EARLY AND LATE APPLICATION OF SKIN HOMOGRAFT IN MANAGEMENT OF MAJOR BURN PATIENTS: A COMPARATIVE STUDY

APPLICATION PRÉCOCE OU TARDIVE DES HOMOGREFFES EN CAS DE BRÛLURE ÉTENDUE: ÉTUDE COMPARATIVE

Megahed M.A.,[1] Elkhouly H.R.A.[2]✉

[1] Department of Plastic and Reconstructive Surgery, Faculty of Medicine, Menoufia University, Shibin Al Kawm, Menoufia, Egypt
[2] Department of Plastic and Reconstructive Surgery, Damietta Specialized Hospital, Damietta, Egypt

SUMMARY. Our objective is to compare the effect of early and late application of skin homograft regarding complications and mortality rate. Burn is a type of physical trauma to skin or tissue. Burn can lead to loss of skin, resulting in deep, widespread skin wounds or even death. This prospective comparative study was done at the Plastic and Reconstructive Surgery Department of Menoufia University Hospitals from December 2017 to July 2020. It was conducted on 31 patients with major burns, classified into two main groups: the early homograft group (8 patients) and the late homograft group (23 patients). All studied patients and donors were subjected to a full history, general and local examination, and investigations such as complete blood counts (CBC), blood glucose level, kidney and liver function tests, electrolytes, and coagulation profile. Additionally, pre-operative preparation along with intra-operative and post-operative care were done. There was a significant decrease in temperature, HR, RR, SIRS score, TLC and K measurements, along with a decrease in rejection % and LOS (length of hospital stay) in the early homograft group compared to the late homograft group ($p < 0.05$ respectively). Additionally, there was a significant increase in albumin and Na measurements ($p < 0.05$, respectively). The use of homograft in major burn patients improved their overall condition by improving laboratory and respiratory data post-operatively. However, early usage of the homograft, especially in the first three days, improved laboratory data, SIRS score, percentage of rejection, and length of hospital stay.

Keywords: burn, homograft, early and late application

RÉSUMÉ. *Notre objectif était de comparer les conséquences sur les complications et la mortalité d'une application précoce ou tardive d'homogreffes. Les brûlures, exemple-type de traumatisme physique cutané ou tissulaire entraînent une destruction cutanée pouvant conduire au décès. Cette étude comparative a été réalisée dans le service de chirurgie plastique et reconstructrice du CHU de Menoufia entre décembre 2017 et juillet 2020 auprès de 31 patients séparés en un groupe de 8 patients recevant précocement des homogreffes et un de 23 les recevant tardivement. Nous avons répertorié l'histoire complète, les examens général et local, les numérations globulaires, glycémies, fonctions rénale et hépatique, bilans électrolytiques, coagulation, prise en charge pré-, per- et post-opératoires, des patients comme des donneurs. Dans le groupe « précoce », on constatait une diminution ($p < 0,05$) des fréquences respiratoire et cardiaque, des scores SIRS, des globules blancs, kaliémies, du pourcentage de rejet des homogreffes et des durées d'hospitalisation, par rapport au groupe « tardif». Concomitamment, albuminémies et natrémies étaient plus élevées dans le groupe « précoce ». Si l'utilisation des homogreffes a un effet positif chez les brûlés sévères, ceci est particulièrement net quand elles sont mises en place dans les 72 heures suivant la lésion.*

Mots-clés *: brûlure, homogreffes, application précoce, application tardive*

✉ Corresponding author: Heba Refaat Abd El-Razek Elkhouly. Tel.: +20 01063736310; Email: hebakhouly@gmail.com
Manuscript: submitted 20/04/2024, accepted 01/05/2024

Introduction

Burns are a complex surgical problem. The aim of surgical procedures in burn patients are prevention or control of infection, conservation of all viable tissue, maintenance of form and function, timely closure of all wounds, early return to rehabilitative therapy, and decrease in mortality. One of the major transformative concepts in burn care since the 1970s is the survival advantage that early burn wound excision and grafting confers.[1]

