OPEN

PRS GLOBAL OPEN

ORIGINAL ARTICLE
Reconstructive

Development and Validation of Scoring System to Predict Secondary Amputations in Free Flap Reconstruction

Efstathios Karamanos, MD
Hassan Ahmad, MD
Ahmed A. Makhani, BBA
Ameesh N. Dev, BS
Noah Saad, MD
Bao-Quynh Julian, MD
Husain AlQattan, MD
Howard Wang, MD
Douglas Cromack, MD

Background: Need for amputation is a potential complication when limb salvage is attempted. The present study aimed to develop a risk assessment tool to predict the risk of future amputation when counseling patients about their reconstructive options.
Methods: All patients undergoing a free flap lower extremity soft tissue reconstruction by the senior author from 2005 to 2019 were retrospectively identified. Patient's demographics, comorbidities, and technical aspects of the operation were extracted. Logistic regressions were used to create a predictive scoring system for future amputation.
Results: A total of 277 patients were identified. Of these patients, two-thirds (183) were used to derive the scoring system and one-third (94) were used to validate the score. In total, 25 of 183 patients (14%) underwent an amputation. A stepwise forward logistic regression identified age > 55 years, smoking, acute wound, aggressive fluid resuscitation intra-operatively, inability to use a superficial vein for drainage, and inability to use the posterior tibialis artery for anastomosis as independent predictors of need for future amputations. The beta co-efficients were used to create the scoring system, and the patients were categorized into mild, moderate, and severe risk based on their cumulative score. The validity of the scoring system was verified by using the one-third validation cohort.
Conclusions: In patients undergoing free flap reconstruction of the lower extremity, the need for future amputation is 14%. The use of a scoring system can guide the surgeon's and patient's decision regarding limb salvage. *(Plast Reconstr Surg Glob Open 2020;8:e3211; doi: 10.1097/GOX.0000000000003211; Published online 20 November 2020.)*

INTRODUCTION

While lower extremity reconstruction following trauma or chronic osteomyelitis is challenging for the plastic surgeon, it has undergone significant changes during recent decades. Many hospitals are now following a multi-disciplinary approach, while the indications to attempt limb salvage are continuing to broaden. With the advent of microsurgery, more wounds are amenable to reconstruction. After vascular reconstruction and osseous fixation, soft tissue coverage is of outmost importance in acute trauma. Similarly, following adequate irrigation and debridement of chronic wounds, soft tissue coverage is paramount if limb salvage is to be attempted. Despite these modern advances, amputation is still a relatively common outcome and represents an undesirable complication for that group of patients.[1–3]

Several trauma-related scoring systems have been created in an attempt to facilitate with triage and to identify the patients who should undergo immediate amputation versus attempt at salvage.[1,4] However, there are currently no scoring systems to assess the probability of failure of soft tissue coverage following the initial limb stabilization. In addition there is no scoring system to evaluate the probability of success of soft tissue reconstruction in a chronically infected lower extremity. We hypothesized that several factors can create a reliable scoring system that can guide the clinician and the patient in deciding whether soft tissue coverage should be attempted either after initial trauma stabilization or in chronically infected wound in the lower extremity.

From the Division of Plastic and Reconstructive Surgery, Department of Surgery and the Department of Orthopedic Surgery, UT Health San Antonio, San Antonio, Tex.

Received for publication August 6, 2020; accepted September 1, 2020.

DOI: 10.1097/GOX.0000000000003211

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

METHODS

After Institutional Review Board approval, all patients undergoing a free flap reconstruction of the lower extremity from 2005 to 2019 were retrospectively identified. Patients were excluded if they underwent a pedicled flap reconstruction (such as a gastrocnemius or a soleus flap), if they underwent reconstruction of their upper extremity, or if they had missing records. The following variables were extracted: age, gender, race, history of infection, intra-operative findings, and post-operative complications. The follow-up was at least 12 months.

For a confidence interval of 95% and a margin of error of 5%, with a population proportion of the outcome (amputation) estimated at 13% based on previous literature, the sample size needed was 174 patients. The primary outcome was the need for amputation. Secondary outcomes included infectious complications, hospital length of stay, and need for further surgery.

