Covering the massive burn: a case series and review of the literature

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The term massive burns is used to indicate burns that cannot be covered by the patient's own skin by a single harvesting. Massive burns therefore are a subclassification of major burns (i.e. burns > 25% TBSA) and are typically managed in a tertiary burns centre. They have been variously defined as burns extending over more than 30%,[1,2] 35%,[3] 40%[4] and 50%[5,6] of the total body surface area (TBSA). As 20% of a patient's body surface area (such as the face, hand, feet and perineum) is not suited to provide donor sites, a maximum of 40% TBSA can be covered with the patient's own skin, and therefore it makes most sense to define a massive burn as a burn over 40% TBSA. Massive burns provide a number of treatment challenges. The large amounts of fluids required to resuscitate these patients puts them at risk for oedema formation in the tissues, burn wound progression and compartment syndromes.[7] Although early total excision has been suggested as the standard-of-care in high-income environments, this is associated with a massive onslaught onto the patient's physiological reserves requiring resources that are scarce in middle- and low-income countries (LMICs). Many units under these circumstances practise a staged-excision approach, but this may be associated with a higher sepsis rate.[8] When the patient survives the initial resuscitative stage, the question arises how to cover the burned areas. Although skin is often meshed to enlarge it, it should be appreciated that harvested skin undergoes primary contraction, decreasing its area by 10–20% in a split-thickness skin graft (SSG) and 40% in a full-thickness skin graft;[9,10] the result is that a 1:3 mesh of an SSG only covers 1.8 x the original donor area.[11] Larger expansion rates (1:4 and more) leave large interstitial areas that need to be covered by a temporary skin substitute, such as cadaver skin or a dermal substitute, to prevent them drying out, while the interstitial areas re-epithelialise.[12] Principles for excision of massive burn wounds, such as early total excision versus staged excision, and the order of areas excised in each option are well covered elsewhere[8] and will not be repeated here.

So what are the options to cover patients with massive burns, and how feasible are they in a tertiary burns unit in a middle-income country? In the following we will discuss the various options available to the burn surgeon. We will then relate our experience with covering massive burn at the Tertiary Burns Unit at Inkosi Albert Luthuli Central Hospital, in Durban, South Africa. Finally, we will suggest a protocol for the management of massive burns, as practised in our hospital.

Options for the management of massive skin defects after burn injuries

Option 1: Temporising

It is sometimes insufficiently realised by non-burn surgeons that the early management of deep burns (i.e. deep partial-thickness and full-thickness burns) as proposed by Janzekovic[13] in the 1970s is 'early excision AND immediate grafting': merely excising the burn wound leaves the wound bed exposed, and prone to dehydration, which will result in progression of the burn wound.[8] There are two solutions to this problem.[8] The first is to excise the burn wound in stages, at each stage removing eschar up to 10–15% TBSA, with immediate autografting of the defect. This, however, is not an option in the massive burn patient, as there are insufficient donor sites to cover all excised burn wounds. The other option is to temporise the wounds by covering them with a skin substitute. This may be in the form of an allograft (cadaver skin, amniotic membrane), xenograft (porcine) or semi-synthetic temporary skin substitute (using porcine or bovine collagen). Cadaver skin is in short supply in South Africa. As disease transmission (HIV, hepatitis) is always a possibility with amniotic membrane,[8] this alternative is rarely used by South African burn surgeons. Both xenograft and semi-synthetic dermal substitutes are commercially available in this country, but costs are prohibitive for many units managing burns.

Option 2: Re-harvesting and unusual donor sites

Unusual donor sites, which may be used in massive burns, may be from the scalp, the soles of the feet or the scrotum. In the latter it helps to infiltrate the subcutaneous tissues with saline, which will even out the contours. The option of re-harvesting from the same donor site is usually combined with a temporising approach while the site from which the original split-thickness graft was taken heals, a process which takes on average two to three weeks, depending on the location of the donor site and the thickness of the original graft. Re-harvesting from the same site can be performed to a maximum of three times, but more frequent reharvesting will increase the risk of later hypertrophic scarring of the donor site. The most commonly used areas from which skin is reharvested are the back and the scalp.

