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Original Research Article

CLINICAL AND WOUND RELATED FACTORS AFFECTING SPLIT THICKNESS SKIN GRAFT UPTAKE IN SOFT TISSUE DEFECTS

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ABSTRACT

Background: Split thickness skin grafting is commonly used for coverage of ulcers and raw areas where primary closure is not possible. Graft uptake depends on local wound condition, infection status and patient related factors. Identification of predictors of poor graft uptake may help in better preoperative preparation. The aim is to assess the clinical, laboratory and wound related factors affecting split thickness skin graft uptake in patients with soft tissue defects.

Materials and Methods: This prospective observational study included 166 patients undergoing split thickness skin grafting for ulcers and raw areas. Demographic profile, wound etiology, wound size, anatomical site, comorbidities, laboratory parameters and preoperative wound culture status were recorded. Graft uptake was assessed clinically on postoperative day 7. Good graft uptake was defined as >=80% uptake and poor graft uptake as <80% uptake. Data were analysed using chi-square test and multivariable logistic regression.

Results: Good graft uptake was seen in 125 patients (75.3%), while poor graft uptake was seen in 41 patients (24.7%). Good uptake was seen in 90 patients (81.8%) with wounds <=10 x 10 cm compared with 12 patients (50.0%) with wounds >20 x 10 cm. Diabetic foot ulcers had lower good uptake, seen in 14 patients (46.7%). Culture-positive wounds showed poor uptake in 29 patients (47.5%), while sterile wounds showed poor uptake in only 12 patients (11.4%). On multivariable analysis, culture-positive wound, wound size >20 x 10 cm, serum albumin <3.5 g/dL and diabetes mellitus were independent predictors of poor graft uptake.

Conclusion: Poor split thickness skin graft uptake was mainly associated with culture-positive wound, large wound size, hypoalbuminemia and diabetes mellitus. Preoperative correction of infection, nutritional status and glycaemic control may improve graft outcome.

Keywords: Split thickness skin graft, graft uptake, wound culture, diabetic foot ulcer, serum albumin, wound size, soft tissue defect

INTRODUCTION

Split thickness skin grafting is a commonly used reconstructive procedure for covering ulcers and raw areas where primary closure is not possible.[1] It is useful in traumatic wounds, burns, diabetic foot ulcers, post-excision defects and chronic wounds. In routine practice it is preferred because it can cover a large area and donor site healing is usually satisfactory.[2] Successful graft uptake depends mainly on a healthy vascular wound bed. Graft survival occurs through plasmatic imbibition, inosculation and revascularisation.[1,2] Any disturbance in these stages can lead to partial or complete graft loss.

Several local factors affect graft uptake. Infection, hematoma, seroma, shearing movement and poor wound bed preparation are important causes of graft failure. Diabetic foot wounds also have delayed

healing because of impaired vascularity, infection risk and altered cellular repair.[3]

Preoperative wound culture is a useful practical parameter. Pseudomonas aeruginosa has been associated with poor healing after split thickness grafting in chronic ulcers.[4] Quantitative culture studies have also shown lower graft uptake with Pseudomonas aeruginosa and Staphylococcus aureus.[5]

Systemic factors also influence wound healing. Diabetes mellitus, anaemia, hypoalbuminemia and poor glycaemic control can delay healing and reduce graft survival. Serum albumin is commonly used as a simple clinical marker of nutritional status. Correction of modifiable factors before grafting may improve the final outcome.[6] Negative pressure wound therapy is used in selected wounds for wound bed preparation and graft stabilization. Recent randomized trial meta-analysis reported better graft take and lower graft loss with negative pressure dressings compared with conventional dressings.[7] However, its routine use in all patients is still not necessary, and patient selection remains important.[8] Although split thickness skin grafting is a routine procedure, graft loss is still seen in many patients. Many risk factors are identifiable before surgery. Hence, the present study was planned to assess clinical, laboratory and wound related factors affecting split thickness skin graft uptake in patients with soft tissue defects.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Surgery and Plastic Surgery of a tertiary care teaching hospital. The study included patients undergoing split thickness skin grafting for ulcers and raw areas. A total of 166 patients undergoing split thickness skin grafting were included. The sample size was used for practice manuscript preparation and simulated analysis. Patients aged 18 years and above undergoing autologous split thickness skin grafting for traumatic wounds, burn wounds, diabetic foot ulcers, post-excision raw areas, venous ulcers and other soft tissue defects were included. Patients not willing to participate, patients undergoing grafting other than autologous split thickness skin grafting, wounds requiring flap cover, exposed bone or tendon without adequate granulation, and patients lost before postoperative day 7 assessment were excluded. Demographic details, wound size, wound site, etiology, comorbidities, hemoglobin, total leukocyte count, serum albumin, random blood sugar, serum creatinine, wound culture status and organism isolated were recorded. Wound bed status and use of negative pressure wound therapy were also noted. Recipient wound bed was prepared by debridement until healthy bleeding granulation tissue was obtained. Split thickness skin graft was harvested using standard technique from an appropriate donor site. The graft was meshed where required, placed over the recipient bed and secured with sutures or staples. Dressing and immobilization were done according to wound site and surgeon preference. Graft uptake was assessed clinically on postoperative day 7. Good graft uptake was defined as >=80% uptake. Poor graft uptake was defined as <80% uptake. Postoperative infection, seroma or hematoma, complete graft loss, need for re-grafting and hospital stay were also recorded. Data were entered in Microsoft Excel and analysed using statistical software. Categorical variables were expressed as frequency and percentage. Association between categorical variables was assessed using chi-square test or Fisher exact test as appropriate. Multivariable logistic regression was used to identify independent predictors of poor graft uptake. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 166 patients undergoing split thickness skin grafting for ulcers and raw areas were included in the study. Graft uptake was assessed clinically on postoperative day 7. Good graft uptake was defined as graft uptake >=80%, while poor graft uptake was defined as graft uptake <80%.