Statistical Analysis

The two groups (need for amputation versus no need for amputation) were compared for differences in their baseline demographics and clinical characteristic, using a univariate analysis. Dichotomous variables were compared using Fisher's exact test or chi-squared test, as appropriate. The continuous variables were examined for normality of distribution using the Shapiro-Wilks test. Normally distributed variables were compared using the Student's *t*-test, while non-normally distributed variables were compared via the Mann-Whitney U test. A forward logistic regression was then performed using the need for amputation as the dependent variable to identify the independent predictors of future amputation. Any of the previously tested variables from the univariate analyses that differed at $P < 0.2$ were included in the regression. A simplified clinical risk assessment tool was derived by assigning point values to the ratios of the regression co-efficients. A composite score was subsequently defined as the summation of these point values. The c-statistic for the model was calculated to assess whether discriminative capacity was preserved.[5–7] Next, to classify the population into different risk categories based on the proposed scoring system, a plot was created for the predicted probability and the score (used as an ordinal variable). Based on the plot, different groups were assigned.

To assess the validity of the model, one-third of the study (which was previously separated from the analysis) was used. The score was calculated for each patient and a multivariate logistic regression was performed, with the dependent variable being the need for amputation. Adjusted odds ratios (AOR) with 95% confidence intervals (95% CI) were derived for each risk assessment group based on the scoring system.

RESULTS

During the study period a total of 277 patients were identified. Of these patients, 183 (2/3) were used for the derivation of the scoring system, while the remaining 94 (1/3) were used to validate the score. The mean age of the study group was 42, while 32% were men. The majority of the flaps were muscle flaps (60%) and the mean dimension was 24 cm (Table 1). Diabetes mellitus was present in 27% of the patients, while active smokers were 43%. Acute wounds accounted for 59% of the cases, while the mean operative time was 568 minutes. A total of 11% of the patients had an occlusion of their posterior tibialis (PT) artery due to peripheral vascular disease, necessitating the use of the peroneal artery or the anterior tibialis as the recipient vessels for microsurgical anastomosis (Table 1).

Table 2 depicts the results of the multivariate analysis to predict future amputation. Older age (>55 years), not using the great saphenous vein (GSV) as an outflow, occlusion of PT, presence of an acute wound, liberal intra-operative fluid administration (>7 ml/kg/hour), a history of previous infection, and smoking status all predicted the need for future amputation. The adjusted odds ratios and the regression co-efficients are depicted in Table 2.

Table 1. Demographics and Clinical Characteristics

	No Amputation (n = 161)	Amputation (n = 22)	Overall (n = 183)	*P*
Age (y)	41 ± 15	52 ± 16	42 ± 16	0.003
Age > 55 y	35 (21.7)	13 (59.1)	48 (26.2)	<0.001
Male gender	51 (31.7)	7 (31.8)	58 (31.7)	1
Type of flap				
Perforator	67 (41.6)	8 (36.4)	75 (41.0)	0.818
Muscle	94 (58.4)	14 (63.6)	108 (59.0)	0.818
Biggest flap dimension (cm)	23 ± 9	25 ± 10	24 ± 10	0.494
No. anastomosed veins				
1	90 (55.9)	15 (68.2)	105 (57.4)	0.36
2	71 (44.1)	7 (31.8)	78 (42.6)	0.36
GSV used for venous outflow	39 (24.2)	1 (4.5)	40 (21.9)	0.036
Co-morbidities				
Diabetes mellitus	41 (25.5)	9 (40.9)	50 (27.3)	0.134
Smoking	66 (41.0)	13 (59.1)	79 (43.2)	0.108
Type of wound				
Acute	91 (56.5)	16 (72.7)	107 (58.5)	0.148
Chronic	70 (43.5)	6 (27.3)	76 (41.5)	0.148
Occlusion of posterior tibialis artery	12 (7.4)	8 (36.3)	20 (10.9)	0.008
Arterial reconstruction	38 (23.6)	5 (22.7)	43 (23.5)	0.742
Intra-operative fluid administration > 7 ml/kg/h	76 (47.2)	18 (81.8)	94 (51.4)	0.002
Operative time (min)	563 ± 182	605 ± 220	568 ± 187	0.315
History of previous infection	29 (18.0)	8 (36.4)	37 (20.2)	0.044

Table 2. Multivariate Analysis for Need for Future Amputation

Variable	AOR (95% CI)	Cumulative R^2	Adjusted *P*	Co-efficient
Age > 55 y	6.52 (1.81, 23.74)	0.342	0.003	1.8
GSV not used for venous outflow	10.09 (1.23, 13.21)	0.531	0.009	4.2
Occlusion of posterior tibialis artery	12.76 (2.29, 17.25)	0.629	0.004	5.4
Acute wound	4.76 (1.13, 16.12)	0.683	0.048	1.7
Intra-operative fluid administration > 7 ml/kg/h	8.05 (1.77, 12.56)	0.699	0.007	3.1
History of previous infection	1.61 (1.05, 2.34)	0.705	0.047	1.2
Smoking	2.16 (1.57, 8.20)	0.708	0.043	1.6

Other variables entered in the model: Diabetes. Area Under the Curve (AUC) (95% CI): 0.964 (0.933, 0.976).