If surgery is not performed or is delayed in patients with deep burns, this will have its consequences. In the past, patients with burns used to be treated with dressings and topical antimicrobial agents for weeks until the eschar separated spontaneously. If the patient survived, the granulating wound would then be covered with split thickness skin graft, a process that could take 3-5 weeks. Patients with severe burns treated in this way, particularly those with over 20% TBSA burns, were more likely to die of sepsis due to the massive release of inflammatory mediators from the burn. This was further exacerbated by subsequent infection of the wounds. With the traditional approach, patients' hospital stay was prolonged, and patients were more liable to develop problems like hypertrophic scarring and contractures due to the problems associated with delayed wound healing.[2,3,4]

In our previous study, we showed the benefits of skin homograft as coverage for major burn patients who have a paucity of autologous skin. This study proved how skin homograft improves their overall condition by improving laboratory and respiratory data post-operatively. Furthermore, it reduces the raw area which consequently reduces fluid and electrolyte loss, besides aiding in rapid wound healing. Moreover, we discovered a significant reduction in the SIRS score, which reduces sepsis and improves morbidity and mortality.[5]

Human skin homograft has long been used for wound coverage and is one of the most successful and widely used dressings for burn wounds worldwide.[6] It can aid in the improvement and preparation of the granulation tissue in the recipient bed. A human skin allograft is integrated into the recipient tissue bed and covered by epidermal cells from the recipient.[7]

The aim of this study is to compare the outcome in patients managed with early excision and homografting versus delayed excision and homografting.

Patients and methods

The current prospective study was done at the Plastic and Reconstructive Surgery Department, Menoufia University Hospitals, from December 2017 to July 2020. Thirty-one patients were enrolled in the present study, with an age range from 8 months to 65 years old. The patients presented with major burns and were managed by homograft, and follow-up was done for six months. Eligible patients were chosen based on a set of the following criteria:

Inclusion criteria:

- Major burn patients with limited donor site availability for autograft.
- Deep dermal burn patients.

Exclusion criteria:

- Superficial burn patients that are suspected to heal conservatively without intervention.
- Patients with severe inhalation injury or severe medical conditions that interfere with the operation.
- Patients having less than 15% total burn surface area (TBSA) in adults, or less than 10% TBSA in children.
- Patients who refused the operation.

The 31 major burn patients were further classified according to time from burn to homograft into 2 independent groups:

- Group A (Early homograft group), in which the wound excision (escharectomy) and graft were performed early (within 3 days), consisting of 8 cases.
- Group B (Late homograft group), in which the wound excision (escharectomy) and graft were performed late (after 3 days), consisting of 23 cases.

All participants were informed about the study's purpose, laboratory, or radiological investigations. Consent was taken from all participants. At the completion of the study, all patients were informed about the results of the examinations performed and received proper recommendations and treatment. The

current work has followed The World Health Organization (WHO) and the Declaration of Helsinki recommendations in terms of protecting the well-being and the rights of the studied people as revised in 2013.

For the recipients

All the patients had major burns in various body areas. Therefore, all of them received their primary survey and resuscitation treatment.

- Full history was taken from all patients.
- General examination including: general condition of patients and vital signs; head and neck examination - inhalation injury was diagnosed by history, presence of facial burn, singed nasal hair, carbonaceous sputum, and laryngeal edema; chest, abdominal and pelvic examination, upper and lower limbs examination.
- Local examination.

Burn areas were examined carefully to detect:

- Total burn surface area (TBSA), calculated according to Lund and Browder's chart, including only partial-thickness and full thickness burn. Therefore, it is almost 100% of the total size of the burn that has been mentioned in the current study.
- The burn wound depth was categorized only into two major groups; either superficial, which was excluded, or deep which was included. Finally, the whole total burn area was excised to be covered with the homograft.
- Presence of any debris, chemicals or other foreign bodies within the wound.
- Signs of infection within the wound (e.g., purulent or malodor discharge, redness, or swelling around the wound).

