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Use of bilaminar grafts as life-saving interventions for severe burns: A single-center experience

Johnny Ionut Efanov [a], *Bianief Tchiloemba* [b], *Antoine Duong* [a], *Annie Bélisle* [a], *Ali Izadpanah* [a], *Edouard Coeugniet* [a], *Michel Alain Danino* [a,*]

[a] *Centre Hospitalier de l'Université de Montreal, Hôpital Notre-Dame, Quebec,Canada*
[b] *Department of Medicine, McGill University, Montreal, Quebec, Canada*

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ABSTRACT

Background: Skin coverage remains a significant hurdle in large-sized burns. Recent advances have allowed to grow Bilaminar Cultured Skin Autografts (BCSGs) from patients' own donor sites. The aim of this study was to report long-term outcomes in patients with large-sized burns having received BCSGs.

Methods: Nine patients received BCSGs from January 2010 to May 2015. Except one patient who died during hospitalization, all patients were contacted. Four agreed to partake in the study. Patients were tested with the Vancouver Scar Scale (VSS), QuickDASH questionnaire and Burn Specific Health Scale (BSHS). Incisional biopsies of BCSGs were compared with patients' autografts.

Results: From nine patients, mean age was 40 years and mean TBSA was 70.3%. For the four patients included, score averaged was 2.25 on the VSS, 29.5 on QuickDASH, 36/36 for psychosocial items and 63/84 for functional abilities on the BSHS. Compared with autografts, BCSGs demonstrated better pliability VSS and functionality. Biopsies showed no evidence of malignancy or atypical changes, but areas of hyperpigmentation.

Conclusion: This is the first report investigating the long-term outcome of a newly developed BCSG. BCSGs demonstrated comparable results with patients' autografts, functional outcomes on self-reported questionnaires and excellent psychological states. Precaution given the extensive unexpected hyperpigmentation must be taken and a randomized controlled study is underway.

1. Introduction

Severe burns provoke devastating injuries associated with elevated short-term mortality and long-term morbidity rates. Moreover, they comprise a significant proportion of healthcare resources when compared with other traumatic and acute care hospitalizations [1]. Of the many factors responsible for poor outcomes, wound coverage plays a critical role in patients' prognosis. Limited, and sometimes inexistent, donor sites have urged surgeons and scientists to develop various techniques for grafting of large-sized burn victims [2]. A promising avenue arose with the advent of cultured-epithelial autografts (CEAs) demonstrating improved outcomes in burn

* *Corresponding author at*: 1560 Sherbrooke Est, H2L 4M1 Montreal, Quebec, Canada.
E-mail address: alain.danino.chum@ssss.gouv.qc.ca (M.A. Danino).
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care [2]. However, several limitations persist, namely the complexity of application, fragility of specimens and high costs [3,4]. In addition, their susceptibility to infections have been reported as a significant inconvenience, further hindering their widespread use [5].

The pursuit for a perfect replica of human skin continues to animate research endeavors worldwide. A novel approach entitled Bilaminar Cultured Skin Grafts (BCSG) has been developed by a laboratory focusing on experimental organogenesis as a potential alternative to epithelial cultured autografts [6]. BCSGs differ from CEAs because they are cultured from two different types of cells. Indeed, keratinocytes are purposed to reconstruct the epidermal layer whereas fibroblasts are cultured to build the dermis. Both cell types are harvested from patients with severe burns and cultured separately in the laboratory. After maturation of both layers, the specimens are superimposed onto one another to form bilaminar skin. Larouche et al. referred to the construct as Self-Assembled Skin Substitute (SASS) and demonstrated great flexibility, minimal scarring and permanent coverage of full thickness wounds on athymic mice for 90 days [7]. Further refinements in technique have also allowed for reduced production times to about 1 month after harvesting of patient cells [8].