Based on the regression co-efficients, the scoring system to predict the need for future amputation was calculated. History of previous infection resulted in a 1-point addition to the score. Advanced age, smoking status. and presence of an acute wound, all resulted in a 2-point addition. Liberal fluid resuscitation added 3 points, not being able to use the GSV as an outflow added 4 points, and finally, occlusion of the PT due to peripheral vascular disease added an additional 5 points (Table 3). Three categories were then derived based on the predictive model of the cumulative score: mild risk: 1–6 points, moderate risk: 7–11 points, and severe risk: 12–19 points (Fig. 1). The predicted probability of need for future amputation was calculated for each category from the previously performed regression (17%, 29%, and 54% respectively; Table 3, Fig. 1, and Fig. 2).

For assessment of the applicability of the scoring system, the study population was divided into four categories and the probability of need for future amputation was calculated for each group using the AOR (95% CI) that was derived from the multivariate analysis. The process was performed for both the derivation and the validation cohort (Table 4).

Table 5 shows the impact on hospital resources of those patients that ended up needing a future amputation. Patients that needed an amputation were more likely to require multiple readmissions, multiple returns to the OR, and had a significantly longer cumulative length of stay (Table 5) compared with their counterparts.

DISCUSSION

In this study, we used retrospective data on patients undergoing free flap reconstruction of the lower extremity for both traumatic injuries and chronic wounds to create a risk assessment scale to help surgeons identify patients that would be at risk for future amputation. The developed scale identified 7 important patient and clinical factors (age > 55 years, smoking, a history of prior infection, presence of an acute wound, liberal intraoperative fluid resuscitation, a lack of greater saphenous vein for drainage, and the inability to use the tibialis artery for reconstruction) as independent risk factors for prediction. Our efforts to verify the validity of our data denotes the utility of the development and use of such models to predict and guide outcomes.

Clinical risk calculators such as the Mangled Extremity Score (MESS), the Predictive Salvage Index, Limb Salvage Index, and the Nerve Injury, Soft tissue, Skeletal Injury, Shock, and Age of patient (NISSSA) scores have been widely used to delineate lower extremity limb salvage operations versus a primary amputation.[1] Although prospective evaluation of these studies has shown high specificity[2] for the prediction of limb salvage, to date there are no reports in the literature describing a risk assessment tool to predict secondary amputation following initial lower extremity reconstruction for traumatic injury or in the setting of chronic wounds. Our study is the first to categorize the variables that would influence this outcome and may guide surgical decision-making.

Our scoring system assigns a value of 2 points for age > 55 years, smoking status, and presence of an acute wound, 3 points for aggressive intraoperative fluid administration (>7 ml/kg), 4 points for patients who did not have GSV used as an outflow, and 5 points for the occlusion of the posterior tibialis artery. The correlation between these variables and outcomes can be supported by the current literature, and is consistent with the notion that flap survivability is dependent on factors that influence the balance of tissue perfusion.

A 10-year review of lower extremity flap revision identified advanced age as a risk factor in flap failure, suggesting the correlation was due to decreased ischemia tolerance in this population.[3,8] Advanced age was identified as a component of both the MESS and NISSSA models as well as the Mangled Upper Extremity Score (age > 40 years) as a correlative factor for failed upper extremity salvage.[9,10] Though none of the above-mentioned models identified smoking status as an independent risk factor, the deleterious effects of smoking on subcutaneous tissue oxygenation as well as nicotine-induced vasoconstriction contributing to flap failure is well documented.[7,11]

Table 3. Scoring System for Predicting Future Amputation

Variable	Points	Classification
History of previous infection	1	
Age > 55 y	2	
Smoking	2	Mild risk: 1–6, probability: 17%
Acute wound	2	Moderate risk: 7–11, probability: 29%
Intra-operative fluid administration > 7 ml/kg/h	3	Severe risk: 12–19, probability: 54%
GSV not used for venous outflow	4	
Occlusion of posterior tibialis artery	5	

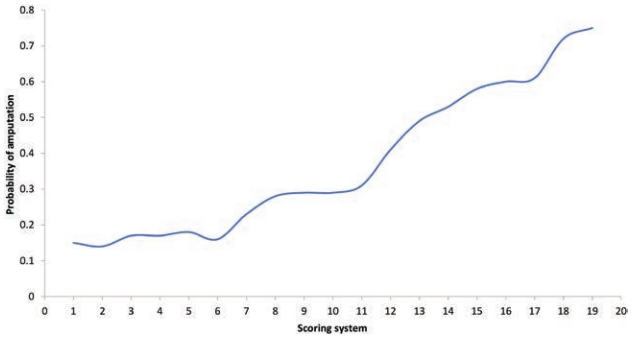

Fig. 1. Probability of amputation based on the scoring system.