Investigations

Laboratory. Complete blood count (CBC) including; haemoglobin (HB), white blood cells (WBCs) and platelets, arterial blood gases (ABGs), PH, PCO_2, sodium (Na) potassium (K), albumin, electrolytes, Creatinine, and blood urea to evaluate kidney function, SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamate pyruvate transaminase) and prothrombin time to evaluate the hepatic function.

Radiological. Chest x-ray in case of chest infection or inhalation injury suspicion.

Instrumental. Bronchoscopy if inhalation injury was suspected.

SIRS was detected in patients who were managed by homograft pre-and post-op when two or more of the following criteria were met:

- Temp. >38 or <36 °C.
- RR >20 breaths/min.
- HR >90 beats/min.
- $Paco_2$ <32mmHg.
- WBCs >12000 or <4000.

These investigations were done pre- and post-operative to monitor the patient's condition continuously, and the investigation parameters were recorded.

For the donors

The source of homograft donors was either first- or second-degree relatives. All the donors signed written consent for the donation of their skin, explaining the procedure, benefits, timing and complications. Full personal, present and past history were taken.

Management: A primary survey was performed on all patients once they reached the hospital. Consequently, the patients went to primary cleansing of the burn wound and debris was removed, then the burn surface area and depth were determined. The wound was covered with Silver Sulfadiazine and gauze dressing, and then the patient's weight was determined. After resuscitation and evaluation of the patient's condition, they were categorised according to the percentage of the burn wound, the presence or absence of inhalation injury, or other comorbidities. Then, some were admitted to the burn ICU, others to intermediate care, and lastly, some were admitted to the ward.

All studied patients received their primary resuscitation treatment, including:

- Proper fluid resuscitation, according to Evans's formula: *First 24 hours*: 2 ml. crystalloids × BW× TBSA + Daily fluid requirements (Glucose 5%). Half of this calculated amount was given in the first 8 hours, while the other half was given in the next 16 hours. *Second 24 hours*: Half the calculated amount of the previous formula + daily fluid requirements (Glucose 5%). The other half of the

previous formula was given in the next 24 hours. Furthermore, Colloid was given according to the patient's needs.

- Broad-spectrum antibiotics to cover gram-positive and gram-negative bacteria and anaerobes according to hospital policy (e.g., penicillin and gentamicin).
- Systemic steroids in the form of dexamethasone IV are also given to reduce the inflammatory reaction and decrease the pain.
- Proper analgesic according to WHO analgesic ladder.
- Proton pump inhibitors (e.g., Controloc) to avoid stress ulcer occurrence.
- Other supportive measures are given according to the patient's condition (e.g., packed RBCs, FFP, bronchodilators, inotropes…).

Monitoring of the patients by pulse, BP, central venous pressure (CVP) after insertion of a central line, and urine output (UOP) after insertion of a urinary catheter was also done.

After stabilisation, the patients were prepared and underwent primary excision of the burn eschar (escharectomy), and then the wound was covered with skin homograft (*Figs. 1 & 2*). The homograft operation was conducted early (within three days) to avoid SIRS, sepsis and septic shock. In some cases, the operation was postponed, either due to a delay in the patient's arrival at the hospital after burn trauma or unavailable donors.

Fig. 1 - Intraoperative burn wound before escharectomy and debridement

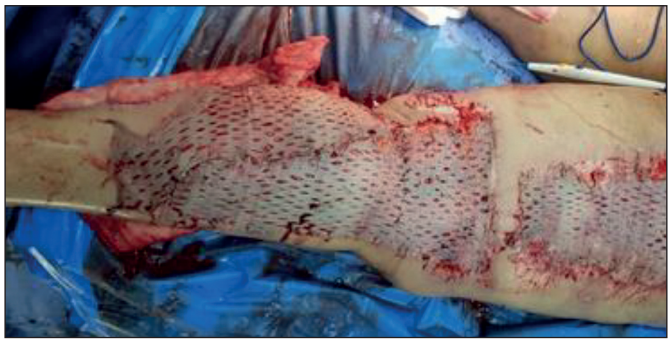

Fig. 2 - Homograft applied and fixed in place

Donor preparations

Pre-operative preparation. Pre-operatively, all donors were evaluated generally and locally before the operation. Anaesthesia consultation was carried out along with full laboratory investigations, including complete blood count (CBC) (e.g., Hb, WBCs, platelets…), electrolytes, blood grouping, fasting, and postprandial blood sugar, albumin and liver function tests, kidney function tests, coagulation profile, virology profile including HIV, hepatitis B, and hepatitis C viral infections.