Table 1: Clinical profile and wound characteristics of study participants

Parameter	Frequency	Percentage
Age group		
<20 years	12	7.2
21-40 years	45	27.1
41-60 years	74	44.6
>60 years	35	21.1
Sex		
Male	130	78.3
Female	36	21.7
Wound size		
<=10 x 10 cm	110	66.3
10 x 11 cm to 20 x 10 cm	32	19.3
>20 x 10 cm	24	14.5
Etiology of wound		
Traumatic wound	94	56.6
Diabetic foot ulcer	30	18.1
Burn wound	22	13.3
Post-excision raw area	16	9.6

Venous ulcer	4	2.4
Site of wound		
Lower limb	118	71.1
Upper limb	32	19.3
Trunk	10	6.0
Head and neck	6	3.6
Comorbidity profile		
No major comorbidity	118	71.1
Diabetes mellitus	29	17.5
Hypertension	15	9.0
Obesity	4	2.4

The clinical profile and wound characteristics are shown in Table 1. Most patients belonged to the 41-60 years age group, comprising 74 patients (44.6%), followed by 45 patients (27.1%) in the 21-40 years age group. There was male predominance, with 130 males (78.3%) and 36 females (21.7%). Most wounds were small to moderate in size. Wounds measuring <=10 x 10 cm were seen in 110 patients (66.3%). Traumatic wounds were the commonest etiology and were present in 94 patients (56.6%). Lower limb was the most common site of wound, seen in 118 patients (71.1%). No major comorbidity was present in 118 patients (71.1%), while diabetes mellitus was the commonest comorbidity, seen in 29 patients (17.5%).

Table 2: Laboratory profile and preoperative wound culture status

Parameter	Frequency	Percentage
Hemoglobin <10 g/dL	29	17.5
TLC >11,000/mm3	44	26.5
Serum albumin <3.5 g/dL	34	20.5
Random blood sugar >200 mg/dL	24	14.5
Serum creatinine >1.2 mg/dL	12	7.2
Healthy granulation tissue	124	74.7
Slough present before final debridement	42	25.3
NPWT used before grafting	32	19.3
Wound culture		
Sterile culture	105	63.3
Culture positive	61	36.7
Organism isolated		
Pseudomonas aeruginosa	35	21.1
Klebsiella species	12	7.2
Staphylococcus aureus	9	5.4
Proteus species	5	3.0

The laboratory profile and preoperative wound culture status are shown in Table 2. Hemoglobin <10 g/dL was present in 29 patients (17.5%). Raised total leukocyte count >11,000/mm3 was seen in 44 patients (26.5%). Serum albumin <3.5 g/dL was present in 34 patients (20.5%). Random blood sugar >200 mg/dL was observed in 24 patients (14.5%). Healthy granulation tissue was present in 124 patients (74.7%). Preoperative wound culture was sterile in 105 patients (63.3%), while culture positivity was seen in 61 patients (36.7%). Among culture-positive wounds, Pseudomonas aeruginosa was the commonest organism, isolated in 35 patients (21.1%).

