Title

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Journal

Journal of Hand and Microsurgery, 10(02)

ISSN

0974-3227

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Publication Date

2018-08-01

DOI

10.1055/s-0038-1626689

Predictors of Digit Survival following Replantation: Quantitative Review and Meta-Analysis

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J Hand Microsurg 2018;10:66–73

Abstract

Introduction Microsurgical replantation following digital amputation has variable success rates. Sociodemographic factors and surgery-related variables have been shown to influence survival rates; however, few studies have evaluated these data systematically across a combined dataset. Therefore, the objective of this study was to analyze the current literature to identify the predictors of replant survival.

Materials and Methods A literature review was performed using the PubMed/Medline database focused on complete digit amputation/replantation studies. Studies were evaluated for patient and surgery-related variables and their respective effects on survival. Statistical analysis was conducted to identify predictors of survival and derive pooled estimates from the combined dataset.

Results Thirty-two studies representing more than 6,000 digit amputation/replantation cases met inclusion/exclusion criteria. Statistical analysis revealed the number of venous anastomosis (0 vs. 1 vs. 2), the number of arterial anastomosis (0 vs. 1 vs. 2), and the mechanism of injury (sharp cut versus blunt cut versus avulsion versus crush) to influence replant survival ($p < 0.05$). The authors failed to find a significant association between survival and the following variables: age, sex, zone of injury, digit number, tobacco use, ischemia time, method of preservation, and use of vein graft.

Conclusion Patient- and surgery-related variables affect digit survival following replantation. The etiology of injury can help risk-stratify patients and assist in an informed decision making process, whereas surgery-related factors can guide surgeon practice to improve clinical outcomes following replantation.

Keywords
- amputation
- digit survival
- microsurgical replantation

Introduction

Digital amputation is a devastating injury and one that affects approximately 45,000 patients in the United States every year.[1] Studies have shown that amputations lead to a decreased quality of life due to the physical, psychological, and financial hardships.[2,3] Microsurgical replantation, however, affords the ability to restore hand function and is attempted under defined indications. Though advances in medicine, improved technology, and identification of prognostics factors have improved results, survival rates continue to vary ranging between 48 and 97%.[4,5]

Predicting success in replant surgery remains a challenging obstacle. To date, numerous authors have studied replant medicine and identified a host of sociodemographic, surgery-related, and injury-related factors influencing digit replant survival. These have included the following: (1) age, (2) sex, (3) zone of injury, (4) digit number, (5) tobacco use, (6) ischemia time, (7) method of preservation, (8) use of vein graft, (9) number of venous/arterial anastomoses, and (10) mechanism of injury.[4,6–9] With the increased quantity of published data and often conflicting results, interpreting the predictors of replant survival has become difficult. Further, few studies to date have analyzed this vast dataset systematically to draw generalized conclusions.

received October 1, 2017
accepted after revision December 2, 2017
published online March 20, 2018

DOI https://doi.org/10.1055/s-0038-1626689.
ISSN 0974-3227.

To date, the predictors of replant survival have yet to be clearly elucidated. Previous meta-analysis studies are limited, and most focus either on distal tip amputations or on patient related variables (vs. surgery-related variables) and often include incomplete amputations.[6,7,10] Therefore, the aim of the this study was to review the current literature and conduct a quantitative statistical analysis to determine which patient- and surgery-related factors predict survival after complete digit amputation. The authors hope that this analysis will provide data to help surgeons risk-stratify replant candidates, manage patient expectations, and improve guidelines for surgical decision making.

Materials and Methods

Search Methodology and Results

The authors performed a literature search using PubMed/Medline databases. The following keywords were used in this search: "finger," "digit," "thumb," "hand," "replant survival," "replantation," "amputation," and "survival." The authors used MeSH terms and keywords and the Boolean operators "AND" and "OR" to create a combined set for the search. Databases were evaluated for all years of publications until 2016 and were last accessed on January 2017. Contact with study authors was attempted, but it did not yield additional data. As shown in ►**Fig. 1**, 1,086 studies were identified from PubMed/Medline database search. Removal of duplicates yielded 644 studies eligible for subsequent screening. Next, 531 studies were excluded based on the described inclusion/exclusion criteria and another 81 studies were excluded due to incomplete data or consolidated data that could not be statistically analyzed. This yielded 32 studies that were ultimately included in this final analysis.