Intra-operative preparations and operative procedure:

- Antibiotic prophylaxis: Antibiotics were given before the operation as 1 gm of 3rd generation cephalosporin direct IV route, one hour pre-operatively.
- Patient positioning: The donors were placed supine as the thigh was the preferred donor site for harvesting.
- Anesthesia: Anesthesia was either spinal (29 cases) or general (2 cases).

After sterilisation of the donor site, split-thickness skin graft harvesting was done using a Humby knife. Then, coverage with a bulky dressing for the donor site wound was performed.

Recipient preparations

Preoperative preparation. Pre-operatively, all recipients were evaluated generally and locally before the operation. An anaesthesia consultation was carried out, along with full laboratory investigations including complete blood count (CBC) (e.g., Hb, WBCs, platelets…), blood grouping, electrolytes, fasting, and postprandial blood sugar, albumin, liver and kidney function tests, coagulation profile, and virology profile including HIV, hepatitis B, and Hepatitis C viral infections. Packed RBCs were also prepared for all recipient patients for the possible need for blood transfusion.

Intraoperative preparations and operative procedure:

- Antibiotic prophylaxis: Antibiotics were

given before the operation as 1 gm of 3rd generation cephalosporin direct IV route, one hour pre-operatively.

- Patient positioning: The donors were placed supine as the preferred donor site for harvesting was the thigh. Meanwhile, depending on the burn site, the recipient's position was either supine or prone.
- Anesthesia: Recipients' anaesthesia was general (30 cases) and spinal (1 case).

For the recipient, sterilisation of the wound was done. Then, tangential excision technique with a Humby knife till well bleeding surface was obtained. The prepared homograft was applied to the recipient patient either immediately or later (kept in the fridge for a maximum of 7 days) according to the burn wound preparation and its liability for taking. The fixation of the homograft with staples was then followed by applying a bulky dressing. Splinting of the joints was usually done with a slap to maintain posture and prevent contracture.

Post-operative care. After the graft's fixation and wound closure, the patient was transferred to the ward, and a normal diet was allowed after complete recovery. Patient monitoring by regular general and local examination, obtaining vital signs, monitoring urine output, laboratory investigations including complete blood count (CBC) (e.g., Hb, WBCs, platelets…), arterial blood gases (ABG), white blood cells (WBCs), albumin, platelets, electrolytes, blood urea, and Creatinine to evaluate the kidney function, SGPT, SGOT, and prothrombin time to assess the hepatic function. These investigations were performed regularly post-operatively up to discharge.

Drugs such as antibiotics were given according to the hospital policy, and proper analgesics and other supportive therapies were given depending on the patient's condition and needs.

The first graft dressing was usually done after 48 to 72 hours. Then, the dressing was left open with a topical antibiotic spray application. Rejection was suspected on day 7 to day 14 post-operative as a form of acute rejection, which may last up to one month. Chronic rejection was also suspected in the long run. Any signs of a local allergic reaction, such as erythema, edema, local infection, or partial or total homograft loss, were detected and documented for each patient. In that case, the patient is kept in the hospital and prepared for another session of homograft (if available) or autograft if possible.

Statistical methodology

Statistical analysis was carried out using MedCalc ver. 18.11.3 (MedCalc, Ostend, Belgium). P-value: level of significance: $P > 0.05$: Non-significant (NS), $P < 0.05$: Significant (S).

Results

A comparative study between the 2 groups revealed non-significant differences regarding age, sex, and all basic clinical data (P-value = 0.1137 and 0.7535, respectively) (*Table I*).