Using the scalp as a donor site is especially useful in children, because of the relatively large surface area of the head. Some consider it the first option for grafts of the face, because of the colour match. Several large international series have shown that the procedure is well tolerated, with little short- or long-term complications, including alopecia.[14-16] However, a study from Cape Town[17] showed a poor result in African children with folliculitis, poor healing of donor sites and alopecia, although this did not reach significance due to the small number of children included. The authors postulated that the poor outcomes were related to the skin type (De la Mettrie types VI–VIII) encountered in African patients. A larger study to confirm these findings would be indicated.

Option 3: Wide meshing

Meshing to a ratio above 1:3 may be used, but – as indicated above – this requires the use of a secondary skin substitute to cover the interstices while these are re-epithelialising ('sandwich technique').[18,19] Although most often cadaver skin is used, any skin substitute will do. A variant of wide meshing is the MEEK technique,[20] which allows an expansion between 1:4 and 1:9. Cicero Parker Meek, in 1958, developed this technique from the earlier practised post-stamp grafts,[21] and it was modified by Kreiss and Paff[22] to the technique currently used. Small split-thickness skin grafts are placed on blocks of cork with the dermal side up. They are then cut into small blocks of 3 x 3 mm by a special dermatome, which will cut the graft, but not the cork. A specially designed glue is applied to the epidermal surface of the cut grafts, which are then glued to a plicated dressing. The cork is removed and the dressing expanded and placed on the wound. The dressing provides a moist surface which will allow the interstices between the micrografts to be populated by epithelial cells migrating from the edges of the grafts, a process which takes three to five weeks.

A recent study comparing 15 patients who had a MEEK procedure with 28 who had a split-skin graft (SSG) found that the scar outcome was significantly superior to that after SSG.[23]

Option 4: Cultured epithelial cells

Epithelial cells can be harvested from the burn patient at the initial operation. They are then cultured either in suspension or using a carrier. This process takes three to five weeks, during which time the wounds must be temporised. During this period, the patient remains at risk for infection and systemic sepsis.[24] The resulting epithelial cells are then either sprayed (suspension) or placed (sheet) onto the wound. Unfortunately, the resulting grafts have proven to be fragile and difficult to handle, and the take is unpredictable with take rates varying between 15 and 85%, with higher rates in wounds that were fresh, had dermal elements or that had been covered by cadaver skin.[24] Recently, better results have been obtained by combining CEA with widely meshed SSGs or MEEK micrografts.[25-28] Because the grafts lack a dermal layer, long-term results have also been poor, with frequent blistering, significant hypertrophic scarring and contracture formation as well as hypopigmentation reported.[29] Furthermore, the procedure is costly.

Option 5: Epithelial cell suspension ('spray-on-skin')

In this technique single or minute clumps (about 50 µm) of skin cells are created, which are then sprayed onto the skin. This is therefore a form of micrografting. The advantages over cultured epithelial cells are that the technique can be applied immediately (i.e. without the three- to five-week waiting time), and that all elements of the skin (epithelial cells, fibroblasts, melanocytes and Langerhans cells as well as their stem cells) are grafted, resulting in better outcomes than cultured epithelial cells.[30,31] There are two techniques. The ReCell® technique (Avita Medical, Australia) separates the cells by an enzymatic technique, using trypsine.[32-34] The Rigenera® technique (Human Brain Wave, Italy) separates the cells mechanically in a specially designed cutter. Rigenera® was originally developed in dental and plastic surgery to generate microsamples of tissue, that were injected as part of a reconstructive procedure to form a nidus for regrowth of tissue such as cartilage and bone.[35-38] We modified the technique to generate micrografts of skin, which are sprayed onto the skin. We routinely combine this with platelet-rich fibrin,[39] generated by ultracentrifuging the patient's blood using the Vivostat® ultracentrifuge and spray system (Lillerød, Denmark). The PRF immediately polymerises on contact with the wound bed, thus 'catching' the skin elements and binding them to the underlying wound bed. The PRF may also provide growth factors (derived from the platelets) and nutrients for the growing skin elements. Recent studies have demonstrated that the Rigenera-generated micrografts accelerate wound healing, probably via an extracellular signal-regulated kinase signalling pathway.[40,41] So far, we have used the spray-on-skin/PRF technique only in combination with wide meshing or the MEEK technique.[39]

