Rate of Healing in Skin-Grafted Burn Wounds

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Background: Skin grafting is a simple and common procedure for achieving wound closure. Despite its widespread use, there is little objective information about the outcomes of skin-grafted burn wounds. The purposes of this study were to determine the length of time it takes to achieve complete wound healing in split-thickness skin-grafted burn wounds and to identify factors that affect time to complete wound healing.

Methods: The authors prospectively collected information from January through September of 2003 on 52 consecutive patients. Time to complete wound healing was defined as the number of days from burn wound skin grafting until the wound was 100 percent epithelialized. Percentage of total body surface area burned, preoperative prealbumin level, sex, age, graft type, burn mechanism, cause of graft loss, and presence of hypergranulation tissue were assessed and correlated with time to complete wound healing.

Results: The time to complete wound healing ranged from 2 to 75 days. Forty-six percent of skin grafts had 100 percent wound closure at postoperative day 7. No grafts were lost to infection. Factors that significantly affected time to complete wound healing were graft loss by seroma, preoperative prealbumin level, presence of hypergranulation tissue, and burns caused by hot solids.

Conclusions: The authors' results suggest that most patients will heal skin-grafted burn wounds within 2 weeks. Meticulous attention to prevention of seroma, hypergranulation tissue formation, and malnutrition might decrease time to complete wound healing. Factors thought to influence time to complete wound healing, such as total body surface area burned, sex, age, graft type, and infection, did not significantly affect the authors' patient group. (*Plast. Reconstr. Surg.* 120: 451, 2007.)

Skin grafting is a simple and common procedure for achieving wound closure. Despite its widespread use, there is little or no objective information about the outcomes of skin-grafted wounds. When queried, most practitioners would assume that skin-grafted wounds heal quickly. Unfortunately, experiences with our patients have suggested that this is often not the case. The actual length of time it takes for complete wound healing of skin-grafted burn wounds is not reported in the literature we reviewed. In addition, factors that might affect the time to complete healing, such as infection, poor nutrition, hematoma, seroma, shear, burn size, and the presence of comorbid conditions, such as diabetes, have been not been well studied.[1,2] Studies that have reported the outcome of skin-grafted wounds used an arbitrary endpoint of a few days to 2 weeks to measure the effects of variables such as graft type, infection, hematoma, shear, nutrition, and diabetic status on graft take.[2–4] Better information is needed to counsel our patients and improve our results.

The purposes of this study were to determine the length of time it takes to achieve complete wound healing in split-thickness skin-grafted burn wounds and to identify factors that affect the time to complete wound healing. The primary endpoint was the length of time from burn wound skin grafting until the wound was 100 hundred percent epithelialized. The risk factors we studied included patient age, sex, premorbid

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conditions, total body surface area burned, prealbumin level, mechanism of burn, and mechanism of graft loss.

PATIENTS AND METHODS

We prospectively collected information from January through September of 2003 on 52 consecutive patients treated at the burn center in a large public teaching hospital. Patients who were critically ill or had multiorgan system failure (i.e., significant organ dysfunction that required alterations of standard of care for that dysfunction) were excluded from the study. For example, patients who had prolonged periods of ventilator support, those who were hemodynamically unstable or required cardiovascular support, and those who had significant renal or hepatic dysfunction were excluded.

On admission to the burn center, resident and attending staff assessed the total body surface area burned and comorbid medical conditions. All patients were treated by a standard protocol. Patients with burns over more than 25 percent of their total body surface area received fluid resuscitation according to the Parkland formula. Cellulitis and sepsis were treated with systemic antibiotics as indicated. Before debridement and grafting, wounds were treated with topical antimicrobials, usually silver sulfadiazine. Most were treated within 1 week of admission by tangential excision of the burn eschar and split-thickness skin grafts to the burn wounds. The grafted wounds were then treated with topical antimicrobial dressings. Meshed grafts were dressed with N-terface (Winfield Laboratories, Inc., Richardson, Texas), burn rolls soaked in 5% Sulfamylon solution (Bertek Pharmaceuticals, Inc., Morgantown, W.Va.), and a compressive wrap. These wounds were irrigated every 8 hours with this solution until the first postoperative dressing change. Irrigation was continued until the majority of the interstices of the meshed grafts were closed. Sheet grafts were dressed with bacitracin-coated Xeroform (Tyco Healthcare/Kendall, Mansfield, Mass.), dry gauze, and a compressive wrap. The sheet grafts were never perforated at the time of surgery. All sheet grafts were assessed on postoperative day 2 for the presence of seroma or hematoma, which, if present, was drained by aspiration. When any significant portion of a patient's wounds remained open, the wound was dressed with silver sulfadiazine until 100 percent epithelialization of the wound was achieved.