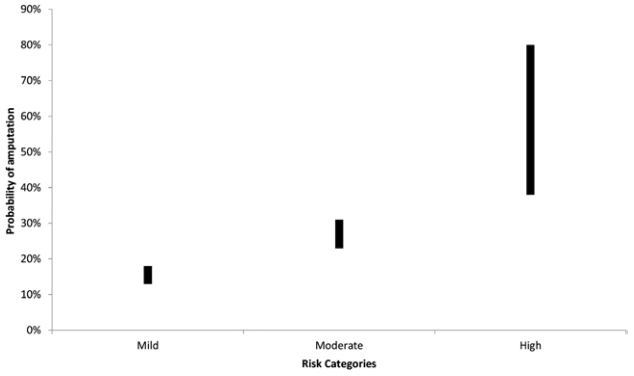

Fig. 2. Probability of amputation based on risk categories.

While current data comparing the influence of acute versus chronic wound classification in associated lower extremity flap failure are limited, traumatic injuries are well known to be associated with a tissue injury and inflammatory cascade. This entails hypercoagulability and acute blood loss, both of which are known to be correlative with flap loss.[8] Similar to this, aggressive fluid administration leading to flap edema, inappropriate venous outflow, and the presence of atherosclerotic calcifications and peripheral vascular disease have all been described as risk factors for flap loss in reconstruction.[8,12] A review detailing lower extremity traumatic injury patterns and their reconstructive outcomes noted the higher incidence of anterior tibialis artery injury and subsequent use of the PT as the predominant recipient vessel in all flap classifications for reconstruction.[13] This suggests the critical role of identifying a nonviable PT in predicting outcomes. This particular finding and the degree of 3 vessel run off were identified most recently in a retrospective study looking at factors influencing secondary amputation following salvage for traumatic injury, by Piwnica-Worms et al.[14]. It is worth noting that this study had a smaller population (129 versus 277 in the present study) and did not attempt to create a scoring system. Of note, although diabetes was a finding of significance in their assessment, we did not include diabetes in our risk assessment score because it was not independently associated with a need of amputation in our study population.[14] The current data regarding diabetes mellitus vary in the literature. In an analysis of free flap failure for traumatic injuries to the lower extremity, Las et al found diabetes to be an independent risk factor, while noting that this was not consistent in the trauma literature otherwise.[15] Similarly, variable findings are noted in the literature regarding the associated risk of secondary amputation following limb salvage for chronic wounds.[12,16]

The presence of this variability highlights the potential limitations and preclusions to generalizability of our scoring system. Our analysis is retrospective and is limited as such. A single surgeon experience entails technical variables that may skew our results. Although our study did categorize acute wounds versus those that were chronic, it includes a model that identifies the risk for secondary amputation following reconstruction for acute traumatic injury as well as reconstruction for a chronic wound. Larger studies may elucidate a model that identifies the risk for the 2 groups separately.

It should be noted that the utility of the scoring systems that delineates primary lower extremity limb salvage operations versus an amputation such as the MESS has been repeatedly called into question.[3,4] This has prompted a number of inquiries that continue to evaluate the validity of such scores, and in turn have incited even more specific questions and studies about this topic, including the development of our own model. In the proper perspective, this can be understood simply as the need for further data collection and persistent revision.

CONCLUSIONS

In patients undergoing free flap reconstruction of the lower extremity, the need for future amputation is significant. We created a risk assessment model that categorized variables that are independent risk factors for this outcome. Our work highlights the impact on resources, variation in current data, and potential utility of such a model. Future studies and development of a scoring system can guide the surgeon's and patient's decision regarding limb salvage.

