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The impact of skin banking and the use of its cadaveric skin allografts for severe burn victims in Singapore

Alvin Chua*, Colin Song, Andrea Chai, Lennard Chan, Kok Chai Tan

Department of Plastic/Burns Surgery, Singapore General Hospital, Outram Road, S169608 Singapore, Singapore

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Abstract

The skin banking programme was set-up in Singapore in 1998 to provide a ready source of allografts for patients with severe burns. The process and problems in establishing a local skin bank will be described together with a retrospective review of skin allograft recipients to determine the efficacy of the programme. For the skin bank set-up, pertinent issues related to legislation, methods, logistics, quality assurance and donation rate are discussed. In this retrospective review, a comparison between patients who had early complete excision with skin allograft transplantation and those who received conventional staged excision and coverage, was analysed in terms of clinical profile and outcome using statistical methods. The former group presented a significant reduction of mortality rate and hospital stay by 29% and 10 days, respectively. The establishment of the skin bank has helped in the management of severe burn patients by facilitating early excision and allografting. In a Burn Centre, therefore, it is essential to have an ample supply of skin allograft for burn victims in readiness for mass disaster situations.

Keywords: Skin bank; Skin donation; Early excision; Mortality; Length of hospital stay

1. Introduction

Skin banking in Singapore started in 1998 with the primary purpose of providing severely burned patients with a ready source of skin allograft for expedient wound coverage after early excision of burn wounds. The use of cadaveric skin allografts as temporary biological coverage for transplantation on massive thermal injury is practised in many major Burn Centres. Its relative low cost and availability permits early complete excision of the burn wound which has been shown to reduce mortality, length of hospital stay and even blood loss [1–5]. The secondary objective of the skin bank is to have an available source of skin allografts for research purposes.

Since the establishment of the skin bank at the Singapore General Hospital (SGH) in 1998 upto September 2003, a total of 100,612 cm^2 of processed skin allografts has been used to treat 51 burn patients. Thirty-five local cadaver donors have provided 70,410 cm^2 of allografts; the balance coming from accredited overseas tissue banks. Without the prompt response and help from these overseas tissue banks, the treatment of severely burned patients would have been significantly compromised.

The aims of this paper are two-fold. Firstly, to describe SGH's experience in establishing a skin bank. Secondly, to provide a retrospective analysis of mortality rate and length of hospital stay, comparing skin allograft recipients at our centre who had early complete excision and transplantation against those who received conventional staged excision and coverage.

2. Skin bank set-up and methods

2.1. Legislation/guidelines

The legislation governing human organ/tissue donation in Singapore was passed in 1972 under the Medical (Therapy, Education and Research) Act or MTERA. MTERA is an opt-in system. Individuals can choose to pledge, during their lifetime, their organs/tissues to be used for transplantation, education or research after their death. Alternatively, relatives/next of kin may decide to donate the organs of the deceased who in his or her lifetime had not signed up as a pledger.

* Corresponding author. Tel.: +65 63214974; fax: +65 62209340.
E-mail address: gplcwc@sgh.com.sg (A. Chua).

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Skin donation falls under MTERA, hence there was no problem with legislation as a start for the skin bank set-up in terms of donor harvesting. However, there were no official guidelines on tissue banking in Singapore with regards to donor selection, retrieval, processing, storage, distribution and documentation/tracking of skin allograft until March 2003. Accordingly, the American Association of Tissue Banks (AATB-1998) guidelines [6] were adopted.

2.2. Resources for skin bank set-up

Laboratory space, equipment and consumables at the then existing skin research facility relevant for skin banking were utilised for the initial set-up funded by the Singapore Totalisator Board.

In 2001, funding came from the Ministry of Health (MOH) under the Health Service Development Programme to formally develop the skin bank as well as a skin tissue culture laboratory for Singapore's only Burns Centre. With this funding, the laboratory space for the Centre expanded with additional manpower and new equipment. Overseas visit and training by accredited tissue banks for local skin bank personnel were embarked upon to align processes and protocols to international standards. As well, public education on skin donation started with this injection of funds through brochure distribution, website publicity and televised interviews to increase awareness and donor pledging.