A data sheet containing a burn diagram was used to document the location and type of split-thickness skin graft used (mesh, sheet, or both). Preoperative data collected on this sheet included the patient's age, sex, premorbid conditions (e.g., diabetes, obesity), drug and/or alcohol serum positivity, preoperative prealbumin level, mechanism of burn (flame, liquid, or solid), percentage of total body surface area burned, presence of preoperative infection, and date of injury. Operative data collected included date of surgery and type of graft used. On a separate data sheet, the percentage of graft take at postoperative days 7 and 15, presence of hypergranulation tissue, mechanism of graft loss, and need for regrafting were documented for each inpatient dressing change. The condition of the graft at time of discharge and at each outpatient clinic visit was documented until the skin-grafted wound was 100 percent epithelialized. The number of days from date of surgery to the time the wound was 100 percent epithelialized was defined as the time to complete wound healing.

We compared the time to complete wound healing among subgroups defined by the selected risk factors (age, sex, comorbid conditions, alcohol or drug use, prealbumin level, mechanism of burn, total body surface area burned, preoperative infection, graft type, hypergranulation tissue, mechanism of graft loss, and need for regrafting) using the Mann-Whitney rank-sum test. This test was chosen because the length of time to complete wound healing was not normally distributed. We studied the relationship between risk factors measured in continuous scale with length of time to complete wound healing using the Spearman's correlation coefficient. On the basis of the findings of the univariate analysis, we selected variables that were significant at $p < 0.20$ into the nonparametric multiple regression analysis to identify the independent risk factors that correlated with length of time to complete wound healing. The percentage of variation explained by the independent predictors (R^2) was derived and tested for statistical significance. SAS statistical software was used for all statistical analyses.

RESULTS

The study included 52 consecutive patients (36 male and 16 female patients) ranging in age from 9 months to 75 years (average age, 30 years). Three patients had diabetes on presentation and 10 tested positive for alcohol and/or drugs on admission. Preoperative prealbumin levels were obtained for 41 patients, and of these, 17 had values lower than 15 g/dl. Twenty-four, 17, and four patients sustained flame, liquid, and solid burns, respectively. Thirty-four patients sustained burns

over 10 percent or less of their total body surface area, and 18 sustained burns over more than 10 percent. Eleven patients had preoperative infections requiring systemic antibiotics. Eighteen patients received meshed grafts, 26 received sheet grafts, and eight received both meshed and sheet grafts. Seventy-one percent of patients experienced graft loss in the form of seroma ($n = 20$), hematoma ($n = 8$), or shear ($n = 9$). Nine patients developed hypergranulation tissue at the site of graft loss. Only three patients required regrafting in areas of graft loss. No grafts were lost to infection (Table 1).

The number of days to complete wound healing ranged from 2 to 75 days. Forty-six percent of skin grafts had 100 percent wound closure at postoperative day 7. Most grafts (88 percent) had take of 95 percent or more, and only 12 percent had less than 95 percent take at postoperative day 7. By postoperative day 15, 46 percent of grafts had 100 percent take. Eighty-four percent of grafts had take of 95 percent or more at postoperative day 15. Only 12 percent had less than 95 percent take at postoperative day 15 (Table 2).

The number of postoperative days to complete wound healing among subgroups was compared for all patients using the Mann-Whitney rank-sum test. No significant difference in time to complete wound healing was found among patients subgrouped by age, sex, diabetes, alcohol and/or drug use, prealbumin level, flame or liquid burn, total body surface area burned of 10 percent or less or of more than 10 percent, preoperative infection, graft type, graft loss by hematoma or shear, and need for regrafting. Patients who experienced graft loss by seroma and those who developed hypergranulation tissue at the site of graft loss demonstrated a statistically significant increase in time to complete wound healing, while patients who sustained burns by hot solids demonstrated a statistically significant decrease in time to complete wound healing (Table 1).