We further analysed and compared 31 (paired) homograft patients according to the serial measurements (pre and post-operative); with entering a grouping factor (Early or Late reconstruction), there was marked

Table I - Comparison between the two groups as regards basic clinical data

Variable			Early homograft group (8)	Late homograft group (23)	P value
Age (years)		Median (IQR)	2.7 (1.8 – 9)	6 (3 – 22.2)	= 0.1137
Gender	Female	No (%)	4 (50%)	10 (43.5%)	= 0.7535
	Male	No (%)	4 (50%)	13 (56.5%)	
Smoking		No (%)	0 (0%)	1 (4.3%)	= 0.5553
Hypertension		No (%)	0 (0%)	2 (8.7%)	= 0.3963
Diabetes mellitus		No (%)	0 (0%)	1 (4.3%)	= 0.5553
Bronchial asthma		No (%)	0 (0%)	4 (17.4%)	= 0.2137
HCV		No (%)	0 (0%)	1 (4.3%)	= 0.5553

decrease in temperature, HR, RR, SIRS, TLC in the early homograft group compared to the late homograft group, during the serial pre and post-operative measurements (P-value = 0.039, 0.015, 0.011, 0.022, 0.009, respectively) (*Figs. 3-7*). There was a marked increase in albumin and Na in the early homograft group, compared to the late homograft group, during the serial pre and post-operative measurements (P-value = 0.032 and 0.008, respectively) (*Figs. 8 & 9*).

There was a marked decrease in K in the early homograft group compared to the late homograft group during the serial pre and post-operative measurements (P-value = 0.038) (*Fig. 10*).

A comparative study between the two groups revealed a highly significant decrease in rejection % and LOS in the early homograft group compared to the late homograft group ($p < 0.05$, respectively),

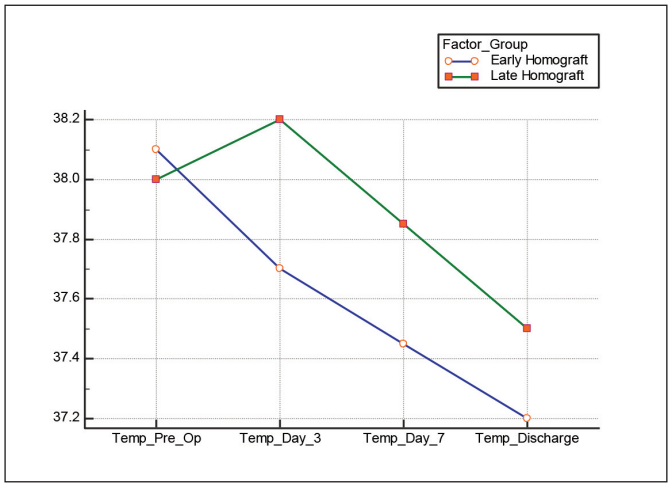

Fig. 3 - Comparison between the two groups of patients regarding serial temperature assessments

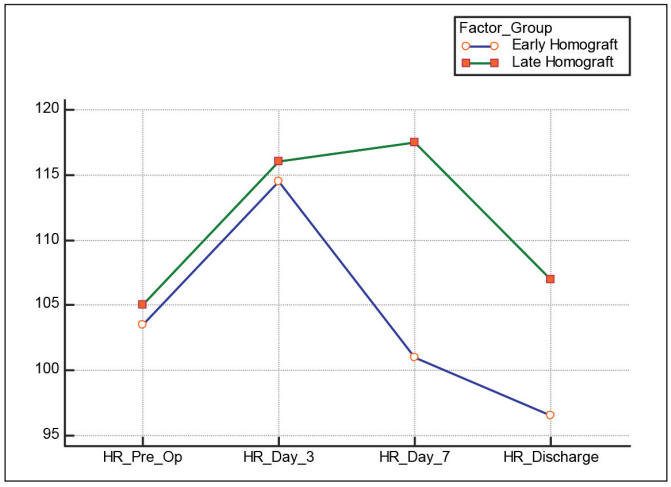

Fig. 4 - Comparison between the two groups of patients regarding serial HR assessments

