Clinical Applications of Allograft Skin in Burn Care

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Abstract: Allograft skin has been widely used for wound management in burn centers. Functional as biologic dressing, it can not only provide ideal temporary wound coverage in extensive burns when autograft is not immediately available but also prepare the wound bed for definitive autografting. In this article, the up-to-date clinical application of allograft in burn care was reviewed, including coverage of extensive burn wounds, combined use with meshed autograft, template for delayed application of cultured epidermal autografts, and the use of human acellular dermal matrix. Although it has potential disadvantages of rejection and disease transmission, allograft skin remains a workhorse in treatment of severe burn wounds.

Key Words: allograft skin, burn care, skin banking, sandwich grafting technique, cultured epidermal autografts, acellular dermal matrix

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HISTORY

The use of allograft in burn management dates back to 1881 when Girdner[10] treated a severe burn patient with allograft skin from a suicide victim. Brown et al[11,12] popularized the use of allograft as biological dressing for extensive burns and denuded area. The widespread use of allograft has become one of the driving forces behind the growth and development of skin banking facilities. In 1971, Bondoc and Burke[13] established the first functional skin bank. The increasing numbers of skin banks over the world not only meet the specific needs of the burn surgeons but also help generate community support for skin donation.[14]

TECHNICAL ASPECTS OF SKIN BANKING

The path of allograft skin from the donor to the recipient includes a series of processes, including procurement, processing, preservation, storage, and distribution of tissue.[15] Once screening of the potential tissue donor is complete and proper authorization has been obtained, procurement of skin from cadavers is carried out by a team of authorized practitioners. At the skin bank, the skin is processed and preserved. As required, the allograft skin is transported to hospitals in secure containers and rewarmed before use.

There are 2 common preservation techniques, cryopreservation and glycerol preservation, and their effects on clinical outcome remain controversial.[16] Both methods have their own advantages and disadvantages.[17,18] Generally, cryopreservation allograft (CPA) has a higher level of tissue viability than glycerol-preserved allograft (GPA), whereas GPA can be stored for longer periods and is more cost effective than CPA.[6,8,17,19,20] Kua et al[17] compared the clinical outcome between these 2 types of allograft skin, and the results were not statistically significant. A recent study concerning cadaver allografts in partial thickness wounds in pig models showed that the take rate and removal rate of skin between CPA group and GPA group were not significantly different despite that the cell viability of CPA was higher than that of GPA.[19] Prospective, randomized, controlled trails are needed to confirm the effect of preservation method of allograft on wound healing process.

INDICATION

With the development of successful procedures for the safe banking of cadaveric skin, allograft has been widely used in the management of patients with severe burn injuries.[2,5–8] The general indications for its use in wound management include temporary biologic coverage in extensive burns when autografts may not be immediately available, dressing for superficial partial-thickness wounds, wound bed preparation for autografting, and template for the delayed application of keratinocytes.[3] Allograft skin possesses many of the desirable properties of autologous skin and plays an important role in treatment of massive burn wounds. As biologic dressings, they can reduce pain and adhere to the wound bed, resulting in temporary wound closure which decreases water, electrolyte, and protein loss, prevents wound desiccation, stimulates vascularization, improves thermoregulation, and protects wounds from bacterial contamination. In addition, allograft can provide dermal matrix, which may improve final graft properties after definitive autografting.[14,21]

CLINICAL APPLICATION

Coverage of Extensive Burn Wounds

Allograft has long been the standard skin substitute applied to patients with major burns for temporary skin coverage. With the versatility and availability of allograft, large burns can now be excised early and quickly. Choi et al[5] analyzed the data of patents with burns covering more than 30% of TBSA from 4 burn centers. A total of 1282 patients were included in their study. These 698 patients were treated by allograft coverage within 7 days of the injury, followed by autografting

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approximately 2 weeks later, whereas 584 patients underwent conventional treatment, with longer intervals between excision and autograft coverage. The results showed that patients in allograft group had a lower 90-day in-hospital mortality than patients in conventional group.

Although allograft is an excellent alternative for temporary wound coverage, it is most frequently used in large burns. Fletcher et al[7] reported that the frequency of allograft use in patients with 30 to 49% TBSA burns was almost equal to that of not use, whereas in patients with 50% to 69% TBSA and more than 70% TBSA, the frequency of allograft use increased up to 91.7% and 92%, respectively. In the study by Choi et al,[5] the frequency of cadaver skin use was 50% in patients with 30% to 49% TBSA burns and 63% in patients with more than 50% TBSA burns. In the study of Blome-Eberwein et al,[20] the average TBSA in allograft group was 41.58% compared with 20.16% in nonallograft group. The available clinical data tend to set 30% TBSA as a threshold below which management with autograft alone is expected and set 50% TBSA as a threshold above which the use of allograft is common.

Sandwich Grafting Technique

Allograft skin can be used as an overlay on top of widely meshed autograft or over expanded postage stamp autografts.[2,22] This technique is also described as sandwich grafting, in which the allograft functions as biologic dressing that protects the wound bed in the interstices of widely meshed autograft.[23,24] Moreover, the allograft would slowly separate from the wound because of the gradual rejection process, allowing the underlying autograft to complete epithelialization. Vloemans et al[22] performed sandwich grafting on 129 major burns, of which 57.6% achieved partial or complete healing, and found that sandwich grafting technique could improve the take rate of meshed autograft. In the study by Khoo et al,[2] the complete healing without regrafting was achieved 44.4% in patients treated by sandwich grafting technique, and the mean autograft take was 74.4%.

