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Original Research

Pre-injury level of anxiety is associated with the rate of digit replant failure: A prospective cohort study

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ABSTRACT

Background: Previous studies have demonstrated that age, smoking, Tamai's level of amputation, causes of injury and ischemia time were associated with the success rate of digit replantation. The primary objective of this study is to investigate whether mental status including anxiety and depression is associated with the rate of digit replant failure.

Methods: This study included 134 digits from 102 patients who received digital replantation after complete amputation from 1 September 2013 to 1 September 2015. The Zung self-rating anxiety scale (SAS) and the Zung self-rating depression scale (SDS) were used to assess the pre-injury level of anxiety and depression for each patient. All participants were followed up for at least 1 month. Failure was defined as necrosis of replanted finger which required revision amputation or flap cover of the skeleton.

Results: Multivariate logistic regression analysis showed that increased level of pre-injury anxiety was an independent risk factor correlated with success rate (odds ratios [OR] = 7.69, 95% confidence interval [CI]: 1.93–30.30) in this series. The relative risk of anxiety group was 4.48 (95% CI: 1.38–14.49) compared to normal group. Digits with double arterial anastomosis in anxiety patients showed a higher survival rate while the number of veins repaired showed no significant effect on survival rate.

Conclusions: Increased level of pre-injury anxiety was an independent risk factors for digit replantation failure. Double arterial anastomosis increased the success rate of replanted digits in anxiety patients.

Level of evidence

Level II, prospective study.

1. Introduction

Replantation of digit represents a hallmark in hand surgery, which requires microsurgical anastomosis of arteries, veins and nerves and repair of fracture and tendon rupture. Advances in microsurgery have allowed an increased survival rate of digital replantation. The survival rates of digital replantation have been reported to range from 70% to 90%, depending on different indications [1–3]. Arterial thrombosis followed by venous congestion is the leading direct cause of replant failure [4]. Replant failure requires revision amputation or flap cover of the exposed skeleton, which bring extra economic burden and pain to patients. Given not all patients will benefit from replantation, the controversy over the benefits and costs between replantation and revision amputation still remains [1]. Previous studies have demonstrated that the success rate of digit replantation was affected by age, smoking, amputation level, cause of injury and ischemia time [2,5,6].

Recent studies have revealed an emerging role of mental status including anxiety and depression in regulation of microvascular function [7–9]. Both anxiety and depression were associated with increased mortality in individuals with coronary heart disease (CHD) by affecting the coronary flow [10–12]. Pre-surgical depression and anxiety also showed an adverse effect on vascular anastomosis in patients receiving coronary artery bypass graft surgery [13,14]. It remains unclear whether mental status affects the success rate of digital replantation.

2. Materials and methods

We performed this study at our hospital. Approval of institutional ethics committee was obtained prior to initiation of the study. All patients were initially evaluated in the emergency department. Patients

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with any of the following criteria were excluded: multiple amputations on a single digit, peripheral arterial diseases, injury on artery in the ipsilateral arm or forearm. The standard protocol for preservation of the amputated part is to wrap it in saline-moistened gauze and place it in a watertight bag and on ice. Because in most cases the parts were not correctly preserved, for the purpose of this study, we also excluded the digits which were correctly preserved before arrival at our hospital. All 109 adult patients who underwent digital replantation in our medical group after complete amputation from 1 September 2013 to 1 September 2015 were assessed and 102 of those were enrolled in this study. Complete amputation was defined as complete separation of the distal part with no bridging tissue. Previous studies have demonstrated that the success rate of digit replantation was affected by age, amputation level, cause of injury and ischemia time [2,5,6]. Hence, the following parameters and were recorded before replantation: age, gender, smoking status, Tamai's level of amputation, causes of injury and warm ischemia time. Antibiotic prophylaxis was routinely used in all the patients. In addition, papaverine was routinely used.