2.3. Skin donation and donor selection

Donations to the skin bank were totally dependent on the efforts of the renal transplant counsellors from SGH at the beginning. They would seek consent from next-of-kin of non-pledgers for skin donation and alert the skin bank of donors. All 35 local skin donors from the past 6 years were a result of this multi-organ donation programme.

However, the number of brain-dead donors from the multi-organ donation programme was limited as compared to the potential donor pool that the skin bank can retrieve, which in essence includes harvesting from fresh cadavers. It was recommended by AATB that tissue excision be commenced within 15 h of cardiac death if the cadaver has not been refrigerated.

To address the skin donor shortage problem, the Skin Bank in August 2003 on the advice of the MOH, collaborated up with the Singapore Eye Bank (which has existing trained counsellors) to cover all death cases at SGH for potential cornea and skin tissues donation.

Donor exclusion criteria for both the above two programmes were adopted from the AATB standards. However, additional criteria (Table 1) were implemented by the hospital due to the outbreak of severe acute respiratory syndrome (SARS) in Singapore in March 2003.

Table 1
Additional donor exclusion criteria for skin donation

Due to the outbreak of SARS, the following exclusion criteria have been added:

- Febrile patients (temperature >37.5 °C) anytime in the last 10 days where SARS cannot be excluded
- Patients stricken with pneumonia and lymphopenia
- Immunocompromised patients, i.e. ESRF, chronic steroid therapy, cancer patients on chemotherapy
- Patients with recent history of travel to SARS affected areas for emergency surgery, even if afebrile
- Patients with history of contact with SARS patients on home quarantine
- All suspect or probable SARS patients requiring emergency operations but were not fit for transfer to the SARS-designated hospital
- Patients from hotspots or isolation wards

2.4. Skin retrieval

The skin retrieval team usually consists of two duty doctors (registrar and medical officer), one skin bank officer and a staff nurse. All skin retrievals took place in a sterile operating theatre (OT) for the multi-organ donation cases. Due to the constraint of cost, a clean room within the SGH Burn Centre was allocated for skin harvesting in the event that only tissues (skin and cornea) donation is consented in the hospital. For such cases, skin preparation, back table set-up and draping are performed in an aseptic manner, keeping with OT criteria.

Paraffin oil is used as a lubricant for easy and consistent skin retrieval using an electric dermatome [Zimmer], normally set at a depth of 0.38 mm (0.015 in.). Skin strips of average size of 100 cm^2 (8 cm × 12.5 cm) are taken and placed in a 1000 ml sterile container [Sanplatec] filled with transport medium—Dulbecco's modified eagle medium (DMEM) [Gibco] supplemented with an antibiotic/fungicide mixture [Biowhittaker]: penicillin (50 IU/ml), streptomycin (50 μg/ml) and amphotericin B (0.125 μg/ml).

Areas of harvesting on the cadaver's body are restricted mainly to the back, buttocks and the lower limbs. This is to ensure that concerns over "raw" appearance on donor's exposed areas will not be an issue for the donor family in an open casket.

During harvesting, a random skin sample (about 0.5 cm^2) is isolated in a small sterile bottle for three standard microbiology tests—aerobic, anaerobic and fungi cultures. A blood sample from the donor is also sent for tests—HIV, syphilis, hepatitis B and C and cytomegalovirus.

The skin tissues are subsequently transported to the skin bank in an ice box. The yield of skin retrieval averages at 2000 cm^2 per cadaver.

2.5. Skin processing

At the skin bank, the harvested skin is rinsed with 0.025% sodium hypochlorite [Orion] mixed in phosphate buffer saline (PBS) [Gibco] to remove excess lubricant as well

as dead skin cells. Another random skin sample is isolated for microbiology tests after rinsing. The remaining rinsed tissues are divided into average sizes of 200 cm^2 and transferred into 150 ml sterile specimen containers [Deltalab] filled with fresh DMEM medium (antibiotics/fungizone added). Appropriate donor identification, date and size of tissue are labelled on each specimen container and placed under 4 °C storage for 10 days as fresh skin tissues. Medium is changed every 3 days. Exceptional release is given to fresh tissues for burn patient's use by the surgeon-in-charge if microbiology tests are negative 3 days after rinsing and serology tests are confirmed negative.