Inclusion/Exclusion Criteria

Inclusion/exclusion criteria were set to identify quality studies of a specific replant population. Inclusion criteria included the following: studies representing prospective or retrospective analyses, studies detailing treatment protocols with survival rates, and studies presenting individual patient data (to be pooled for analysis). The authors then focused their search to include human subjects (versus animal models) representing all age groups that had complete digital amputations (vs. partial amputations or upper extremity amputations). Exclusion criteria included the following: studies combining partial and complete replant data, studies evaluating revascularization data alone, studies with insufficient sample size (i.e., case studies/series/$n < 5$), and studies representing reviews/meta-analyses. If studies additionally included partial amputation/replantation data or amputations proximal to the digit, the data were stratified to include only cases that met the inclusion/exclusion criteria.

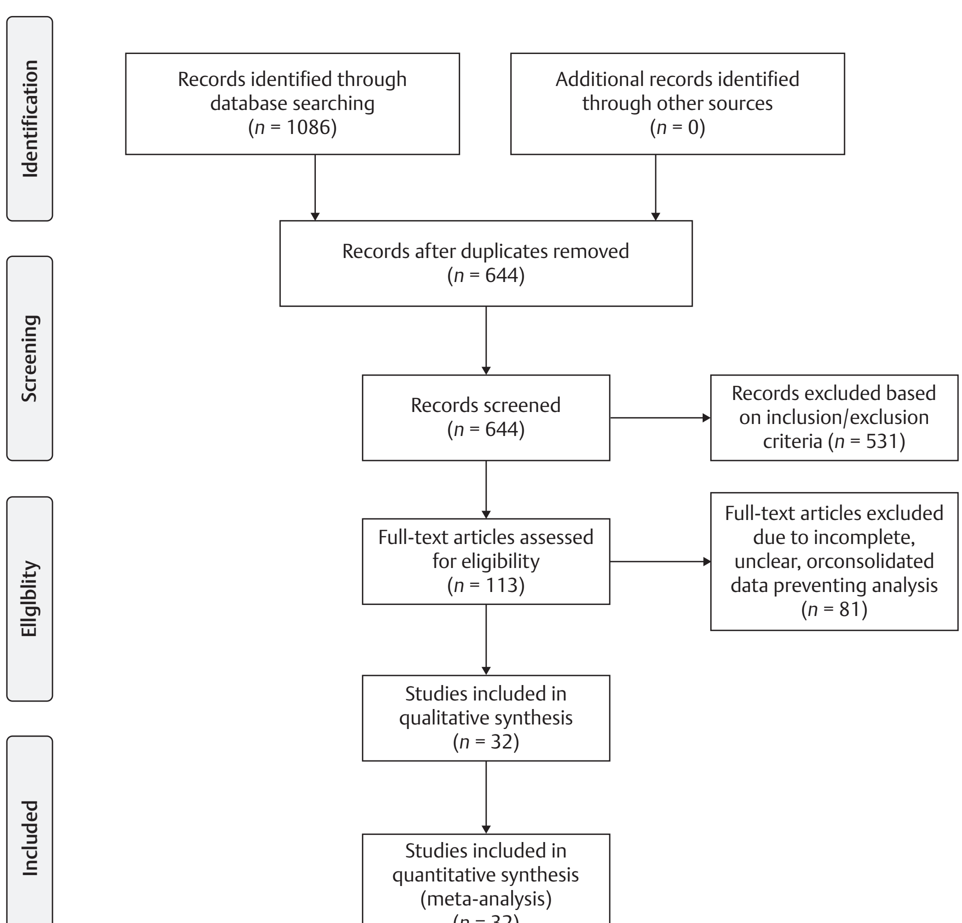

Fig. 1 Study selection process.

Data Extraction and Statistical Analysis

Studies fulfilling inclusion/exclusion criteria were evaluated for patient- and surgery-related factors relating to digit survival. Patient-related variables included age, sex, mechanism of injury, zone of injury, specific digit injured, whether single or multiple digits were amputated, and tobacco use. Surgery-related variables included ischemia time, number of arterial anastomoses, number of venous anastomoses, use of vein graft, and method of preservation. Data collection was verified independently by two authors for accuracy. Data were pooled across the different studies and incorporated into statistical analysis. Summary statistics using Student's *t*-test, analysis of variance (ANOVA), and chi-square tests were used where appropriate to evaluate outcomes between treatment groups. Statistical significance was set with $p < 0.05$, with all tests two sided.

