

# Controlled continuous systemic heparinization increases success rate of artery-only anastomosis replantation in single distal digit amputation

## A retrospective cohort study

Jun Yong Lee (MD, PhD)<sup>a</sup>, Hak Soo Kim (MD)<sup>a</sup>, Sang Taek Heo (MD, PhD)<sup>b</sup>, Ho Kwon (MD, PhD)<sup>a</sup>, Sung-No Jung (MD, PhD)<sup>a,\*</sup>

### Abstract

Replantation is a prime indication for distal digital amputation, as it helps restore hand aesthetics and functions; however, venous anastomosis is often not feasible. Previous studies used systemic anticoagulation in distal digital artery only anastomosis replantation surgery to improve replantation success rate, however, which yielded limited level of clinical evidence. This study aimed to compare controlled continuous heparinization (CCH) and intermittent bolus heparinization (IBH) for surgical outcome and clinical variables after single distal digital artery only anastomosis replantation surgery.

A single-institution, retrospective cohort study was performed. Out of 324 patients who underwent digital replantation surgery, we focused the study for the Zone I and II single distal digital amputation patients excluding confounding factors. Sixty-one patients were included in this study and underwent artery-only anastomosis replantation surgery with postoperative CCH (34 patients) or IBH (27 patients) protocols. The CCH group targeted activated partial thromboplastin time (aPTT) at 51 to 70 seconds, monitoring aPTT levels every eight hours and administering 100mg of aspirin per day. The IBH group received 300mg of aspirin per day and underwent IBH (12,500U). Both groups received intravenous prostaglandin E1 drips (10 µg). To verify the factors affecting the success rate of the heparin protocol, patient factors, clinical factors, and operative factors were extracted from the medical records. Statistical analysis with inverse probability of treatment weights propensity score methods compared treatment outcomes and clinical variables.

The CCH group's replantation success rate was higher (91.17% vs 59.25%), and the transfusion rate was increased ( $P=0.032$ ). However, the significant decrease in hemoglobin levels ( $>15\%$ ) did not differ between the groups ( $P=0.108$ ). Multivariable logistic regression analysis with potent univariate variables ( $P < .10$ ) revealed that CCH was a statistically significant variable in replantation success rate ( $P=0.004$ ). Neither the major bleeding complications nor the significant decrease in patients' platelet levels were observed in both groups.

Our study suggests that CCH after artery-only anastomosis replantation surgery in Zone I and II distal digital replantation is a safe method to improve the replantation success rate and may provide a guideline for use of the anticoagulation method following artery-only anastomosis distal digital replantation surgery.

**Abbreviations:** aPTT = activated partial thromboplastin time, CCH = controlled continuous heparinization, DIP = distal interphalangeal joint, HIT = heparin-induced thrombocytopenia, IBH = intermittent bolus heparinization, IPTW = inverse probability of treatment weights.

**Keywords:** amputation, anticoagulation, finger injury, hand surgery, heparin, microsurgery, replantation

Editor: Perbinder Grewal.

Funding: The statistical analysis conducted in this study was supported by the Department of Biostatistics of the Catholic Research Coordinating Center, The Catholic University, Korea.

The authors report no conflicts of interest.

Supplemental Digital Content is available for this article.

<sup>a</sup> Department of Plastic and Reconstructive Surgery, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea, <sup>b</sup> Department of Internal Medicine, School of Medicine, Jeju National University, Jeju, Republic of Korea.

\* Correspondence: Sung-No Jung, Department of Plastic and Reconstructive Surgery, Uijeongbu St. Mary's Hospital, College of Medicine, Catholic University of Korea, 271 Cheonbo-ro, Uijeongbu-si, Gyeonggi-do, 11765, Republic of Korea (e-mail: jsn7190@catholic.ac.kr).