Applicability in patients with severe burns received a temporary approbation by our regulation authority in 2010. A Special Access Program for bilaminar skin was approved where treating physicians could request authorization to use this product as a life-saving device on a case-by-case basis depending on the severity of burns and the lack of alternative treatments. With the program coming to an end, the primary objective was to determine qualitative and quantitative outcomes of patients treated with BCSG. We hypothesized that objective scar evaluations and patient-reported outcomes would be favorable. A secondary objective was to measure the total costs associated with the technique and discuss its impact in the context of reported outcomes.

2. Methods

A retrospective study was conducted on all patients treated for severe burns with bilaminar skin autografts in our regional burn unit from January 2010 to May 2015. Treatment funding was provided by a Special Access Program depending on indications postulated by treating surgeons. For example, patients suffering from burns with a total body surface area (TBSA) superior to 50% wherein conventional therapies were insufficient to maintain a patient alive were offered BCSGs as life-saving procedures. Three institutions with burn units participated in the program in Canada, including two adult and one pediatric hospitals. Current work presents data from patients treated at one of the adult burn units covering a population of 4 million.

After identification of patients treated with BCSGs, a study proposal was granted approval by our institution's ethics review board, in accordance with the declaration of Helsinki, to evaluate scarring characteristics, patient-reported outcomes, biopsied specimens and procedural costs. All patients were contacted by telephone and invited to present to the hospital for evaluations stated above. Only patients who agreed to come in person were included, thus excluding those who refused due to distant geographical locations or personal reasons.

Data collection consisted of patient demographics and injury characteristics such as age, gender, ethnicity, occupation, socioeconomic class, total body surface area (TBSA) of the burns with depth, etiological mechanism of burn, year of the trauma and the total surface area of BCSG transplanted (cm^2). Additionally, patient pre-operative and post-operative data was gathered such as the anatomical region where the BCSG was applied, duration of stay at the ICU, days post-admission prior the BCSG insertion, vacuum assisted therapy utilization, wound bed preparation prior BCSG grafting, post-operative wound healing issues for autografts and receiving sites, BCSG healing issues, major medical complications during hospitalization and BCSG grafting technique. Both the medical and the demographic data were recorded from patients' medical charts and verified for accuracy during patient interviews. Finally, total costs associated with the use of bilaminar grafts were calculated from operative invoices reimbursed by Health Canada. A cost benefit analysis including aspects such as operative room costs, duration of hospitalisation and return to work were beyond the scope of the current study.

When patients with BCSG agreed to partake in the study, they were interviewed by three evaluators. Evolution of scar formation was evaluated in all patients with the Vancouver Scar Scale (VSS), by comparing scores obtained over regions treated with BCSG and regions treated with autografts. The VSS is a validated tool used to quantify scar pliability, vascularity, pigmentation and height with a high degree of inter-rater reliability [9,10]. In the current work, these four subsets were analysed for all patients at one to four years following application of bilaminar autografts.

Furthermore, in patients where BCSGs and autografts were inset in the upper extremity, a patient-reported outcome questionnaire was performed to evaluate functional improvements and limitations as well as residual pain attributed to the bilaminar graft. The Quick Disabilities of the Arm, Shoulder and Hand (Quick-DASH) was administered for that purpose, which is a validated 11-item questionnaire measuring physical function and symptoms in people with musculoskeletal disorders of the upper extremity [11]. Answers are given based on a one-to-five scale, with an overall score ranging from 0 (no disability) to 100 (most severe disability).

Additionally, psychosocial and functional outcomes, as reported by patients treated with BCSG, were measured with the Burn Specific Health Scale-Brief (BSHS-B). In this questionnaire, there are 9 items scored from 0 (extreme) to 4 (none) relating to functional health specific to burn injuries and 21 items score from 0 (extremely) to 4 (not at all) relating to psychological well-being [12]. A higher score on both scales indicates a better state of health as reported by the patient. Also, a household questionnaire was produced to compare and evaluate patients' satisfaction level of bilaminar grafts in comparison with autograft. Aspects measured by the questionnaire include aesthetics, function, sensation and healing process. Question items can be found in Table 1.

At the end of the interview process, photographs of BCSGs and autografts were taken followed by incisional biopsies on

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