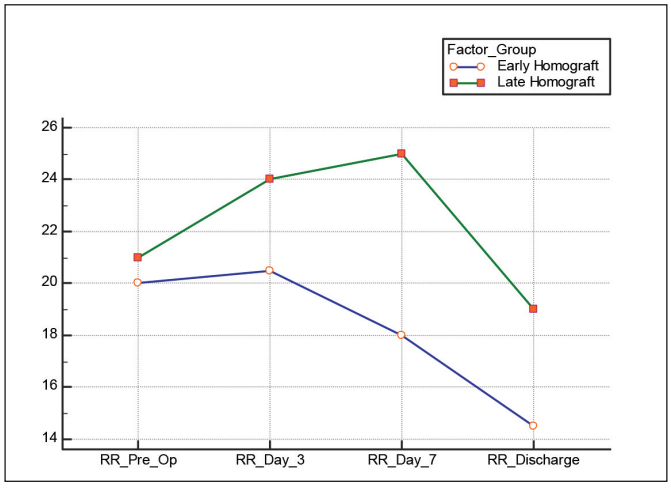

Fig. 5 - Comparison between the two groups of patients regarding serial RR assessments

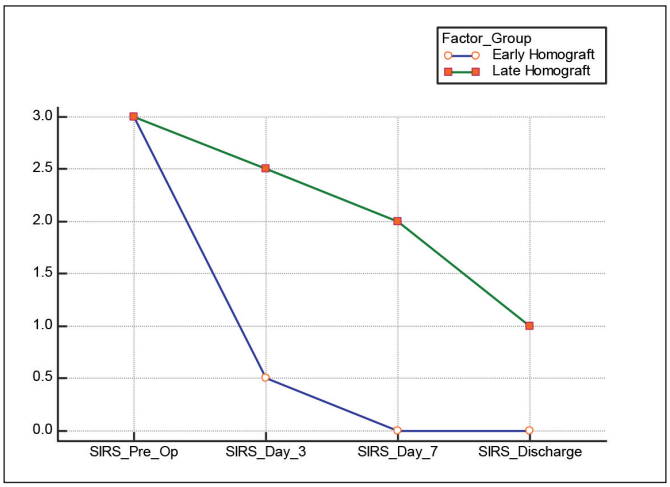

Fig. 6 - Comparison between the two groups of patients regarding serial SIRS score assessments

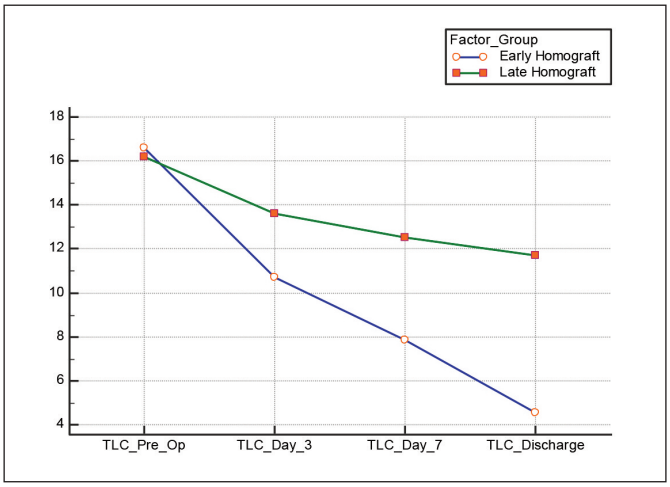

Fig. 7 - Comparison between the two groups of patients regarding serial TLC assessments

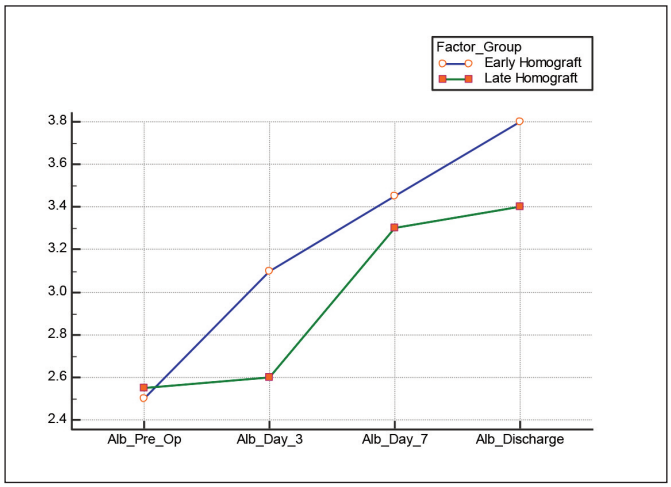

Fig. 8 - Comparison between the two groups of patients regarding serial albumin assessments