Option 6: Dermal regeneration templates

Although split-thickness grafting is considered in many burn centres the treatment of choice for larger deep partial- and full-thickness burns, the lack of a full dermis puts the patient at risk for hypertrophic scarring and contracture formation. Dermal regeneration templates (Pelnac®, Integra®) consist of an acellular collagen matrix (either of porcine or bovine origin) that closely resembles the fibre pattern of human skin. The template is covered by a silicone film, which serves as a temporary epithelial substitute.[29] The matrix is incorporated into the wound bed by ingrowth of vessels and fibroblasts over the course of one to three weeks. Completeness of this process is indicated by separation of the silicone layer, after which a split-skin graft can be grafted onto the template. The incorporation of artificial dermis has been shown to minimise contracture and enhance skin elasticity.[42] Recently, variants have been developed (Matriderm®, Integra Ultra-Thin®) that allow immediate grafting onto the dermal template.[43-45]

Emerging options

A number of novel options will possibly be available in the near future. Stem cells have been investigated in the management of burns.[47] They are usually mesenchymal or adipose-derived. They may be injected locally or systemically early after the burn (before day four). A review from 2017[46] reported 'a trend towards improved microscopic appearance', but results were conflicting between the included studies. Epithelial stem cells are either derived from the basal layer of the epidermis (unipotent) or from the bulge portion of the hair follicles (multipotent). Multipotent stem cells can differentiate into multiple cell lines, such as epidermal, and sebaceous cells. Epithelial stem cells are an important component of spray-on-skin.

Progress in bio-engineering has involved populating dermal templates with epithelial cells or fibroblasts.[24] Where such keratinocytes have to be autologous, fibroblasts are immunologically tolerant, and allogenic fibroblasts are usually accepted without rejection in the long term. New developments in this area are the manufacturing of skin containing all dermal elements, such as vessels, hair follicles and nerve endings. A variant of this is 3D-printed skin,[47,48] which is now commercially available in Germany and the USA.

The Durban experience

The Burns Unit at Inkosi Albert Luthuli Central Hospital is the Tertiary Burns Unit for the Province of KwaZulu-Natal, a province with a population of about 10 million people. We estimate that about 10 000 people are admitted with a diagnosis of burn injury annually in this province. People with massive burns are typically referred to the tertiary burns unit, although limited bed space may indicate a period of temporisation in a lower-level hospital. We have previously reported on the epidemiology of burns referred to our unit, as well as on the problems we face with the referral of our patients.[49] One of these problems was the lack of ICU facilities for burn patients in our hospital which meant that patients with inhalational injury had to be managed in regional hospitals until they no longer required ICU care, after which they were transferred to our unit. Since 2018 burns patients requiring ICU care are accommodated in our trauma ICU (provided there is space) and we have since then managed massive burns from the time of burn. Yet, a number of massive burn patients are never discussed with us, but only referred if and when they survive.

Methods

We identified all patients with massive burns (defined as burns over 35% for this study) admitted to the adult burns ward (age > 12 years) between January 2018 and July 2019. The adult burns unit is a ten-bed unit providing tertiary burn care to a province of roughly 10 million people. We defined a massive burn as a burn with a TBSA of > 35% rather than > 40%, because many of these patients are referred late after attempts of grafting by lower-level centres, and have compromised donor sites. The following information was collected from our database: demographics (gender/age), mechanism of burn, delay to referral from base hospital, mortality, operative technique, length of stay in the tertiary unit, costs of procedure.