When sandwich grafting technique is used, GPA skin is preferred because it contains less viable cell and causes a diminished inflammatory response compared with CPA. Rejection of the allograft before epithelialization could lead to maceration of the wound bed and secondary infection, resulting in loss of the autograft layer.[23]

Template for Delayed Application of Keratinocytes

The first clinical application of cultured epidermal autografts (CEA) for treatment of severe burns was reported by O'Connor et al[25] in 1981. Since then, this technique has been adopted in several centers in care of burn patients with limited skin graft donor sites.[26–28] However, the early use of CEA in covering full-thickness burn wounds without dermal elements often had a poor take rates.[29–31] The outcome was significant improved when Cuono et al[32] introduced the method of 2-stage procedure involving the use of allograft for wound bed preparation, followed by grafting of CEA. The use of allograft for temporary wound coverage can result in lower infection rate and higher CEA take.[33–35] Sood et al[36] reported their 18-year experiences using Cuono's method in 88 patients with large burn wounds, and 72.7% graft take rate with 91% overall survival rate was achieved. A recent systematic review showed that the combined use of allograft and CEA remained the most popular method in application of CEA.[37]

Human Acellular Dermal Matrix

Human acellular dermal matrix (HADM) is biological scaffold derived from cadaveric skin. It maintains the structural and biochemical properties of extracellular matrix while containing no cellular components.[38] Human acellular dermal matrix provides a structural support and a biological environment suitable for regeneration of the underlying tissue. The use of HADM in combination with thinner autograft was evaluated as an option for full-thickness wound coverage.[39] Compared with conventional split-thickness skin grafts (STSGs), HADM provides a dermal source that can prevent or reduce contracture and scar formation during wound healing.[40–43] In addition, the donor site will heal more quickly because of the thinner autograft required. A randomized controlled clinical trial of HADM showed that the composite graft of HADM with thinner STSG could provide acceptable esthetic outcomes, good functional recovery, and less scar formation at the donor site.[44] The main disadvantage of the use of HADM is that both the HADM and the overlying skin graft require revascularization.[45] Data from a multicenter clinical trial showed that when standard STSG was used, the autograft take rate in HADM/STSG group was somewhat lower than that in STSG group.[46] Thus, it is recommended using ultrathin skin graft with HADM to reduce metabolic demands and easier revascularization.[45]

POTENTIAL DISADVANTAGES OF ALLOGRAFT USE

Rejection

Although possessing many advantages in wound covering, allograft is considered as a temporary coverage and graft rejection is somewhat inevitable.[47] Allograft skin contains numerous dendritic cells, which play a significant role in rejection.[48] Clinically, the peeling off or nonadherence of skin allograft to the wound bed is regarded as the sign of rejection, which is likely to occur within 2 weeks after its application.[2]

Many authors have reported different experiences about the time to allograft rejection, ranged from 11 days to 4 weeks.[7] However, data from recent large clinical trials indicated that the average time interval for allograft exchanges occurred more frequently than expected.[2,7] The average duration of GPA adherence to the wound bed in the study by Khoo et al[2] was 8.4 days, and the average time of CPA exchange was 7.5 days as reported by Fletcher et al.[7]

Many efforts have been put to prolong skin allograft survival via reducing allograft antigenicity or suppressing immune system of the patients.[47] It is generally believed that using glycerol to preserve the allograft can reduce the antigenicity of allograft skin.[49] Histologic evaluation confirmed that GPA presented less severe microscopic early inflammation that CPA; however, the graft performance between GPA and CPA did not show any difference.[19] Pharmacologic agents have also been used to prolong the skin allograft survival, such as azathioprine, antithymocyte globulin, steroids, and cyclosporine.[14,50,51]

Disease Transmission

A major concern regarding the use of allograft is the risk of disease transmission. Despite the development of skin processing, microbial contamination of allograft skin persists, and it remains the main reason for tissue discard in skin banks.[52,53] Thus, microbial testing is imperative for skin banks to ensure the safety of the allograft. Meanwhile, with the growth of skin banking worldwide, there have been an increasing number of practices reported for skin disinfection, such as combined use of broad spectrum antibiotics and antifungal agents, low temperatures, disinfection with 0.1% peracetic acid, or with 25 kGy of gamma irradiation.[54] Viral disease transmission by skin allografts has also been reported in rare cases.[55,56] Generally, reported rates of disease transmission are very low and sporadic, and the advantages of allograft treatment are considered to greatly outweigh such risks.

CONCLUSIONS

Allograft skin has been used in burn care for more than 100 years. Although various kinds of skin substitutes have been developed for clinical and research use, the major role of allograft skin in severe burn wounds remains. Research will be an important avenue of investigation that is toward modifying the immunologic problems related to the rejection of the allograft.[57] The ever growing interest in regenerative medicine, stem cell therapies, and acellular dermal matrix may provide novel application for allograft skin in the treatment of burn wounds.

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