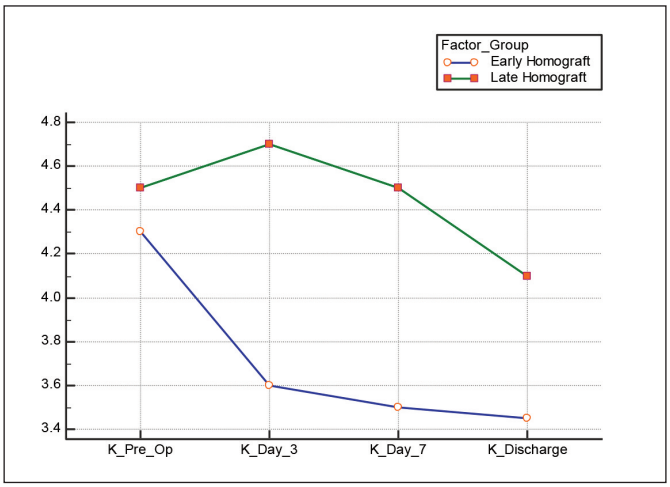

Fig. 10 - Comparison between the two groups of patients regarding serial K assessments

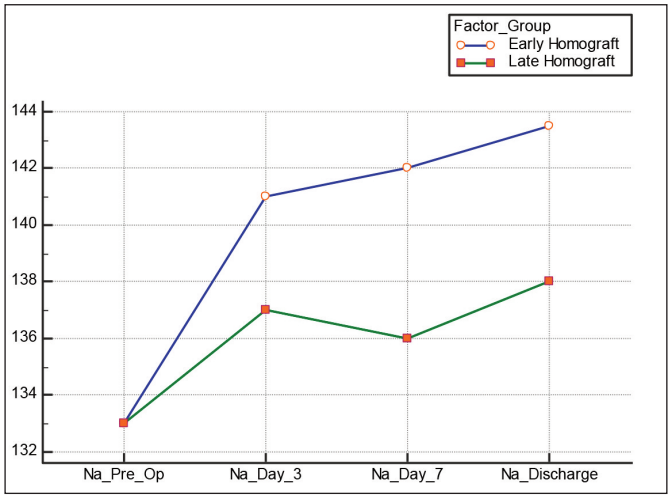

Fig. 9 - Comparison between the two groups of patients regarding serial Na assessments

and a non-significant difference as regards wound infection and mortality ($p > 0.05$) (*Table II*).

Discussion

Burn injury may lead to extensive skin loss. Finding an ideal skin substitute for burn patients becomes essential.[8] The best burn wound dressing in partial-thickness and full-thickness burns is split-thickness skin autograft. However, in major burns, there is a limited donor site for the skin autograft,[9] and in this case, homograft is used as a temporary biological dressing.[10]

Our study did not find significant differences between the two groups regarding serial HB assessment. However, a previous study found a significant difference between both groups regarding preoperative haemoglobin levels in the early surgery group (11.99±1.57) compared to the delayed surgery group patients (9.33±1.66). This can be explained as the early surgery group underwent surgery before affection of general condition by burn insult, no recurrent dressing oozing, no frequent blood samples, less duration of exposure to erythroid inhibitory substances and decreased incidence of burn wound infection and nosocomial infection.[11]

In the present study, the mean length of stay was significantly decreased in the early skin homograft group compared to the late skin homograft group. A previous meta-analysis, which analysed six randomised controlled trials comparing early grafting

Table II - Comparison between the two groups as regards post-operative outcome data