Fifty percent of patients (13 of 26) who received sheet grafts developed seromas. The mean time to complete wound healing for these patients was 38 days (±22 days). Patients with sheet grafts who did not develop seromas healed within 13 days (±20 days), which was significantly faster ($p = 0.007$) compared with patients with sheet grafts who did develop seromas. Only one patient with meshed grafts developed a seroma, and this did not significantly prolong time to complete wound healing.

In patients with small burns (≤10 percent total body surface area), the preoperative prealbumin level correlated inversely with the number of days to complete wound healing. This inverse relationship was not observed in patients with larger burns (Table 3).

Among the risk factors that had a p value of less than 0.20 in the univariate analysis, the nonparametric multiple regression analysis identified prealbumin level as the most significant independent

Table 1. Comparison of Days to Complete Wound Healing in Patient Subgroups

Parameter	No.	Mean Days to CWH (±SD)	Median	p*
All patients	52	29 ± 22	25	
Age				0.99
<18 years	14	30 ± 20	30	
≥18 years	37	30 ± 24	21	
Sex				0.46
Male	36	30 ± 21	28	
Female	16	26 ± 25	16	
Diabetes				0.33
Yes	3	47 ± 36	61	
No	49	28 ± 21	25	
Alcohol/drugs				0.53
Yes	10	26 ± 25	14	
No	42	30 ± 22	26	
Prealbumin level				0.13
<15 g/dl	17	37 ± 26	28	
≥15 g/dl	24	24 ± 20	20	
Flame burn				0.26
Yes	24	32 ± 21	30	
No	28	26 ± 24	18	
Liquid burn				0.57
Yes	17	28 ± 24	21	
No	35	30 ± 22	29	
Solid burn				0.05
Yes	4	8 ± 5	7	
No	48	31 ± 22	28	
TBSA burned				0.94
>10%	18	28 ± 21	23	
≤10%	34	30 ± 24	27	
Preoperative infection				0.97
Yes	11	29 ± 23	21	
No	41	29 ± 23	25	
Graft type				0.25
Mesh	18	30 ± 22	26	
Sheet	26	26 ± 23	18	
Both	8	37 ± 19	34	
Hypergranulation tissue				0.02
Yes	9	38 ± 21	45	
No	43	26 ± 21	21	
Seroma				0.01
Yes	20	38 ± 20	30	
No	29	22 ± 22	13	
Hematoma				0.19
Yes	8	38 ± 25	44	
No	41	26 ± 22	21	
Shear				0.94
Yes	9	29 ± 22	17	
No	40	28 ± 23	23	
Regraft necessary				0.12
Yes	3	50 ± 20	40	
No	49	28 ± 22	21	

CWH, complete wound healing; TBSA, total body surface area.
*The p values are based on the Mann-Whitney U test or the Kruskal-Wallis test.

Table 2. Comparison of Graft Take at Postoperative Days 7 and 15

Graft Take	No. of Patients	Percentage of All Patients
Day 7		
100%	24	46
99–95%	22	42
94–85%	3	6
<85%	3	6
Day 15		
100%	24	46
99–95%	20	38
94–85%	5	10
<85%	1	2
No data available	2	4

Table 3. Correlation between Prealbumin Level and Number of Days to Complete Wound Healing

Patient Group	No.	Spearman Correlation Coefficient	*p*
All patients	41*	−0.403	0.009
TBSA burned >10%	15	−0.161	0.566
TBSA burned ≤10%	26	−0.478	0.014

TBSA, total body surface area.
*Only patients with preoperative prealbumin data were included.

factor ($R^2 = 0.15$; $p = 0.017$) that predicted time to complete wound healing. The presence of hypergranulation tissue was the second most significant independent factor (partial $R^2 = 0.07$; $p = 0.085$). For patients with more than 10 percent of their total body surface area burned, the presence of hypergranulation tissue was the most significant independent predictor of time to complete wound healing ($R^2 = 0.27$; $p = 0.0131$). For patients with burns over 10 percent or less of their bodies, the prealbumin level was the most significant independent predictor of time to complete wound healing ($R^2 = 0.17$; $p = 0.043$).