This study was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[11]

Results

The current analysis included 32 studies representing more than 6,000 digital replants. Study characteristics are summarized in ►**Table 1**. Digit replant survival rate ranged from 48 to 97% across all studies. Studies were most commonly published between years 2000 and 2016 but ranged from 1985 to 2016. Studies were most commonly published in the United States or an Asian country and included data from the following geographical regions: Brazil, China, Greece, India, Italy, Japan, Korea, Taiwan, United Kingdom, and United States (California, Connecticut, Kentucky, Massachusetts, Missouri, Ohio, North Carolina). When the authors stratified for practice type, they found that 26 studies represented the university hospital setting, five studies represented general hospital practice setting, and one study evaluated the NIS (National [Nationwide] Inpatient Sample) national database comprising both general and university setting practices.

The impact of patient- and surgery-related factors on replant survival after statistical analysis is shown in ►**Tables 2 and**► **3**. Here, the authors found (1) the number of arterial anastomoses, (2) number of venous anastomoses, and (3) mechanism of injury to predict digit survival following replantation ($p < 0.05$). When the authors explored the role of arterial anastomoses in replantation, they found that 14 studies[12–25] evaluated the relationship between arterial anastomoses and replant survival. After analyzing the pooled dataset, the authors found a significant difference in survival rates for digits replanted with zero versus one versus two arterial anastomoses ($p < 0.05$). They found digit replant survival rates of 50.3% with zero arterial anastomosis, 84.2% with one arterial anastomosis, and 90.0% with two arterial anastomoses (►**Fig. 2**). Survival in the "zero anastomosis" group most commonly represented distal fingertip and pediatric amputations. Few studies documented the need for intraoperative arterial revision or their technique for arterial anastomosis. Though few studies have shown digit survival without arterial anastomoses, improved survival rates can be achieved with increased number of anastomoses.

To evaluate the need for adequate venous drainage in replanted digits, the authors evaluated the relationship between venous anastomoses and replant survival. Here, the authors analyzed 14 studies[12,14–22,24–27] that explored the relationship between venous anastomoses and replant survival. After conducting statistical analysis, they found a significant difference in survival for digits replanted with zero versus one versus two anastomoses ($p < 0.05$). The authors found 61.1% survival rates for digits replanted with zero venous anastomosis, 73% for those with one venous anastomosis, and 92.3% with two venous anastomoses (►**Fig. 3**). Several studies evaluated survival following three venous anastomoses replants; however, the sample size was too limited to generalize conclusions. Similarly, too few studies stratified for type of venous anastomosis (suture vs. coupler). Ultimately, though nonanastomoses techniques (i.e., leeches, heparinization, etc.) and dermal/subdermal plexus can provide a level of venous drainage, survival rates are improved with increased number of venous anastomoses.

Next, the authors explored the relationship between the etiology of amputation (sharp cut, blunt cut, avulsion, crush mechanisms) and survival rates following replantation. They pooled data from 20 studies,[4,13,15-17,19-22,25,27-36] and after conducting this statistical analysis, they found the mechanism of injury to predict replant survival ($p < 0.05$). They found a significant difference in survival rates across the mechanisms of injury with sharp lacerating injuries having the highest rates of survival (87.2%), followed by blunt lacerating injuries (83.0%), avulsion injuries (71.2%), and crush injuries (69.4%) (►**Fig. 4**). Too few studies stratified for severity of injury or other concomitant life-threatening injuries that may have influenced replant survival. The mechanism of injury can relate with severity of injury during amputation and influences survival rates following replantation.