Variable			Early homograft group (8)	Late homograft group (23)	P value
Rejection (%)		Median (IQR)	20 (16.2 – 45)	75 (50 – 100)	0.033*
Length of hospital stay (days)		Median (IQR)	14 (13 – 15)	28 (21 – 37.5)	0.0019*
Wound infection	+ve	No (%)	1 (12.5%)	9 (39.1%)	0.1721
Mortality rate	+ve	No (%)	1 (12.5%)	3 (13%)	0.9690

and delayed grafting, concluded that hospital stay was significantly reduced in the group that had early grafting.[4] However, our study showed no significant difference between both techniques regarding hospital stay. This may be due to the difference in inclusion criteria of the included patients, as the patients had less than 15% total body surface area burns and were otherwise healthy.[12] The present finding suggests that early excision and grafting by reducing the hospital stay would lead to greater availability of beds to the general population. Hence, as a corollary, the overall efficiency and output of the system will be increased without actually increasing the number of beds dedicated to burn care.

Regarding infection, we found that infection was increased among the late skin homograft group compared to the early skin homograft group, although this difference was still non-significant. A previous study showed that culture-positive wounds were more frequent in the delayed grafting group.[13]

Conclusion

Using homograft in major burn patients improved their overall condition by improving laboratory and respiratory data post-operatively. However, early usage of the homograft, especially in the first three days, improved laboratory data, SIRS score, percentage of rejection, and length of hospital stay.

BIBLIOGRAPHY

1 Gallaher JR, Mjuweni S, Shah M, Cairns BA, Charles AG: Timing of early excision and grafting following burn in sub-Saharan Africa. Burns, 41(6): 1353-9, 2015.

2 Saaiq M, Ahmad S, Zaib MS: Burn wound infections and antibiotic susceptibility patterns at Pakistan Institute of Medical Sciences, Islamabad, Pakistan. World J Plast Surg, 4(1): 9-15, 2015.

3 Orgill DP, Ogawa R: Current methods of burn reconstruction. Plast Reconstr Surg, 131(5): 827e-836e, 2013.

4 Ong YS, Samuel M, Song C: Meta-analysis of early excision of burns. Burns, 32(2): 145-50, 2006.

5 Mrgahed MA, Elkashty SM, Nassar AT, Elkhouly HRA: Evaluation of the use of skin homograft for management of major burn patients. Egypt J Plast Reconstr Surg, 45(4): 247-257, 2021.

6 Bravo D, Rigley TH, Gibran N: Effect of storage and preservation methods on viability in transplantable human skin allografts. Burns, 26: 367-378, 2000.

7 Halim AS, Khoo TL, Mohd Yussof SJ: Biologic and synthetic skin substitutes: an overview. Indian J Plast Surg, 43(Suppl): S23-S28, 2010.

8 Yussof MSJ, Halim AS, Saad MAZ, Jaafar H: Evaluation of the biocompatibility of a bilayer chitosan skin regenerating template, human skin allograft and Integra implants in rats. Br J Surg, 98: 212, 2011.

9 Shevchenko RV, James SL, James SE: A review of tissue-engineered skin bio-constructs available for skin reconstruction. J Royal Soc Interface, 7: 229-258, 2010.

10 Mahdavi-Mazdeh M, Nozary HB, Tavakoli SAH, Ayaz M et al.: Human split-thickness skin allograft: skin substitute in the treatment of burn. Int J Org Transplant Med, 4: 96-101, 2013.

11 EL-Menoufy T, Taha O, Tohamy AM, Kamal M, EL-Sonbaty M: Early excision and skin graft versus delayed skin grafting for patients with deep thermal burn up to 15% of the body surface area: a prospective comparative study. Egypt J Plast Reconstr Surg, 43(2): 221-226, 2019.

12 Ayaz M, Bahadoran H, Arasteh P, Keshavarzi A: Early excision and grafting versus delayed skin grafting in burns covering less than 15% of total body surface area: a non-randomized clinical trial. Bull Emerg Trauma, 2(4): 141-145, 2014.

13 Saaiq M, Zaib S, Ahmad S: Early excision and grafting versus delayed excision and grafting of deep thermal burns up to 40% total body surface area: a comparison of outcome. Ann Burns Fire Disasters, 25(3): 143-147, 2012.