DISCUSSION

There is little objective information about the length of time it takes for complete wound healing of skin-grafted burn wounds. In the past, surgeons considered a procedure to be successful if the graft take was greater than 90 to 95 percent or if the wound healed without an additional procedure. Although there is abundant information in the literature regarding skin graft healing and factors that contribute to major skin graft loss, most authors measure these outcomes at arbitrary time points in the healing process of the skin-grafted wounds, such as postoperative day 7 or postoperative day 14.[2–5] Until now, there has been no prospective information about the time it takes for skin-grafted burn wounds to become 100 percent epithelialized. This study provides that information as well as a description of the role played by risk factors previously known to contribute to graft loss or decreased graft take in time to complete wound healing.

We want to emphasize that these results describe excellent surgical outcomes, but they are not perfect. Only about half (46 percent) of our patients were completely healed at 2 weeks. While the unhealed areas were small, less than 5 percent of the grafted area, they required daily care. Although our patients were generally very happy with their results, the pain and inconvenience of unhealed wounds and the daily dressing changes delayed their recovery.

The patients we studied were not the sickest patients with the greatest likelihood of graft failure. By excluding critically ill patients from our study, we hoped to remove the complicating systemic effects of organ dysfunction. While it is true that critically ill patients are more likely to have alterations in their wound-healing capabilities, they are a very heterogenic group. In addition, the purpose of this study was to examine the process of skin grafting as a procedure, not the success of skin grafting in patients with multiorgan system failure. To collect meaningful data with regard to skin graft healing in critically ill patients, we would need a significantly larger cohort of patients. Although this would certainly make an interesting follow-up to our current study, by removing these complex factors, we hoped to avoid obscuring our data outcomes by reporting results from a more homogeneous group of patients.

The greatest surprise of these results was the complete absence of graft loss due to infection. Contrary to these results, previous studies have reported infection as one of the most common causes of graft loss.[1,3,6,7] The development of new topical antimicrobial agents, such as 5% Sulfamylon solution (Bertek Pharmaceuticals) and Acticoat (Smith and Nephew, Memphis, Tenn.), appears to have changed this state of affairs. This does not mean that all skin-grafted wounds require antimicrobial dressings. To the contrary, many practitioners do not routinely use topical antimicrobial agents on skin-grafted wounds and get excellent results. The burns wounds that we treat are at higher risk for infection than usual. The wounds are larger, they contain necrotic tissue before debridement, and the injury results in local and systemic immunosuppression. The result is a higher risk of infection. Our results suggest that each practitioner must decide whether his or

her patient is similarly at higher risk for graft infection. If so, these data suggest that a topical antimicrobial agent can reduce those risks and prevent infectious graft loss.

There were many factors that did not affect skin graft take and healing in our study. We did not find a statistically significant correlation between time to complete wound healing and patient age. This is contrary to previous wound-healing studies that demonstrated prolonged wound closure and decreased wound tensile strength with increasing age.[2,5,8–11] Similarly, we did not find a statistically significant correlation between time to complete wound healing and patient sex or drug or alcohol positivity on admission. This may suggest that the poor outcomes associated with these lifestyles may reflect poor nutrition or compliance rather than a direct, primary effect. Although diabetes mellitus has been shown by many authors to cause delayed wound healing and poor skin graft take, we did not find a statistically significant correlation between the presence of diabetes and time to complete wound healing.[1–4,7,12] This may have been due to the aggressive treatment of hyperglycemia in our inpatients. We acknowledge that this nonsignificant finding could be related to the small number of cases in the series and the low incidence rate.

In addition, we found no statistically significant correlation between preoperative infection and delay in complete wound healing. Preoperative infections were considered present in any patient who had clinical evidence of infection localized to the burn wound (i.e., pain, erythema, purulent drainage, and accompanying systemic signs of fever, malaise, or sepsis). These infections were treated with systemic antimicrobial agents according to culture results. Positive wound cultures were not considered to indicate infection unless the above signs were present. The lack of delayed wound healing in this group likely reflects our treatment algorithm of systemic and local antibiotic use until resolution of signs of acute infection, followed by the use of local antimicrobial treatments on the skin-grafted wound. We were surprised by the relatively large number of patients we identified with preoperative infections (21 percent; $n = 11$), but this was likely due to the large population of uninsured and homeless patients treated in our facility. These patients often experience delays in seeking or receiving treatment that may predispose them to preoperative infection.