Table 3: Association of wound factors with graft uptake on postoperative day 7

Variable	Graft uptake <80% n=41	Graft uptake >=80% n=125	p-value
Wound size			0.004
<=10 x 10 cm	20 (18.2%)	90 (81.8%)	
10 x 11 cm to 20 x 10 cm	9 (28.1%)	23 (71.9%)	
>20 x 10 cm	12 (50.0%)	12 (50.0%)	
Etiology of wound			0.002
Traumatic wound	17 (18.1%)	77 (81.9%)	
Diabetic foot ulcer	16 (53.3%)	14 (46.7%)	
Burn wound	4 (18.2%)	18 (81.8%)	
Post-excision raw area	2 (12.5%)	14 (87.5%)	
Venous ulcer	2 (50.0%)	2 (50.0%)	
Site of wound			0.155
Lower limb	33 (28.0%)	85 (72.0%)	
Upper limb	4 (12.5%)	28 (87.5%)	
Trunk	2 (20.0%)	8 (80.0%)	
Head and neck	2 (33.3%)	4 (66.7%)	

The association of wound factors with graft uptake on postoperative day 7 is shown in Table 3. Overall, 41 patients had graft uptake <80%, while 125 patients had graft uptake >=80%. Wound size showed significant association with graft uptake (p=0.004). Good uptake was seen in 90 patients (81.8%) with wounds <=10 x 10 cm, but only 12 patients (50.0%) with wounds >20 x 10 cm had good uptake. Etiology

of wound was also significantly associated with graft uptake (p=0.002). Post-excision raw areas had the highest good uptake, seen in 14 patients (87.5%). Traumatic wounds and burn wounds also showed good uptake in 77 patients (81.9%) and 18 patients (81.8%), respectively. Diabetic foot ulcers showed poorer outcome, with good uptake in only 14 patients (46.7%). Site of wound was not significantly associated with graft uptake (p=0.155).

Table 4: Association of clinical and laboratory factors with graft uptake on postoperative day 7

Variable	Graft uptake <80% n=41	Graft uptake >=80% n=125	p-value
Comorbidity profile			0.006
No major comorbidity	21 (17.8%)	97 (82.2%)	
Diabetes mellitus	14 (48.3%)	15 (51.7%)	
Hypertension	4 (26.7%)	11 (73.3%)	
Obesity	2 (50.0%)	2 (50.0%)	
Hemoglobin <10 g/dL	13 (44.8%)	16 (55.2%)	0.006
TLC >11,000/mm3	18 (40.9%)	26 (59.1%)	0.005
Serum albumin <3.5 g/dL	16 (47.1%)	18 (52.9%)	0.001
Random blood sugar >200 mg/dL	12 (50.0%)	12 (50.0%)	0.002
Culture-positive wound	29 (47.5%)	32 (52.5%)	<0.001
Sterile wound culture	12 (11.4%)	93 (88.6%)	<0.001

The association of clinical and laboratory factors with graft uptake is shown in Table 4. Comorbidity profile showed significant association with graft uptake (p=0.006). Patients without major comorbidity had good uptake in 97 patients (82.2%). In patients with diabetes mellitus, good uptake was seen in only 15 patients (51.7%), while poor uptake was seen in 14 patients (48.3%). Hemoglobin <10 g/dL, raised TLC >11,000/mm3, serum albumin <3.5 g/dL and random blood sugar >200 mg/dL were significantly associated with graft uptake. Culture-positive wound showed strong association with poor graft uptake (p<0.001). Poor uptake was seen in 29 patients (47.5%) with culture-positive wounds. In contrast, sterile wound culture showed good uptake in 93 patients (88.6%).

Table 5: Multivariable predictors of poor graft uptake

Predictor	Adjusted OR	95% CI	p-value
Wound size >20 x 10 cm	3.4	1.20-9.72	0.021
Culture-positive wound	5.8	2.35-14.25	<0.001
Serum albumin <3.5 g/dL	3.1	1.16-8.45	0.024
Diabetes mellitus	2.7	1.01-7.32	0.048
TLC >11,000/mm3	2.2	0.89-5.66	0.087
Hemoglobin <10 g/dL	1.9	0.72-5.18	0.190
Lower limb wound site	1.8	0.62-5.39	0.271

