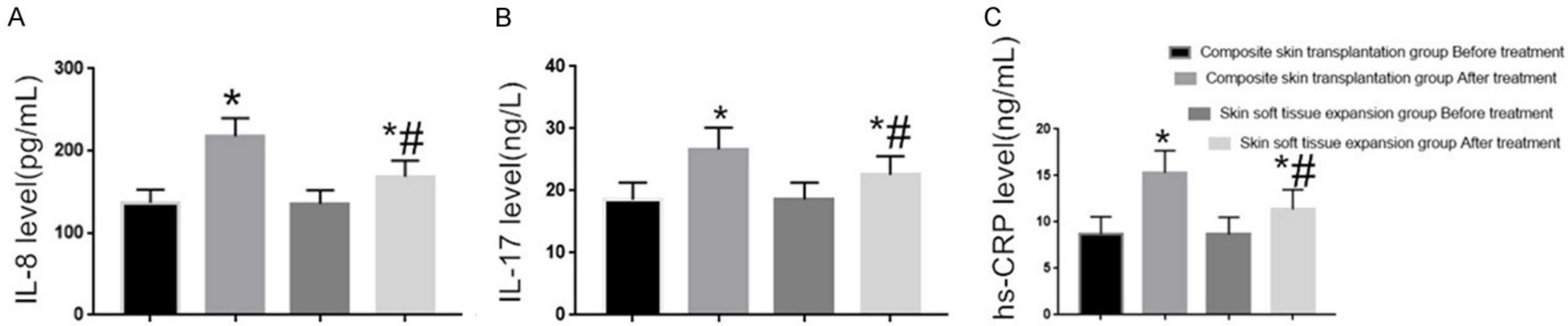

Figure 3. Comparison of IL-8, IL-17 and hs-CRP levels. A: Level of IL-8; B: Level of IL-17; C: Level of hs-CRP. Compared with the same group after treatment, *P<0.05; compared with the composite skin graft group, #P<0.05. IL-8: interleukin-8; IL-17: interleukin-17; hs-CRP: hypersensitive C-reactive protein.

Table 3. Comparison of the treatment efficiency (n, %)

Group	n	Markedly effective	Effective	Ineffective	Overall response rate
Composite skin graft group	58	23	21	14	44 (75.86)
Soft-tissue expansion group	58	32	21	5	53 (91.38)
χ^2					5.098
P					0.024

Table 4. Comparison of complications (n, %)

Group	n	Distal necrosis of flap	Infected wound	Erythema	Total incidence
Composite skin graft group	58	8	7	7	22 (37.93)
Soft-tissue expansion group	58	5	4	3	12 (20.69)
χ^2					4.161
P					0.041

source of stress response, surgery may cause high-energy damage to patients and induce inflammatory responses in the body. IL-8, IL-17 and hs-CRP are clinically common markers used to assess the inflammatory response of the body. IL-17, a proinflammatory cytokine produced by activated T cells, promotes the generation of IL-6, IL-8 and other inflammatory cytokines, thereby inducing an inflammatory response [19, 20]. Hs-CRP, a C-reactive protein mostly synthesized by liver tissue, is a broad-spectrum marker for inflammatory response of the body [21, 22]. A result of this study showed that elevations in IL-8, IL-17 and hs-CRP levels were smaller in magnitude in burn patients with soft-tissue expansion, which indicates soft-tissue expansion was associated with a smaller inflammatory response in burn patients.

In addition, the incidence of complications was also statistically analyzed in burn patients in this study. The result suggested that the incidence of complications was lower in burn patients treated with soft-tissue expansion, which further reflected the higher safety of soft-tissue expansion.

Although soft-tissue expansion is more effective than composite skin grafting, it has the disadvantages of longer treatment duration and higher costs. Moreover, it is still associated with higher rates of complications. Therefore, future clinical studies should be directed at shortening the surgical duration and decreasing the incidence of complications, so as to reduce the psychological and economic pressure of patients and improve the safety of soft-tissue expansion.

In conclusion, the application of soft-tissue expansion in plastic and reconstructive surgery for burns accelerated wound healing and blood circulation recovery in the patients. The surgery-induced stress response and inflammatory response were less in these patients. The surgery was more markedly effective and safer. Hence, soft-tissue expansion is of important for clinical application.

Disclosure of conflict of interest

None.

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