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Medicine (2016) 95:26(e3979)

Received: 14 January 2016 / Received in final form: 22 May 2016 / Accepted: 26 May 2016

<http://dx.doi.org/10.1097/MD.0000000000003979>

## 1. Introduction

Workplace regulations and safety training programs to prevent accidents have decreased the incidences of nonfatal workplace amputations.<sup>[1]</sup> Accidental fingertip injuries and amputations, however, still occur in daily life. About 1% of all trauma patients in the United States undergo amputation, and 70% of those traumatic amputation patients have a finger amputated.<sup>[2]</sup> Most digital amputation patients experience mental stress upon seeing their amputated fingers and are concerned about possible disability and disfigurement to their hands. Because cosmetic appearance appears to play as great a role as recovery of physical function in the psychological sequelae of the amputation,<sup>[3]</sup> digital amputation patients with cosmetic disfigurement are prone to experience post-traumatic stress disorder.<sup>[4]</sup> Therefore, successful replantation of the amputated finger is important not only to restore function for the patient but also to remedy the patient's mental trauma.

When clinically feasible, finger replantation surgery—especially in distal amputation—is the treatment of choice after digital amputation, because successful replantation helps restore the aesthetics of the patient's hand as well as its previous functions.<sup>[5–8]</sup> If replantation surgery fails, however, the lost body part cannot be reconstructed aesthetically and functionally, leaving the patient's hand disfigured. Since the first successful digital replantation in 1968, numerous studies have shown that amputation distal to the flexor digitorum superficialis insertion is an excellent indication for replantation surgery because restoration of hand functions and aesthetics is expected after successful replantation.<sup>[8–10]</sup> For the distal replanted part, survival of the digital length is more important than distal interphalangeal (DIP) joint motor function, as DIP motion only partially accounts for overall hand function.<sup>[11]</sup> Therefore, increasing the survival rate of the replanted part is the most important aspect of the distal digital replantation surgery.

The survival of the distal finger replantation depends on the arterial anastomosis and can be improved with a venous anastomosis.<sup>[7]</sup> However, in fingertip amputation distal to the DIP joint, venous anastomosis may not be feasible; the damage may be too severe, or the surgeon may lack experience in microsurgical techniques required to repair crushed fine digital veins. In such cases, the surgeon has no choice but to replant the finger without venous anastomosis. This so-called artery-only replantation requires pharmacologic agents to maintain blood flow through the crushed digit to the outflow at the fingertip until venous outflow is reestablished naturally. Maintaining this blood flow is as vital to successful replantation as performing fine microsurgical anastomosis of the vascular pedicle.

There have been many debates about these pharmacologic agents and their protocols for maintaining blood flow into the replanted part. Among these agents, heparin has a long application history not only in the field of microsurgery but also in vascular accidents such as myocardial infarction. Previous research has shown that heparinization after microvascular anastomosis in replantation surgery is usually performed via intermittent bolus intravenous injection.<sup>[6,8,12]</sup> However, because heparin shows variable pharmacokinetics among patients, its administration method and the monitoring of its bioavailability are important to maintain blood flow into the replanted part via systemic heparinization.<sup>[13]</sup> To date, however, supporting clinical data for monitored continuous heparinization after artery-only anastomosis finger replantation surgery is lacking. Continuous heparin infusion with monitoring of its bioavailability after Zone

I and II fingertip artery-only replantation may improve the replantation success rate by preventing clotting-induced venous congestion common in artery-only anastomosis finger replantation surgery.

This study compares the surgical outcomes and clinical variables of controlled continuous heparinization (CCH) and intermittent bolus heparinization (IBH) following Zone I and II artery-only anastomosis finger replantation surgery.

## 2. Methods

This study was conducted under the approval of the institutional review board of Uijeongbu St. Mary's Hospital (UC13RISI0126). From December 2003 to October 2011, a single-institution, retrospective cohort study was performed. In this study, we used Tamai's classification, which divides the distal digital amputation into Zone I (fingertip to the base of the nail) and Zone II (base of the nail to the DIP joint).<sup>[14]</sup> The study included patients who underwent single artery-only anastomosis for replantation of Zone I and II single digit amputation and who showed continuous exsanguinations of blood at the replanted fingertip immediately following surgery. The study excluded patients who had concomitant injuries to other areas of the hand or body, patients with degloving injuries, and patients who received venorrhaphy or revisional operations more than 24 hours postoperatively. To take into consideration the learning curve of the operator, each surgeon's first 5 cases were also excluded (Table 1).