Statistical analysis revealed that the following variables failed to influence replant survival: age, sex, zone of injury, digit number, tobacco use, ischemia time, method of preservation, and use of vein graft. The authors found that 19 studies evaluated the role of sex and survival,[4,12,13,15-17,20-22,24,25,27-30,32,34,35,37] 13 studies evaluated the zone of injury,[13,15-18,21,23,26,27,33,34,36,38] 15 studies evaluated digit number,[4,13,15,17,20-22,24,29,32,33,35,39-41] 5 studies evaluated tobacco use,[4,13,15,22,34] 2 studies evaluated ischemia time,[13,32] 2 studies evaluated method of preservation,[15,34] and 6 studies evaluated the use of vein grafting.[12,13,15,17,20,24] Despite several individual studies finding statistically significant correlations between these variables and replant survival, these variables did not maintain significance when evaluated across the pooled dataset ($p > 0.05$). Several studies presented conflicting data whereas others presented nonsignificant data that ultimately negated significance on statistical testing.

Discussion

In this study, the authors performed a review of the literature and quantitative systematic analysis evaluating the risk factors for survival following digit replantation. Here, they found the number of venous anastomosis, the number of

Table 1 Study characteristics

Study	Year	Location	Setting	Survival rate (%)
Adani et al[12]	2013	Italy	University	88
Baker and Kleinert[17]	1994	United States (Kentucky)	University	69
Berlin et al[39]	2014	United States (Connecticut)	Nat'l database	73
Breahna et al[33]	2016	United Kingdom	General hospital	70
Chai et al[28]	2008	China	University	92
Chen et al[29]	2013	Taiwan	University	90
Chen et al[30]	2014	Taiwan	University	92
Cheng et al[5]	1985	China	General hospital	97
Fufa et al[13]	2013	United States (Missouri, Ohio)	University	57
Goldner et al[20]	1989	United States (North Carolina)	University	81
Gordon et al[35]	1985	United States (California)	University	71
Hattori et al[21]	2003	Japan	University	86
Heistein and Cook[34]	2003	United States (Ohio)	University	53[a]
Hirase[23]	1997	Japan	University	92
Huang and Yeong[14]	2015	Taiwan	University	81
Ito et al[26]	2010	Japan	University	87
Kim et al[31]	1996	Korea	University	78
Koshima et al[24]	2005	Japan	University	81[a]
Lee et al[38]	2000	Korea	University	77
Li et al[15]	2008	China	University	82
Lin et al[37]	2010	Taiwan	University	68
Lin et al[25]	2004	Taiwan	University	94
Malizos et al[27]	1994	Greece	University	83
Matsuda et al[18]	1993	Japan	General hospital	75[a]
Mulders et al[4]	2013	United States (Massachusetts)	University	48[a]
Shi et al[49]	2010	China	University	91
Urbaniak et al[19]	1985	United States (North Carolina)	University	86
Venkatramani and Sabapathy[16]	2011	India	General hospital	88
Woo et al[32]	2015	Korea	General hospital	86[a]
Yamano[36]	1993	Japan	University	80
Yin et al[22]	2015	China	University	87
Zumiotti and Ferreira[41]	1994	Brazil	University	70

[a] Represent study survival rates after excluding incomplete amputation/revascularization cases (Koshima et al[24] and Mulders et al[4]) and excluding amputations proximal to MCPJ (Matsuda et al[18], Woo et al,[32] and Lin et al[37]).

arterial anastomosis, and the mechanism of injury to predict replant survival. They failed to find a significant association between survival and the following variables: age, sex, zone of injury, digit number, tobacco use, ischemia time, method of preservation, and use of vein graft. Taking all these data together, this study identifies both significant and nonsignificant variables in replant survival that can be used to improve patient outcomes.

Adequate arterial inflow is necessary to avoid ischemia. In this study, the authors found number of arterial anastomosis to predict survival. This likely represents the need for adequate arterial inflow necessary to meet the metabolic demands of the amputated segment.[9] Studies suggest that adequate capillary perfusion pressures are necessary for tissue viability and thus the necessity of restoring arterial inflow. Furthermore, the results support traditional opinion that suggest that one arterial anastomosis is necessary for replant survival, but two anastomoses can improve survival rates.[42] Several authors have reported survival rates without arterial anastomosis, however, these results primarily

Table 2 Quantitative analysis of patient-related factors on replant survival

Factor	Studies	Comparison	OR	*p*-Value
Age	14	Child vs. adult	0.81	NS
Sex	19	Male vs. female	1.02	NS
Mechanism of injury	20	Sharp cut	Ref	< 0.05
		Blunt cut	0.95	
		Avulsion	0.82	
		Crush	0.80	
Digit number	15	Thumb	Ref	NS
		Index	0.94	
		Middle	1.00	
		Ring	1.01	
		Small	0.93	
Zone of injury	13	Tamai zones:		NS
		I	Ref	
		II	1.01	
		III	0.87	
		IV	0.99	
Tobacco use	5	Tobacco use vs. no tobacco	0.80	NS
Ischemia time	2	< 6 h	Ref	NS
		6–10 h	1.49	
		> 10 h	1.34	
Method of preservation	2	Cold vs. warm/room temperature	0.94	NS

Abbreviations: NS, not significant; OR, odds ratio.