Multivariable logistic regression findings are shown in Table 5. Culture-positive wound was the strongest independent predictor of poor graft uptake. Patients with culture-positive wounds had 5.8 times higher odds of poor graft uptake compared with those having sterile wounds (adjusted OR 5.8, 95% CI 2.35-14.25; p<0.001). Wound size >20 x 10 cm was also an independent predictor of poor graft uptake (adjusted OR 3.4, 95% CI 1.20-9.72; p=0.021). Serum albumin <3.5 g/dL remained significantly associated with poor graft uptake (adjusted OR 3.1, 95% CI 1.16-8.45; p=0.024). Diabetes mellitus was also an independent predictor (adjusted OR 2.7, 95% CI 1.01-7.32; p=0.048). Raised TLC, hemoglobin <10 g/dL and lower limb wound site did not remain statistically significant in the adjusted model. Postoperative complications were more frequent in patients with poor graft uptake. Surgical site infection was seen in 24 patients (14.5%). It was present in 14 patients (34.1%) with poor graft uptake compared with 10 patients (8.0%) with good graft uptake. Seroma or hematoma was seen in 13 patients (7.8%). Complete graft loss was seen in five patients (3.0%) and re-grafting was required in 12 patients (7.2%). Hospital stay >7 days was seen in 39 patients (23.5%), with higher frequency in the poor uptake group.

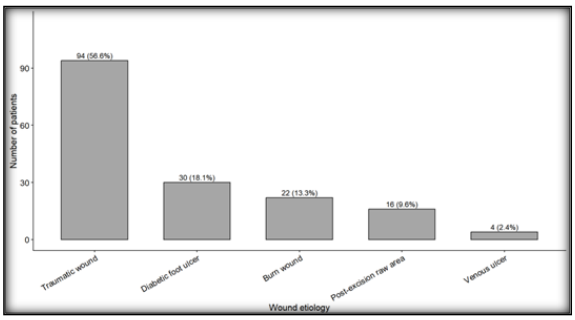

Figure 1: Distribution of wound etiology among patients undergoing split thickness skin grafting

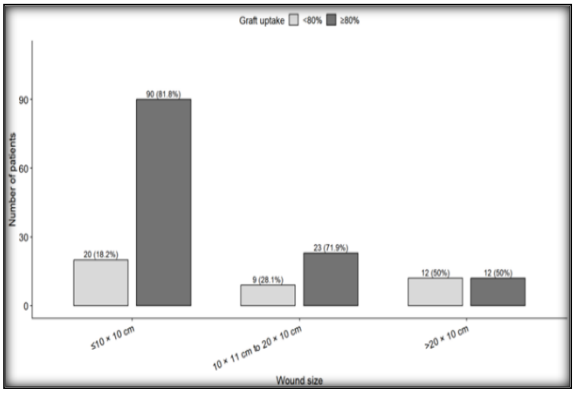

Figure 2: Graft uptake according to wound size

DISCUSSION

Split thickness skin grafting is a routine reconstructive procedure for ulcers and raw areas. In the present study, good graft uptake was seen in 125 patients (75.3%), while poor graft uptake was seen in 41 patients (24.7%). This shows that STSG gives acceptable short-term outcome in most patients, but graft loss remains a relevant problem in routine practice. Most patients in the present study were males, 130 patients (78.3%), and the commonest age group was 41-60 years, 74 patients (44.6%) [Table 1]. This pattern is expected in a surgical unit where traumatic raw areas are common. Traumatic wounds were the commonest etiology, seen in 94 patients (56.6%) [Table 1].

Wound size showed significant association with graft uptake [Table 3]. Good uptake was seen in 90 patients (81.8%) with wounds <=10 x 10 cm. In contrast, only 12 patients (50.0%) with wounds >20 x 10 cm had good uptake. Larger wounds may have more discharge, uneven granulation, shearing and bacterial colonisation. These factors can reduce graft adherence and delay inosculation. Etiology was also significantly associated with graft outcome [Table 3]. Post-excision raw areas had good uptake in 14 patients (87.5%), while diabetic foot ulcers had good uptake in only 14 patients (46.7%). McCartan and Dinh reported that split thickness skin grafts were 78% successful in closing 90% of optimized diabetic foot ulcer wounds by eight weeks.[3] Our lower uptake in diabetic foot cases may be due to infection, raised blood sugar, neuropathy and delayed wound bed preparation.

The anatomical site of wound did not show significant association in the present study [Table 3]. Lower limb was the commonest site, seen in 118 patients (71.1%), and good uptake was seen in 85 patients (72.0%). Reddy et al. studied 70 lower limb skin grafts in 50 patients and reported that about one-third of lower limb grafts failed, with increased BMI, peripheral vascular disease and immunosuppressant medication as important risk factors.[8] This supports that lower limb grafting needs careful wound selection and postoperative protection. Comorbidities showed significant association with graft uptake [Table 4]. Patients without major comorbidity had good uptake in 97 patients (82.2%). In diabetic patients, good uptake was seen in only 15 patients (51.7%). Diabetes mellitus remained an independent predictor of poor graft uptake in multivariable analysis, with adjusted OR 2.7 (95% CI 1.01-7.32; p=0.048) [Table 5]. This is biologically acceptable because diabetes affects angiogenesis, collagen formation, leukocyte function and infection control.

