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Human acellular dermal matrix allograft: A randomized, controlled human trial for the long-term evaluation of patients with extensive burns

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ABSTRACT

The potential of acellular dermal matrix (ADM) to improve cosmetic and functional outcomes has been demonstrated; however, there have been few clinical comparative studies assessing the long-term morphological, histological and functional changes after ADM placement. This study was designed to retrospectively evaluate the long-term outcomes of the cograft acellular dermal matrix with autologous thin split-thickness skin for the coverage of wounds in extensively burned patients. Thirty burn patients treated with a composite graft of ADM with autologous split-thickness skin from January 2007 to December 2009 were enrolled in this study. Another group of thirty patients who received only an autogenous split-thickness skin implant served as the control. Our study revealed that the collagen in the dermis treated with ADM were ordered, and the proportion of collagen III/I was much higher in the control group than in the ADM group. The basement membrane was prominent and continuous. Meanwhile, the VBSS (Vancouver Burn Skin Score) was used to evaluate skin quality, which shows a significant differences between the two group ($P < 0.001$). Then the functional level was evaluated by the BI (Barthel Index), and the ADM group was much better than the control group ($P = 0.005$). Based on these results, we concluded that the composite graft of ADM with autologous thin split-thickness skin was suitable for repairing the defects in functional areas after a burn. This technique might facilitate wound management with acceptable esthetic outcomes, good functional recovery and less scar hyperplasia at the donor site.

1. Introduction

Burn wound coverage techniques have been greatly improved; patients with more than 90% total body surface area (TBSA) burns can now expect a fighting chance for survival [1–3]. Nevertheless, the lack of donor sites in major burn patients and secondary hypertrophic scar formation remain two major clinical challenges. The problem of the lack of donor sites is that the need for donor sites sometimes

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exceeds the available unburned skin; to approach this problem, autologous thin-thickness skin grafts were developed. The intermediate meshed split skin graft for recipient site wound closure after excision of the burned area remains the gold standard for treatment. However, split-skin harvest and transplantation are accompanied by frustrating consequences, such as wound contraction, donor site morbidity, and hypertrophy [4–6]. The lack of a dermal component in burn wounds after treatment with split-thickness autografts resulting in the poor quality of healing in recipient sites created the need for alternative graft sources [7].

The advent of allo-dermal replacement has revolutionized the therapeutic potential for the success rate and quality of healing in split-skin transplantation. In 1981, a composite of bovine collagen and chondroitin-6-sulfate from shark cartilage with an outer silicone covering was first engineered as an organotypic dermia for skin grafting [8]. In the same year, Sarber et al. developed a type of skin equivalent that is composed of natural collagen extraction and fibroblasts according to a specific mixing ratio [9]. Composite skin grafting was used extensively thereafter. In 1985, Heck reported using allogeneic dermis for wound closure [10]. He found that allogeneic dermis grafts caused immunological rejection mainly due to cellular immunity [11]. Subsequently, all of the cellular components of the dermis and epidermis were processed for removal, and the extracellular matrix and basement membrane (BM) were preserved. Such ''decellularized'' allografts had been effectively used alone or in combination with cultured autologous keratinocytes for the closure of burns and chronic wounds in the next year and were considered to have the potential to be a permanent dermal alternative [11]. Until 1995, Wainwright used composite transplantation to repair burn wounds with acellular and allogeneic dermis and reticular autologous thin-split grafts; this method avoided immune rejection [12]. Subsequently, upon histological observation, researchers found that the epithelial cells were well covered and that there was less scar proliferation with good effect. Since then, composite skin grafts have been widely used in both wound healing and scar plastic surgery [13–16].

However, there is a lack of literature regarding the long-term follow-up data of randomized, controlled human studies, especially in the aspects of histological changes, contour and function. In the present study, we used the Vancouver Burn Scar Scale (VBSS) and Barthel Index (BI) Scale to conduct a long-term evaluation of contour and functional outcomes following co-transplantation of a split-thickness skin graft (STSG) with human acellular dermal matrix.

2. Materials and methods

2.1. Clinical data

This study was reviewed and approved by the institutional ethics committee. A total of 60 patients who sustained burns provided consent to participate in this study over 3 years (2007–2009), and patients with electrical burns, fourth-degree burns, burns as components of multiple traumas (patients with fractures or central nervous system, thoracic and abdominal trauma), elderly patients with co-morbid diseases such as chronic cardiovascular disease, diabetes mellitus or hypertension, and those who had significant inhalation injuries or needed intensive care were excluded from the study. Eligible patients were randomized at admission to either ADM or STSG group. Randomization was performed following a predetermined random order produced in groups of 10. This preordered format was maintained by the primary investigator. Patients who were excluded were assigned randomization but not included in the subsequent analysis. The 2 groups are as follows: the acellular dermal matrix (ADM) group ($n = 30$), in which the wounds were successfully covered with ADM and autologous epidermis, and the control group ($n = 30$), in which the wounds were covered with autologous split-thickness skin. The general patient characteristics are listed in Table 1; the types of grafts used for burn treatments are listed in Table 2. Of the 30 patients in the experimental group, 25 were male and the remaining 5 patients were female; their ages ranged from 3 to 52 years, with an average age of 30.53 ± 10.73 years. Thirty sites from 20 patients underwent surgical burn wound excision and were grafted with acellular dermal substitutes and covered with thin split-thickness skin that was not expanded. A similar procedure was conducted on five sites of four patients with mature granulation tissue in later burn stages and on seven sites of six patients with scar plasticity. The skin graft sites included the neck, hand, elbow, shoulder, popliteal site, knee and foot back, among others. The largest area of composite skin graft was 600 cm^2; the minimum area was 40 cm^2. Of the control group, the mean age of the 30 patients was 25.30 ± 15.88 years with a range of 2–57 years; 24 patients were males, and 6 were females.

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2.2. Materials

This investigation involved commercial ADM products from Jie-Ya Life Tissue Engineering (Beijing, China) that were approved by the Chinese Food and Drug Administration for transplantation. ADM is a dermal collagen matrix extracted from human skin by removing the majority of the cellular

Table 1 – General patient characteristics.

Type	Number	
	ADM group	Control group
Average age	30.53 ± 10.73	25.30 ± 15.33
Male/female	25/5	24/6
Scar plasticity	6 (20%)	2 (6.67%)
Granulation tissue	4 (13.33%)	11 (36.67%)
Burn	20 (66.67%)	17 (56.67%)