Ethical permission for retrospective studies involving the trauma/burn database was covered by the UKZN-BREC ethics committee (Class Approval BE 207/09). Ethical approval for micrograft treatment was obtained from the Hospital Medical Human Research Committee, and all patients gave informed consent prior to participation in the procedures.

Results

We identified 14 patients with burns over 35% (see Table 1). Median age was 35 years (range 12–50 years). The male:female ratio was 10:4. Median burns size was 49% TBSA (range 35–70). Mechanism of injury was fire burns in 12 patients, and a chemical and electrical burn in the remaining two patients. Three patients had an inhalational injury and were ventilated in our trauma ICU.

Four patients died (mortality 20.4%). The majority of patients (nine patients, or 64.3%) were admitted after 21 days post-burn, with a delay ranging from 24 to 389 days. When the length of stay, divided by the percentage burn was calculated for survivors admitted within 21 days, the result showed an average LOS of 1.5 days per % TBSA burned. For survivors admitted after this period the LOS was 10.5 days/% TBSA burned.

Table 1: Patients with massive burns admitted in 2018 and 2019

Pt	Age	Gender	HIV	Mechanism	%TBSA	Inhalation	Delay	SSG	DRT	MEEK	SoS	PRF	LOS_{BC}	LOS_{TOTAL}
1	15	M	N	Shack fire	40	N	90+	Y				Y	200+	290+
2	51	M	N	Flame	70	N	1			Y	Y		80	81
3	41	F	Y	Flame, explosion	45	Y	25						Died - 25	50
4	40	F	Y	Flame	50	N	24						futile	24
5	12	N	N	Flame	35	N	69			Y	Y	Y	42	77
6	40	M	N	Flame	45	N	120+	y	y	y	y	y	441	561+
7	32	M	N	Flame	38	N	65	Y				Y	30	95
8	27	M	N	Multitrauma	40	N	0						Died - 30	30
9	32	M	Y	Flame	35	N	389			Y	Y	Y	177	566
10	48	M	Y	Field fire	48	Y	0			Y	Y	Y	Died - 51	51
11	40	M	Y	Flame	50	Y	4	Y			Y	Y	107	111
12	32	M	N	Electrical	45	N	5	Y	Y				55	60
13	50	F	Y	House fire	42	N	42			Y	Y	Y	16	58
14	34	M	N	Chemical	35	N	108	Y	Y	Y	Y	Y	124	232

HIV – patient positive for HIV, %TBSA – percentage of the total body surface area burned, SSG – split-skin graft, DRT – dermal regeneration template, MEEK – Meek micrografting technique, SoS – spray-on-skin, PRF – platelet-rich fibrin, LOS_{BC} – length of stay in tertiary burns centre (in days), LOS_{TOTAL} – total length of stay (burns centre plus referring hospital in days)

Table 2: Costs of various procedures

Item	Cost	Cost/daily admission cost
MEEK 10% TBSA	R16 800	5.6
Rigenera® ECS (spray-on-skin)	R6 700	2.2
ReCell® ECS (spray-on-skin)	R38 000	12.7
Vivostat® PRF (platelet-rich fibrin)	R7 000	2.3
Integra® Dermal Substitute 10% TBSA	R150 000	50
Biobrane® 10% TBA	R7 000	2.3
24-hour admission to Tertiary Adult Burns Ward	R3 000	1

%TBSA – percentage of the total body surface area burned, MEEK – Meek micrografting technique, ECS – epithelial cell suspension

A variety of techniques were used in the management of these patients. Seven patients were managed with a combination of MEEK, spray-on skin and platelet-rich fibrin (PRF) (one of which subsequently demised), one with a combination of wide meshing, spray-on-skin and PRF, and two with wide meshing and PRF only. The last patient was covered with a dermal substitute after the initial burn wound excision, followed by split-skin grafting after two weeks. Three of the patients who died did not survive until the wounds could be covered.