After initial evaluation, all open wounds were irrigated with saline solution and dressed with sterile gauze. The amputated digit was then preserved in an appropriate fashion to facilitate further replantation. The patients were taken to the operating room for further wound irrigation and debridement, and digital replantation. After brachial plexus anesthesia and before replantation, pre-injury depressive and anxious symptoms in the past week were assessed using the Zung self-rating depression scale (SDS) and the Zung self-rating anxiety scale (SAS), respectively [15]. All the outcomes were reported by patients. Each scale contains 20 items scored based frequency (1, rarely; 2, some of the time; 3, very often/often; 4, almost/always). The total score for the 20 questions was multiplied by 1.25, with the integer score as a standard score. A standard score below 50 was considered to indicate absence of depression and anxiety. For the Chinese population, these scales are also valid and reliable instruments for application [16,17]. The hospital anxiety and depression scale (HADS) is commonly used to determine the levels of anxiety and depression for hospitalized patients and general population [18]. The HADS consists of two subscales which are HADS-anxiety (HADS-A) and HADS-depression (HADS-D). Since the SAS and SDS was inappropriate for application in hospitalized patients, we adopted HADS as a tool for consecutive monitoring of anxiety and depression after surgery. The initial assessment of HADS was also conducted after brachial plexus anesthesia and before replantation. The repeated assessments were conducted one week and one month after replantation. The scores were given by patients based on the experiences in the past week. The optimal cut-off of HADS is controversial [19–22]. As a result, we grouped cases according to the SAS/SDS results in this study.

The numbers of vessels repaired were documented by surgeons who conducted the replantation. All participants completed at least one-month follow-up. Failure was defined as necrosis of replanted finger which required revision amputation or flap cover of the skeleton in the study period.

The significance of differences between groups in each of the variables was assessed using Pearson's Chi-squared test or Fisher's exact test. The variables that independently influenced the survival rate ($P < 0.05$ in univariate analysis) were selected into a multivariate logistic regression analysis to evaluate their effect on the survival rate. All data were presented as mean ± standard deviation.

The work has been reported in line with the STROCSS criteria [27].

3. Results

After excluding seven patients, a total of 102 patients with 134 amputated digits who met the inclusion and exclusion criteria were included in the analysis from 1 September 2013 to 1 September 2015. Age, gender, smoking status, Tamai's level of amputation, causes of injury and warm ischemia time were documented before replantation.

Table 1
Results of univariate logistic regression analysis.

Parameters	Whole cohort (n = 134)	Success (n = 121)	Failure (n = 13)	*P* value
Age				0.75
≤35 years	57	52	5	
> 35 years	77	69	8	
Gender				0.48
Male	115	103	12	
Female	19	18	1	
Injury mechanism				0.52
Blade	37	35	2	
Saw	61	55	6	
Crush	16	13	3	
Avulsion	20	18	2	
Tamai's level				0.22
I	22	17	5	
II	27	24	3	
III	38	36	2	
IV	31	29	2	
V	16	15	1	
Smoking				0.03
Yes	53	44	9	
No	81	77	4	
Warm ischemia time				0.02
< 6 h	54	49	5	
6–12 h	76	70	6	
> 12 h	4	2	2	
Pre-injury anxiety (SAS)				0.01
Yes	32	25	7	
No	102	96	6	
Pre-injury depression (SDS)				0.79
Yes	35	32	3	
No	99	89	10	
Number of arteries repaired				0.82
Single	89	80	9	
Double	45	41	4	
Number of veins repaired				0.80
< 2	32	28	4	
2-3	61	56	5	
≥4	41	37	4	

Pre-injury depressive and anxious symptoms were also assessed using the SDS and the SAS before replantation, respectively. All patients were followed for a minimum of one month. The numbers of veins and arteries repaired were also documented due to their importance for survival rate [23–25].

There were 19 amputated digits from women and 115 amputated digits from men. The average age of the patients was 36.56 ± 9.15 years (range from 18 to 59 years). The highest numbers of replants were amputated at level 3, followed by levels 2 and 4 according to Tamai's classification. Four main mechanisms of injury were identified with saw injuries being the most common. There were 53 injured digits from smokers and 81 injured digits from non-smoker. The warm ischemia time ranged from 2 h to 18 h 30 min in this study. There was a prevalence of 23.5% (24 patients, 32 digits) of anxiety and 24.5% (25 patients, 35 digits) of depression. Univariate analysis showed the smoking, warm ischemia time, and anxiety were related to the success rate ($P < 0.05$). The demographic and clinical characteristics of each replanted digit are summarized and shown in Table 1. All these variables also showed significance in multivariate analysis indicating their independence (Table 2). Analysis based on a cohort grouped according to pre-injury SAS results was then performed. Patient demographic and clinical characteristics were compared between the groups and no significant difference was found except success rate (Table 3). The relative risk of the anxiety group was 4.48 (95% CI: 1.38–14.49). Based on above results, we concluded that the increased level of pre-injury anxiety is an independent risk factor for replant failure.

The level of HADS scores of patients grouped by SDS or SAS results at different time points were shown in Fig. 1. The HADS-A scores increased slightly in the normal group but increased remarkably in

Table 2
Results of multivariate logistic regression analysis.