Efstathios Karamanos, MD
Division of Plastic and Reconstructive Surgery
Department of Surgery
UT Health San Antonio
7703 Floyd Curl Drive
San Antonio, TX
E-mail: ef.karamanos@gmail.com

REFERENCES

1. Schirò GR, Sessa S, Piccioli A, et al. Primary amputation vs limb salvage in mangled extremity: a systematic review of the current scoring system. *BMC Musculoskelet Disord.* 2015;16:372.
2. Shanmuganathan R. The utility of scores in the decision to salvage or amputation in severely injured limbs. *Indian J Orthop.* 2008;42:368–376.
3. Wettstein R, Schürch R, Banic A, et al. Review of 197 consecutive free flap reconstructions in the lower extremity. *J Plast Reconstr Aesthet Surg.* 2008;61:772–776.
4. Loja MN, Sammann A, DuBose J, et al; AAST PROOVIT Study Group. The mangled extremity score and amputation: time for a revision. *J Trauma Acute Care Surg.* 2017;82:518–523.
5. Chien TL, Hsiao FY, Chen LJ, et al. Development and validation of a risk scoring system for cephamycin-associated hemorrhagic events. *Sci Rep.* 2019;9:12905.

Table 4. Probability of Amputation Stratified by Scoring System

Score	Derivation Cohort [AOR (95% CI)]	Validation Cohort [AOR (95% CI)]
0 (reference)	Reference	Reference
1–6	1.56 (1.23, 4.35)	1.52 (1.11, 5.85)
7–11	2.32 (1.51 (7.12)	3.11 (1.78, 7.55)
12–19	5.21 (2.06, 7.23)	4.57 (2.31, 10.43)

Table 5. Impact of Future Need for Amputation on Hospital Resources

	No Amputation (n = 161)	Amputation (n = 22)	Overall (n = 183)	*P*
Readmission				
0	26 (16.1)	0 (0.0)	26 (14.2)	
1	81 (50.3)	4 (18.2)	85 (46.4)	
2	17 (10.6)	2 (9.1)	19 (10.4)	
3	33 (20.5)	5 (22.7)	38 (20.8)	
4	2 (1.2)	3 (13.6)	5 (2.7)	
>4	2 (1.2)	8 (36.4)	10 (5.5)	<0.001
Return to the OR				
0	54 (33.5)	0 (0.0)	54 (29.5)	
1	51 (31.7)	3 (13.6)	54 (2.5)	
2	37 (23.0)	4 (18.2)	44 (22.4)	
3	18 (11.2)	9 (40.9)	27 (14.8)	
>3	1 (0.6)	6 (27.3)	7 (3.8)	<0.001
Cumulative length of stay	18.5 ± 5.5	32.1 ± 12.5	20.1 ± 8	<0.001

6. Karamanos E, Gupta AH, Stanton CN, et al. Clostridium difficile-associated infection in trauma patients: development of the clostridium difficile influencing factors (CDIF) score. *Perm J.* 2018;22:18–013.
7. Karamanos E, Kandagatla P, Watson J et al. Development and validation of a scoring system to predict surgical site infection after ventral hernia repair: a Michigan surgical quality collaborative study. *World J Surg.* 2017;41:914–918.
8. Stepanovs J, Ozoliņa A, Rovīte V, et al. Factors affecting the risk of free flap failure in microvascular surgery. *Proc Latv Acad Sci B Nat Exact Appl Sci.* 2015;70:356–364.
9. Johansen K, Hansen ST. MESS (Mangled Extremity Severity Score) 25 years on. *J Trauma Acute Care Surg.* 2015;79:495–496.
10. Savetsky IL, Aschen SZ, Salibian AA, et al. A novel mangled upper extremity injury assessment score. *Plast Reconstr Surg Glob Open.* 2019;7:e2449.
11. Hwang K, Son JS, Ryu WK. Smoking and flap survival. *Plast Surg (Oakv).* 2018;26:280–285.
12. Wirth P, Schwitzer JA, Kotha VS, et al. Risk factors for amputation following lower extremity free tissue transfer in a chronic wound population. *Plast Reconstr Surg Glob Open.* 2019;7:84–85.
13. Haddock NT, Weichman KE, Reformat DD, et al. Lower extremity arterial injury patterns and reconstructive outcomes in patients with severe lower extremity trauma: a 26-year review. *J Am Coll Surg.* 2010;210:66–72.
14. Piwnica-Worms W, Stranix JT, Othman S, et al. Risk factors for lower extremity amputation following attempted free flap limb salvage. *J Reconstr Microsurg.* 2020;36:528–533.
15. Las DE, de Jong T, Zuidam JM, et al. Identification of independent risk factors for flap failure: a retrospective analysis of 1530 free flaps for breast, head and neck and extremity reconstruction. *J Plast Reconstr Aesthet Surg.* 2016;69:894–906.
16. Schwitzer JA, Janhofer DE, Lakhiani C, et al. Risk factors for amputation following lower extremity free tissue transfer. *Plast Reconstr Surg Glob Open.* 2018;6:69–70.