The surgery was performed under general anesthesia. The amputated finger and stump were thoroughly irrigated with saline. Bone and soft tissue debris were trimmed if necessary, and then the amputated finger was fixated with Kirshner wire. In Zone II replantation, flexor and extensor tenorrhaphy was also performed using Prolene 3–0 sutures when returning of joint function could be expected postoperatively. The proximal arterial stump can be found by careful dissection of the blood pumping point. The amputated digit's arterial stump is normally located opposite the site of the proximal arterial stump. If the opposite arterial stump could not be found, arteriovenous anastomosis was performed. Neuroorrhaphy was not performed routinely, because it can pull or compress the anastomosis site, and distal neurotization can be established as a nerve is transected at the distal part of the finger.<sup>[15,16]</sup> Next, the skin was closed with loose nylon sutures or an onlay split-thickness skin graft. Because we do not perform venous anastomosis, we made a fish-mouth incision at the fingertip for continuous blood exsanguination, thereby controlling the venous congestion until the fingertip circulation was re-established. When the amputated digit was replanted successfully, we could observe continuous bleeding from the fish-mouth incision (Fig. 1). To maintain exsanguination

**Table 1**

### Inclusion and exclusion criteria of the study.

Inclusion criteria	Exclusion criteria
Zone I and II single digit amputation	Concomitant injury at the other part of hand or body
Artery-only anastomosis	Degloving injury
Continuous exsanguination of blood at the replanted fingertip immediately following surgery	Venorrhaphy (or vein graft) or revision surgery more than 24 hours postoperatively
	Surgeon's first 5 cases



**Figure 1.** Fifty-one year old male patient with amputated right middle fingertip by an ornament tacking machine (top left); after artery-only anastomosis replantation surgery with systemic heparinization (top right)—note the fresh blood exsanguinating from the fingertip fish-mouth incision (arrow, top right); 4 months postoperative view, wherein the replanted fingertip has regained its original shape and function (7 mm of 2–point discrimination, bottom left); more growth of the fingernail is expected (bottom right).

at the fish-mouth incision, we put heparin-soaked gauze over the incision site, replacing the gauze with new heparin-soaked gauze when it was soaked with blood. The gauze was soaked with 25,000 U heparin mixed with 40 cc of normal saline solution. To promote external bleeding from the replanted fingertip and to prevent thrombosis in the crushed amputated digit, we used 2 different systemic heparinization protocols.

The authors used the IBH protocol from December 2003 to February 2007 (27 patients), and the CCH protocol from March 2007 to October 2011 (34 patients). The IBH protocol consisted of 300 mg of aspirin per oral dose, intravenous dripping of prostaglandin E1 (Alprostadil, 10 µg), and intermittent intravenous bolus heparin injection (12,500 U of heparin mixed in 40 cc of normal saline) per day. Depending on the amount or flow of bleeding at the fish-mouth incision, intravenous bolus heparin was administered once or twice a day. For the CCH protocol, we adopted continuous intravenous heparinization using an injection pump instead of intermittent bolus heparin injections, and we monitored activated partial thromboplastin time (aPTT) every 8 hours to maintain the target aPTT level (51–70 seconds) while decreasing the aspirin dose to 100 mg per day. Prostaglandin E1 was used as in IBH (intravenous dripping, Alprostadil, 10 µg). After injecting a loading dose of 12,500 U of heparin mixed in 100 mL of normal saline, a heparin solution (12,500 U of heparin mixed in 500 mL of 5% dextrose) was infused continuously at a rate of 20 mL per hour. The infusion rate was regularly adjusted according to the aPTT level every 8 hours. To complete heparinization, the dosage was tapered for 2 days in a stepwise manner. We used our heparin dose adjustment protocol as summarized in Table 2. In both groups, in cases of excess venous congestion showing purplish discoloration of the replanted fingertip, a medical leech was applied to decompress urgent venous congestion.

We defined “success” as a case that showed bleeding, had a viable replanted digit at the time of discharge, and did not undergo any secondary operations such as stump revision during the follow-up period. “Failure” was defined as a case in which the replanted digit showed shrinkage, necrosis, no bleeding on pin-prick, or bluish-to-dark discoloration at the time of discharge.