On the 10th day, unused fresh skin tissues are meshed, double-packed and cryo-preserved. The skin sheets will be trimmed at their edges before they are meshed [Brenner mesher] at a 2:1 ratio. This is followed by the spreading of the skin sheets with the dermis facing up on the 4 in. cotton bandage [Smith & Nephew] which is then gently folded up to fit a plastic pouch—6 in. × 8 in. [Kapak]. Each sheet of cotton bandage contains up to a maximum of four pieces of skin that would make up an approximate size of 200 cm^2 as a standard packing. Random small skin samples are also isolated for microbiology testing at this step.

All the folded gauze is subsequently soaked in DMEM with 10% dimethyl sulfoxide (DMSO) [Sigma] to allow penetration of the cryoprotective agent to the tissues. These soaked tissues are drained dry of excess medium after 20 min of immersion, double packed and sealed into the plastic pouch followed by a foil pouch—8 in. × 10 in. [Kapak] via a medical grade heat sealer [Hawo hd260MS]. The thin and flat configuration of the pouches allows efficient and uniform freezing of the skin tissues at a slow rate of −1 to −5 °C/min using a programmable control rate freezer [Planar KRYO 10]. At −100 °C, the skin pouches are promptly transferred to a −150 °C CFC-free ultralow freezer [SANYO MDF-1155ATN] for storage of up to 5 years.

2.6. Distribution and documentation

The integration of the skin bank and the OT of the Burns Centre at SGH allows ready access of skin allografts in the OT. The allografts are thawed immediately and rinsed in warm saline at 37 °C to remove all residual cryoprotectant. A "skin allograft transplant record" indicating donor's tracking number, patient particulars and date of procedure are updated upon request for skin allograft. The above details are subsequently entered into a standalone database to track inventory of the skin tissues and to manage donors as well as patients' profile for future clinical reference and management.

3. Patients and methods

3.1. Selection of patients

Forty-five patients admitted to SGH Burns Centre between January 1998 and September 2003 with deep dermal to full thickness burns greater than 30% total body surface area (TBSA) were studied. All these patients underwent surgery and had partial (with autograft) to complete skin allograft transplantation following excision of their burn sites.

The above patients were divided into two groups. The study group consisted of patients who had early burns excision with skin autograft/allograft transplantation within 72 h and the excision completed within 7 days post-injury. The control group was made up of patients who had excision done more than 72 h after injury or debridement not completed within 7 days. Critical parameters that would determine the outcome of mortality rate (MR) and length of hospital stay (LOS) were compared between the two groups of patients. The determinants include age, sex, TBSA and presence of inhalation injury.

All other burn management modalities, such as resuscitation, ventilator, topical care, nutrition and ward care are comparable for both groups.

3.2. Statistical methods

The retrospective statistical analyses were performed using SPSS for Windows package version 10.1. The two groups were compared using Chi-square and Mann–Whitney *U*-analysis for patients' profile and clinical outcome, depending on the nature of the data. The methodology chosen is reflected in the results tables and the level of significance was chosen as $p < 0.05$ for all statistical analyses.

4. Results

Tables 2 and 3 show the patients' profile and clinical results, respectively. Continuous data was summarised as the mean ($\bar{A}$) followed by the standard deviation (S.D.) in the form $\bar{A} \pm$ S.D. From Table 2, it can be observed that the two groups of patients essentially have similar profiles. Patients who had early excision and grafting on an average underwent surgery 1.7 days post-injury as compared to 5.5 days for the control group (Table 3). MR reduced significantly from 45% in the latter group to 16% in the study group. Like-

Table 2
Profile of patients who received skin allografts between 1998 and September 2003

	With early excision	Control	*p*-value
N	25	20	–
Age (year)	31.7 ± 12.7	30.6 ± 11.2	NS[a]
Male/female	16/9	12/8	NS[b]
TBSA (%)	52.6 ± 16.6	56.0 ± 18.2	NS[a]
Range (%)	31–85	33–88	–
Full thickness; median (%)	10.4	17.9	NS[a]
Smoke inhalation (Y/N)	12/13	11/9	NS[b]

NS: not significant.
[a] Mann–Whitney *U*.
[b] Chi-square.