Table 3 Quantitative analysis of surgery-related factors on replant survival

Factor	Studies	Comparison	OR	*p*-Value
No. of arterial anastomosis	14	0	Ref	< 0.05
		1	1.67	
		2	1.79	
No. of venous anastomosis	14	0	Ref	< 0.05
		1	1.19	
		2	1.51	
Vein graft	6	Graft vs. no graft	0.99	NS

Abbreviations: NS, not significant; OR, odds ratio.

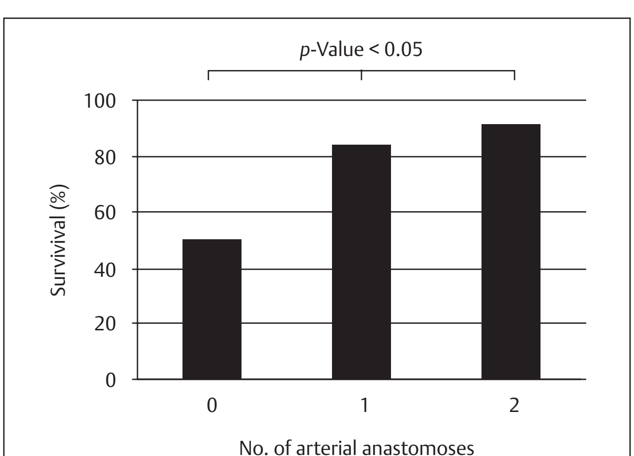

Fig. 2 Effect of arterial anastomoses on survival.

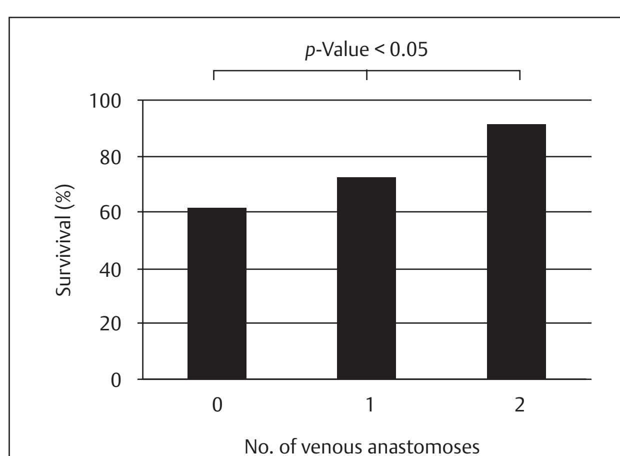

Fig. 3 Effect of venous anastomoses on survival.

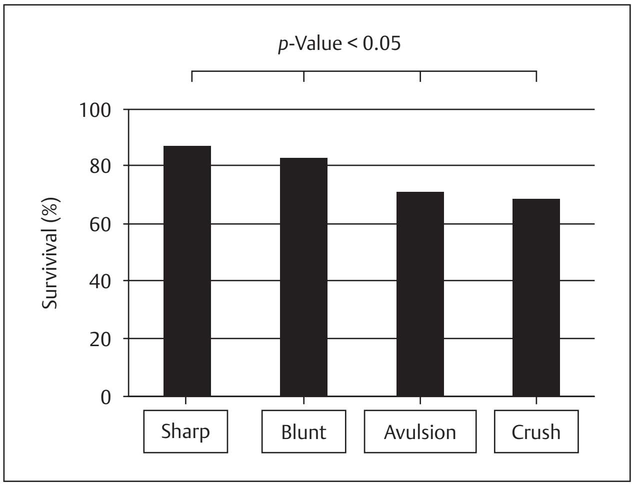

Fig. 4 Effect of mechanism of injury on survival.

represent amputations in the pediatric population or distal fingertip amputations.[16,23] Ultimately, arterial inflow is necessary for replant survival wherein surgeons can improve survival rates intraoperatively by increasing the number of arterial anastomoses.