	P value	OR	95% CI
Smoking (reference: none)	0.026	4.63	1.20–17.86
Warm ischemia time 6–12 h (reference: < 6 h)	0.470	0.60	0.15–2.38
Warm ischemia time > 12 h (reference: < 6 h)	0.015	20.06	1.78–225.58
Pre-injury Anxiety (reference: none)	0.004	7.69	1.93–30.30

Table 3
Pre-surgical and surgical differences between normal and anxiety groups.

Parameters	Normal (n = 102)	Anxiety (n = 32)	*P* value
Replantation outcome			0.01
Success	96	25	
Failure	6	7	
Age			0.28
≤35 years	46	11	
> 35 years	56	21	
Gender			0.40
Male	89	26	
Female	13	6	
Injury mechanism			0.41
Blade	25	12	
Saw	48	13	
Crush	14	2	
Avulsion	15	5	
Tamai's level			0.56
I	16	6	
II	22	5	
III	26	12	
IV	24	7	
V	14	2	
Smoking			0.89
Yes	40	13	
No	62	19	
Ischemia time			0.45
< 6 h	42	12	
6–12 h	56	20	
> 12 h	4	0	
Depression			0.53
Yes	25	7	
No	74	28	
Number of arteries repaired			0.75
Single	67	22	
Double	35	10	
Number of veins repaired			0.62
< 2	25	7	
2-3	48	13	
≥4	29	12	

All cases were grouped according to the SAS assessment on pre-injury anxiety.

patients with pre-injury anxiety (Fig. 1A). This finding revealed that the pre-existing anxiety before injury might further deteriorate in response to the trauma. Surprisingly, the postoperative HADS-D scores showed no significant increase in both groups (Fig. 1B).

Finally, we noticed that double arterial anastomosis increased the survival rate of replanted fingers in patients with pre-injury anxiety while the number of veins repaired showed no significant effect on survival rate (Table 4). This finding provided a potential solution for digital replantation in patients with pre-injury anxiety.

4. Discussion

In this study, we showed that pre-injury anxiety was negatively correlated to the success rate of digit replantation. Although the post-operative anxiety should be the factor actually affected the outcome of replantation, the pre-injury level was clearly more valuable. The post-operative anxiety level could only be assessed one week after re-plantation. It is too late for any intervention to prevent the replant failure in anxious patients since most vascular crisis occurs within

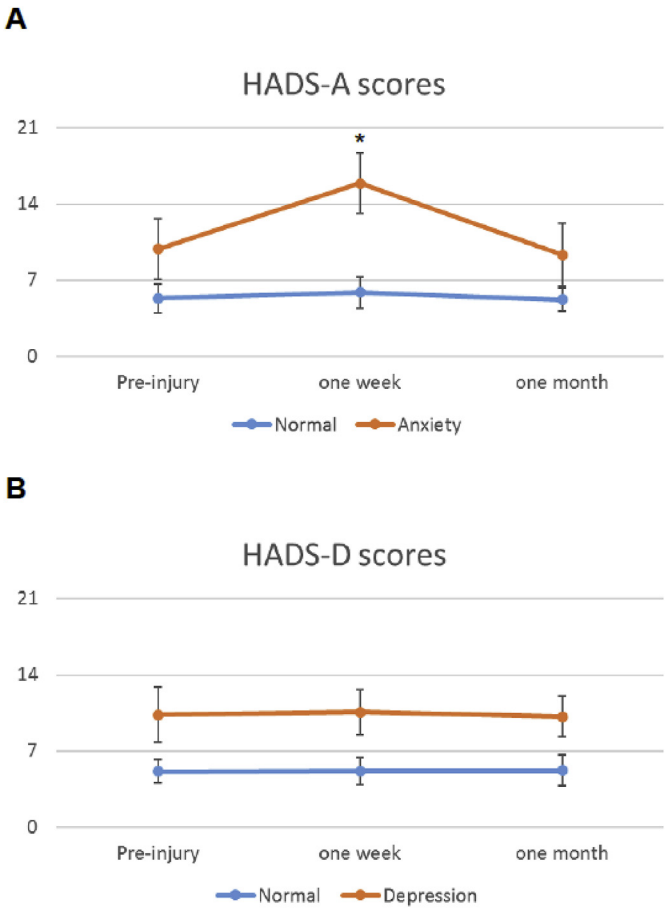

Fig. 1. The consecutive HADS scores. The HADS was scored based on how the patients felt in the past week. (A) patients were grouped according the results of SAS. The scores of HADS-A were shown at indicated time point. (B) patients were grouped according the results of SDS. The scores of HADS-D were shown at indicated time point. *$P < 0.05$ versus pre-injury.