Patients with burns caused by hot solids healed significantly faster than those burned by flames or hot liquid. This was likely due to the defined edges and depth of these injuries. Contrary to previous authors, we did not find a correlation between burn size and time to complete wound healing.[2] This also could be related to the small sample size.

Mechanical barriers between the skin graft and its wound bed are well-known causes of skin graft loss.[1,6,7,13] In our study, seromas were the most common cause of graft loss and led to a significant increase in time to complete wound healing. We also found that the common belief that sheet grafts are more prone to developing seromas is true. Fifty percent of our patients who received sheet grafts developed seromas and had a statistically significant delay in time to complete wound healing. Comparatively, only one patient who received meshed grafts developed a seroma, and it had no affect on time to complete wound healing. These data emphasize the importance of preventing seroma formation, especially beneath sheet grafts, in optimizing graft take and time to complete wound healing.

The presence of abundant granulation tissue also correlated significantly with lengthened time to complete wound healing. Although some authors state that granulation tissue is a requirement for successful skin graft take, our findings agree with those who believe granulation tissue is not necessary and may actually be a hindrance to graft take.[1,2,13] It is unclear to us, however, if the hypergranulation tissue was the cause or consequence of skin graft loss.

Poor nutrition is well known to delay wound healing.[1,7,9,10,14,15] In this study, we used serum prealbumin level as a nutritional marker. Prealbumin is an ideal marker for protein malnutrition because it has a short biologic half-life, responds quickly to changes in nutritional status, and is relatively inexpensive to measure.[14,15] According to a 1995 consensus statement, a prealbumin level of 15 g/dl or higher is considered normal.[15] For this reason, we chose a serum prealbumin level of less than 15 g/dl as a risk factor for delayed time to complete wound healing. We were surprised to find that for patients with burns covering 10 percent or less of their total body surface area, the prealbumin value correlated inversely with days to complete wound healing. The fact that this negative correlation was not found in patients with burns over more than 10 percent of their bodies was also unexpected. Patients with larger and more severe injuries were presumed to be at risk for delayed wound healing due to the metabolic demands of a relatively larger wound. Conversely, patients with smaller burns were considered at low

risk for wound healing delays due to poor nutrition or increased metabolic demand. For this reason, we may have been more aggressive in meeting the nutritional needs of patients with larger burns, while assuming that patients with smaller burns were at low risk because of smaller metabolic demands. Clearly, this assumption was wrong. In addition, when nonparametric regression analysis was performed for all patients with preoperative prealbumin data available, prealbumin level was the most significant predictor of time to complete wound healing. This leads us to conclude that the nutritional status in patients with relatively small skin-grafted burn wounds should be managed as aggressively as that of patients with larger wounds. This finding is important and relevant to any practitioner who grafts wounds.

Although no statistically significant difference was found for time to complete wound healing in all patients grouped by diabetes, prealbumin level less than 15 g/dl or greater than or equal to 15 g/dl, graft type, graft loss by hematoma, or need for regrafting, these subgroups did display a large clinical difference (≥11 days) in time to complete wound healing. Our power analysis showed that the power of the present study to detect mean time to complete wound healing of 11 days or more ranged from 22 to 44 percent. To reach a power level of 80 percent, 64 patients per subgroup would be required to detect the clinically significant difference at a significance level of 0.05. Otherwise, our sample size was sufficient to effectively assess all other outcomes presented above.

CONCLUSIONS

Skin grafting is a simple and effective method for treating wounds. These results demonstrate that nearly half of patients will have 100 percent wound closure at 2 weeks, while the remaining patients will have small areas of unhealed wound that require an average period of 30 days to achieve complete wound healing. Our results suggest that meticulous attention to the prevention and treatment of seroma, hypergranulation tissue formation, and malnutrition might improve these excellent results. In addition, the use of modern topical antimicrobial agents in high-risk patients has made graft loss by infection a problem of the past.

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DISCLOSURE

Warren L. Garner, M.D., is the medical director for Advanced Biohealing, in La Jolla, California, and is a member of their speaker list. There is no financial interest or commercial association for the other authors that might pose or create a conflict of interest with the information presented in this article.

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