Random blood sugar >200 mg/dL was significantly associated with poor graft uptake [Table 4]. Poor uptake was seen in 12 patients (50.0%) with raised random blood sugar. This supports the need for glycaemic optimisation before elective grafting. In diabetic wounds, grafting should preferably be done after infection control, healthy granulation and acceptable blood sugar control. Nutritional status was another important factor. Serum albumin <3.5 g/dL was present in 34 patients (20.5%) [Table 2]. Poor graft uptake was seen in 16 patients (47.1%) with low albumin [Table 4]. On multivariable analysis, low albumin remained an independent predictor of poor graft uptake with adjusted OR 3.1 (95% CI 1.16-8.45; p=0.024) [Table 5]. Protein deficiency may impair collagen formation, angiogenesis and epithelialization. Hence albumin is a useful and simple preoperative marker in routine hospital practice. Wound culture status showed the strongest association with graft uptake.[9,10] Culture-positive wounds were present in 61 patients (36.7%) [Table 2]. Poor graft uptake was seen in 29 patients (47.5%) with culture-positive wounds compared with only 12 patients (11.4%) with sterile wounds (Table 4). On multivariable analysis, culture-positive wound was the strongest independent predictor of poor graft uptake, with adjusted OR 5.8 (95% CI 2.35-14.25; p<0.001) [Table 5].

The importance of culture status is supported by previous studies. Hogsberg et al. reported that only 33.3% of ulcers with Pseudomonas aeruginosa healed compared with 73.1% of ulcers without Pseudomonas aeruginosa at 12 weeks.[4] Geethabanu and Vanaja also reported 100% graft uptake in wounds with no bacterial growth, while mean uptake was 68.88% with Pseudomonas aeruginosa and 75.55% with Staphylococcus aureus.[5] These findings support our result that preoperative culture positivity is a major practical risk factor for poor graft uptake. In our study, Pseudomonas aeruginosa was the commonest organism isolated, seen in 35 patients (21.1%) [Table 2]. This is important because Pseudomonas can persist in chronic wounds and interfere with graft take. Culture-guided antibiotic therapy, repeated debridement and grafting only after healthy granulation may improve the final graft result.[11,12] Raised TLC was significantly associated with graft uptake on univariate analysis [Table 4]. Poor uptake was seen in 18 patients (40.9%) with TLC >11,000/mm3. However, it did not remain significant in multivariable analysis [Table 5]. This may be because TLC is a general inflammatory marker and overlaps with wound culture positivity, diabetes and local infection.[6]

Postoperative complications were more common in the poor graft uptake group. Surgical site infection was seen in 14 patients (34.1%) with poor uptake compared with 10 patients (8.0%) with good uptake. Seroma or hematoma was also higher in the poor uptake group. These findings are expected because infection and fluid collection prevent close graft contact and delay revascularisation.[13,14] Negative pressure wound therapy may help in selected wounds, especially large wounds and irregular recipient beds. Lee et al. included 16 randomized trials with 411 patients and 401 controls and reported 8.3% higher overall graft take with NPWT compared

with conventional dressings. They also reported lower graft loss, lower complication rates and lower reoperation rates.[7] However, Mandili et al. found no statistically significant difference between NPWT and conventional dressing in a small prospective observational study of 18 patients.[15] Therefore, NPWT should be used selectively rather than routinely in all cases.

The present study shows that graft uptake is multifactorial. Culture-positive wound, wound size >20 x 10 cm, serum albumin <3.5 g/dL and diabetes mellitus were independent predictors of poor graft uptake [Table 5]. These factors are clinically useful because most of them can be assessed before surgery. Some can also be modified before grafting. This study has some limitations. Graft uptake was assessed only in the early postoperative period. Long-term scar quality, contracture, pigmentation and functional outcome were not assessed. Quantitative bacterial load was not measured. Vascular assessment of lower limb wounds was not done in detail. Despite these limitations the study provides a practical preoperative profile of factors affecting STSG uptake in routine surgical practice.

CONCLUSION

Split thickness skin grafting showed good short-term outcome in most patients with ulcers and raw areas, but poor graft uptake was seen in nearly one-fourth of cases. Culture-positive wound, large wound size, hypoalbuminemia and diabetes mellitus were the main independent predictors of poor graft uptake. These findings suggest that wound culture, wound size assessment, serum albumin and diabetic status should be considered before elective grafting. Proper wound bed preparation, infection control, nutritional optimisation and glycaemic control may improve graft outcome in routine surgical practice.

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