Table 3
Clinical results of patients who received skin allografts between 1998 and September 2003

	With early excision	Control	*p*-value
Days from burn injury to first operation	1.7 ± 0.8	5.5 ± 3.8	0.001[a]
Mortality (Y/N)	4/21 (16%)	9/11 (45%)	0.049[b]
Length of hospital stay	48.3 ± 28.5	58.5 ± 12.4	0.044[b]

[a] Mann–Whitney *U*.
[b] Chi-square.

wise, LOS reduced from an average of 58.5 to 48.3 days.

The *P*-values reported in this study for MR and LOS are close to 0.05 which is the cut-off value for level of statistical significance. This is partly due to the small sample size of patients available for this mid-term retrospective study. The authors are planning a final 10-year retrospective review where larger number of skin allograft recipients will be available for further analysis.

5. Discussion

5.1. Skin bank set-up

Since the establishment of the skin bank in 1998, it has provided severely burned patients with skin allograft cover that has proven to be life-saving. Thus far, there are no reports of adverse reactions in donor skin recipients, an attestation of the AATB's guidelines in terms of donor selection, skin processing and quality assurance. The recent release of Guidelines for Healthcare Institutions providing Tissue banking by MOH this year is also timely as it would re-align the practices of all tissue banks in Singapore.

The problem of lack of donors for organs and tissues for transplantation cannot be overstated as it is a worldwide phenomenon. Skin donation in Singapore is no exception and in fact during the past 5 years, multi-organ retrievals consistently yield less skin donors compared to cornea donors. This is primarily due to concerns over disfigurement and the longer time that is needed to harvest skin tissues. The onset of SARS also affected donor numbers as stricter criteria were then implemented for donor suitability (Table 1). Other factors for poor yield are mainly due to social and cultural reasons which include religious conviction and Asian superstitions.

The other problem that exacerbated the shortage of skin tissues in Singapore is the lack of canvassing of donors (other than multi-organ donor cases) who have experienced cardiac-death in other local hospitals or institutions, aside from grappling with logistics issues for harvesting of skin. There are currently insufficient resources to extend coverage of such cases beyond SGH as the present skin harvesting team consists mainly of duty doctors from the hospital's plastic surgery department. Moreover, it would be difficult for duty doctors to balance between the demands of urgent trauma cases and the opportunity for skin retrieval.

A centralised agency to co-ordinate donor retrieval and counselling services for all relevant tissue types among the healthcare institutions in Singapore would be welcomed. It would be an efficient and effective way to address resource deficiency issue, thereby increasing tissue donor rate.

5.2. Retrospective study of skin allograft recipients

The above study (Table 3) shows a significant decrease in mortality of 29% for patients who underwent excision within 72 h of burn injury and completed within a week. Similarly, length of hospital stay (LOS) was also shown to reduce significantly by 10 days for patients in the study group. The above results are consistent with retrospective studies conducted by Tompkins et al. [1,2] and Herndon et al. [3,4], respectively.

Tompkins et al. [1] reported a significant decrease of 24% in mortality for adult patients with burns above 70% TBSA and saw a significant reduction of LOS from 32 to 22 days in adults at Massachusetts General Hospital over a 10-year period from 1974 to 1984 [2]. While it was impossible to single out any single treatment factor, Tompkins et al. strongly believed that aggressive, prompt excision of burn eschar even in older patients and the immediate physiologic closure of the wound with grafts were the major forces in that improvement.

Herndon et al. [3] compared conservative versus early excision on patients (aged 17–55 years) with burns above 30% and reported a significant reduction in mortality from 45% to 9% in patients aged between 17 and 30 years old who were without inhalation injury. They concluded that continued comparisons of the two therapies outlined in their study were justified in older patients who had larger burns or in patients who had inhalation injuries. In another study, Herndon and Parks [4] reported a reduction of LOS from 97 to 57 days in children with large burns who had undergone early massive excision.

The positive results in terms of MR and LOS from the study affirm the efficacy of early excision and grafting of massive burn patients in SGH Burns Centre practice. The use of allograft dermis in conjunction with cultured kertinocytes as descibed by Cuono et al. [7] is also in the pipeline for treating severe burns. The establishment of the skin bank in Singapore to provide a ready source of skin allograft for biological coverage is thus an indispensable component in the management of severe burns. Recent events pointing to an increase in terrorism activities within Southeast Asia reinforced the need to address the issue of donor skin shortage with greater urgency. A top–down approach is recommended to stream-

line resources so as to be prepared for event of mass disaster.

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