Venous congestion results from inadequate venous outflow and is commonly encountered following tissue replantation when venous anastomosis may not be technically possible (i.e., ear, lips).[43-45] In this study, the authors found the number of venous anastomosis to predict replant survival. This likely represents the need for adequate venous drainage to prevent venous congestion and subsequent edema, increased interstitial space pressures, arterial insufficiency, and the accumulation of metabolites.[46,47] Though medical leech application, arteriovenous anastomosis, and local heparin administration can improve venous insufficiency,[10] formal venous anastomoses should be prioritized. These data are further supported by the partial amputation/revascularization data that suggest skin bridges may not provide adequate venous outflow and necessitate formal venous anastomoses.[48] To this end, survival of a replanted digit can be optimized intraoperatively by increasing the number of venous anastomoses.

The mechanism of injury often gives insight into the severity of tissue damage in surgical/trauma patients. In this study, the authors found the mechanism of injury to predict survival with sharp and blunt lacerating injuries having higher survival rates than crush/avulsion injuries. The mechanism of injury likely affects replant survival through its effects on the vasculature. The rotational stretching, crushing, and tearing components characteristic of avulsion and crush injuries lead to a larger zone of injury and more severe vessel damage.[9,17] Damaged vessel endothelium and trauma-related contusion of the microvasculature increase the risk for thrombosis and subsequent replant failure.[9,17] The more frequent use of vein grafts in avulsion and crush injuries to circumvent the zone of injury has been cited by the authors as contributing to higher rates of success with these injuries.[8] Lacerating injuries, in contrast, have minimal soft tissue damage and a defined zone of vessel injury that does not extend greatly beyond the laceration itself. As such, survival rates for lacerating injuries are improved. Ultimately, the mechanisms of injury correlate with vessel injury and subsequent replant failure and can be a prognostic factor to help educate patients and improve the patient-physician decision-making process.

Several variables were reported to correlate with survival in the literature; however, they did not maintain significance after this systematic analysis. These variables included age, sex, zone of injury, digit number, tobacco use, ischemia time, method of preservation, and the use of vein grafts. Though many of these variables have physiologic reasons to explain a relationship with survival, they failed to reach statistical significance when analyzing the pooled dataset. This likely represents the lack of a significant relationship with survival and conflicting data across studies. It may also, in part, reflect underpowered statistics for a given variable (i.e., zone of injury) or the nonuniform categorization of variables across studies precluding pooled analyses (i.e., ischemia times). Ultimately, additional research is necessary to evaluate further the role of these variables in replant survival.

This study has several limitations. First, it represents a review of retrospective studies and risks of unmeasured and unaccounted bias. A comprehensive review of literature was performed; however, this study risks incomplete retrieval of identified research and reporting biases of published data. This study included studies from various time periods and countries that may influence the standard of practice. Next, this study was unable to address the role of surgical skill or years of experience in replantation, which can affect success rates. Furthermore, there is significant variability in the method of data collection as various descriptors were not standardized (i.e., different descriptors for zone of injury, different ischemia time intervals). This variability decreases the sample size and may underscore otherwise significant associations. Last, though the data evaluated replant survival, the authors did not evaluate or correlate quality of hand function in these replanted patients.

The significant variables identified in this study can be used to help guide surgeon practice and guide patient decision-making. They can be used in preoperative patient counseling and risk stratification, as well as influence intraoperative proficiency. Additional research and data are needed in the field of replant medicine to better characterize the predictors of survival and functional outcomes following replant. The authors hope that, with additional data and advancing technology, rates of digit replant can be improved and standardized across different injury patterns and patient presentations.

Conclusion

Digital amputation is a debilitating injury and one that has variable rates of survival following replantation. This systematic review of the literature and quantitative statistical analysis showed the number of arterial anastomoses, number of venous anastomoses, and mechanisms of injury to predict replant survival following digit amputation. Though additional research is needed, the authors feel these data can be used to help guide surgeon practice and provide prognostic data to assist further in the physician-patient decision-making process.

Conflict of Interest
None.

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