Table 4
Number of vessels repaired and success rate in patients with pre-injury Anxiety.

Parameters	Success(n = 25)	Failure(n = 7)	*P* value
Number of arteries repaired			0.047
Single	15	7	
Double	10	0	
Number of veins repaired			0.24
< 2	5	2	
2-3	9	4	
≥4	11	1	

several days after replantation. The postoperative anxiety level measured by HADS-A increased remarkably in patients with pre-existing anxiety, highlighting pre-injury anxiety as a valuable predictor to postoperative anxiety and thus a promising indication for prophylactic intervention. The rate of the anxiety and the depression was similar to several studies ([28.29]). Most patients are workers, and the status of the emotion may be associated with their occupations. Long-term exposure to high-risk working environment and unhealthy lifestyle may result the high rate of the above negative emotions. Thus, primary prevention is vitally important to these workers.

Our studies also revealed that replanted digits with double arterial anastomosis in anxiety group had a low failure rate similar to normal group. Given the observational nature of this study, the double arterial anastomosis was mainly conducted in two scenarios. First, there were adequate veins available for repair to guarantee the sufficient drainage

from the amputated part. Second, the first anastomosis was unsatisfactory and the blood supply to amputated part was insufficient. In this aspect, it is still unclear whether double anastomosis is an effective method to increase the survival rate in patients with pre-injury anxiety. A randomized, controlled trial was required in the further to confirm our observation. In addition, psychological intervention might relieve the anxiety and thus theoretically increase the survival rate. It is also interesting to know whether anxiety-alleviating drugs could improve the outcomes for anxiety patients.

The mechanism of the relationship between anxiety and depression and the success rate of digit replantation remains unclear. Previous studies showed that anxiety symptoms are associated with increased inflammation and coagulation process [30]. Certain emotional states, such as anxiety and depression, evoke hemodynamic forces like turbulence and shear stress, which may cause or exacerbate endothelial damage.

Papaverine remains popular for treating intraoperative vasospasm and it was routinely used of all the patients in our study. It is a non-specific vasodilator that acts on the smooth muscle of the arterioles and the capillaries of all vascular beds [31]. We wonder whether papaverine could improve the success rate of digit replantation since relevant research showed substituting lidocaine or nicardipine for papaverine to treat vasospasm did not demonstrate an increased rate of flap loss in breast reconstruction ([32]).

We did not observe any association of pre-injury depression. One possibility was that anxiety instead of depression increased plasma norepinephrine which lead to the smooth muscle contraction of microartery [26]. It is conceivable that constriction of digital arteries might affect the blood supply to the amputated part and increase the risk for thrombosis. Supporting our hypothesis, the estimated failure cause for 6 out of 7 cases in the anxiety group was arterial thrombosis. Comparatively, only 3 out of 6 cases in the normal group were estimated to be related to arterial thrombosis.

There are some limitations of the present study. First, SAS and SDS were self-rating scales. More precisely, the mental status should be assessed by psychological specialists. Second, as an anxiety-provoking factor, injury could lead to an increased recall bias and overestimation on the anxiety level. To minimize the bias, we conducted all the tests after brachial plexus anesthesia to relieve the pain of patients. Third, the underlying mechanism by which anxiety increased the failure rate remains unclear.

5. Conclusion

In conclusion, pre-injury anxiety along with smoking history and prolonged ischemia time could significantly increase the failure rate of digit replantation. Double arterial anastomosis might increase the success rate in anxious patients.

Ethical approval

The ethical approval was given by Ethics Committee of Shanghai Sixth People's Hospital and the registration number is 2013-H-032.

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The funding are all from researchers.

Author contribution

Hanqiang Jin, Xiaoyuan Peng: Data collections, Data analysis, writing, Study design.

These authors contributed equally to this work.

Conflicts of interest

The authors have declared that no competing interest exists.

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Data statement

The collected data used to support the findings of this study are currently under embargo. Requests for data, 6 months after publication of this article, will be considered by the corresponding author.

CRediT authorship contribution statement

Hanqiang Jin: Project administration, Data curation, Formal analysis, Resources, Software, Writing - original draft. **Xiaoyuan Peng:** Conceptualization, Investigation, Methodology, Visualization. **Changqing Zhang:** Funding acquisition, Writing - review & editing, Supervision, Validation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.07.027.

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