The costs of the various procedures are given in Table 2. To put these costs in perspective, they were compared with the cost of a day's admission to the tertiary burn ward at our hospital.

Discussion

The management of massive burns is a challenge, and often considered too costly in resource-limited environments. We have described our experience with the management of massive burns in the province of KwaZulu-Natal, South Africa. We managed 14 patients in a period of 18 months. Although this seems a small series, it has to be appreciated that the average burns unit in a high-income country manages about one or two massive burns in a one-year period. We observed a mortality of four. However, because most patients are referred to our hospital from elsewhere, and these patients sometimes wait in these hospitals until a bed becomes available, early deaths occur in the referring hospital, and are not included in our figures. This is a regrettable situation, in view of the finding that the length of stay in the tertiary unit increases significantly for those patients who could not be admitted and operated upon within three weeks after the injury. Although there were only three survivors admitted within three weeks (out of a total of five), their average length of stay (1.5 days/% TBSA burned) is in keeping with other series of massive burns.[50,51] The average length of stay of those admitted after three weeks (10.5 days/%TBSA) highlights the importance of referring and managing patients with massive burns as soon as possible. Since our previous article we have embarked on an intensive outreach programme, including the use of telemedicine[52] and frequent ward rounds in peripheral hospitals, which serve to improve matters somewhat; however early admission to the burn centre has remained critically dependent on the availability of beds.

We have adapted the Rigenera technique, originally developed as an injectable adjunct to reconstructive surgery, for use with epithelial and dermal cell suspension. We use this technique in conjunction with a wide meshing (1:4) or MEEK micrografting. The exact technique has been described elsewhere.[37] Results so far have been excellent, both in terms of objective parameters as of patient satisfaction.[37]

Throughout the 18 months we have developed a protocol for managing massive burns, which includes the following:

1. Fresh burns are immediately excised and covered with a skin substitute. If an ICU bed is available, a total excision will be attempted, otherwise the excision is done in stages.
2. Older burns (i.e. after three weeks post-burn), who are ready for grafting, are immediately grafted.
3. Older burns, which are not suitable for grafting, are subjected to a period of negative wound pressure therapy, usually lasting for a week, until the wound bed is ready for grafting.
4. A dermal regeneration template is used in fourth degree burns, especially when there is exposed bone (such as ribs), and to cover areas of full-thickness skin loss over joint areas.
5. The wound is then covered by a combination of either wide-meshed split-thickness skin or MEEK micrografts and spray-on-skin. The aforementioned experience with cultured epithelial cells suggests that the combination with wide-meshed SSG or MEEK autografting provides better results, and we have found the same with the Rigenera spray-on technique. The Rigenera spray-on-skin significantly speeds up the time to healing, with most grafts showing near-complete skin coverage by the first dressing change. Whether to use wide meshing or MEEK micrografting depends on the availability of donor sites, availability of equipment, and surgeon's as well as patient's preference.

Although many of these techniques are costly, the picture changes significantly if costs are put into the perspective of the running costs of a tertiary burn centre. Most therapies are in the cost-range of three to six days of hospital stay. Given the massive decreases in hospital-length-of-stay that are obtained by early treatment as opposed to later treatment, we can conclude that these techniques are certainly justified in an LMIC economy.

Conclusion

The management of massive burns, after the initial resuscitation stage and excision of the burns, has evolved in our unit to wide meshing or MEEK micrografting, combined with the use of spray-on-skin and platelet-rich fibrin. This may be combined with a dermal template for certain indications, such as fourth-degree burns with exposed bone, and over joints. We do not know whether the addition of the PRF makes a difference to the final results, and this needs further investigation.

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