To verify the factors affecting the success rate of the heparin protocol, patient factors, clinical factors, and operative factors were extracted from the medical records. Patient factors included demographic variables (sex, age), tobacco use, alcoholic consumption, comorbidities, and hypertension history. Clinical factors were length of hospital stay, transfusion, significant decrease in hemoglobin level (more than 15% decrease from the preoperative level), and medical leech use. Operative factors consisted of operative method (arterio-arterial anastomosis versus arteriovenous anastomosis), surgeon, and surgeon’s condition variables (operation month and operation start time). Major bleeding complications during the hospital stay, such as intracranial or internal organ hemorrhage, and significant

**Table 2**  
Heparin dose adjustment protocol in continuous controlled heparinization.

aPTT	Change rate of infusion
<30	+6 mL/h (650 U/h)
31–40	+4 mL/h (600 U/h)
41–50	+2 mL/h (550 U/h)
51–70	0 (500 U/h)
71–79	–2 mL/h (450 U/h)
80–90	–4 mL/h (400 U/h)

Starting dose of 12,500 U as IV bolus, followed by 12,000 U per 24 hour as a continuous infusion (25 U/mL). aPTT measurement was performed every 8 hr after the initial bolus infusion.

**Table 3****Baseline characteristics.**

	Controlled continuous heparinization (N=34)	Intermittent bolus heparinization (N=27)	P
Sex (Male)	28 (82.4%)	21 (77.8%)	0.655
Age	38.5 ± 14.0	40.0 ± 13.5	0.666
Smoking	16 (47.1%)	13 (48.2%)	0.933
Alcohol	13 (38.2%)	17 (63.0%)	0.055
Comorbidities	3 (8.8%)	0 (0.0%)	0.248
Hypertension	2 (5.9%)	0 (0.0%)	0.498
Length of hospital stay	14.3 ± 3.4	13.3 ± 4.5	0.362
Transfusion	10 (29.4%)	2 (7.4%)	<b>0.032</b>
Significant decrease in Hb level (>15%)	17 (50.0%)	8 (29.6%)	0.108
Leech use	5 (14.7%)	8 (29.6%)	0.157
Operation method (arterio-arterial anastomosis)	20 (58.8%)	15 (55.6%)	0.798
Surgeon			
A	11	18	
B	4	6	
C	0	3	
D	11	0	
E	8	0	
Operation month			0.923
Spring (Apr–May)	7 (20.6%)	6 (22.2%)	
Summer (Jun–Aug)	9 (26.5%)	6 (22.2%)	
Fall (Sep–Nov)	9 (26.5%)	9 (33.3%)	
Winter (Dec–Feb)	9 (26.5%)	6 (22.2%)	
Operation time			0.972
From 00:00 to 05:59	4 (12.1%)	3 (11.1%)	
From 06:00 to 11:59	2 (6.1%)	1 (3.7%)	
From 12:00 to 17:59	14 (42.4%)	13 (48.2%)	
From 18:00 to 23:59	13 (39.4%)	10 (37.0%)	

Data are presented as mean ± SD, and n (%).

P values for differences were determined by *t* test, Chi-square test, and Fisher exact test.

Bold text indicates a statistically significant difference with a *P* value less than 0.05.

decrease in platelet levels (more than 50% decrease from the preoperative level) were collected separately.

### 2.1. Statistical analysis

To decrease selection bias in our comparison of the success rate of the nonrandomized heparinization protocol group, we adopted inverse probability of treatment weights (IPTW) propensity score methods. Categorical and continuous variables were reported as frequencies (%) and means ± standard deviations, respectively. Univariable logistic regression was explained by odds ratio for each variable using IPTW propensity score methods. The final model was determined by creating a multivariable logistic regression model, which included all potent univariate variables ( $P < 0.10$ ). All tests were 2-sided, with a significance level of 0.05. Analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC).

### 3. Results

The patients' baseline characteristics grouped by heparinization protocol are presented in Table 3. Out of 324 patients who underwent digital replantation surgery, 61 patients—49 males and 12 females—were included in this study. The mean age was 39.2 years. There were no significant differences in patient factor variables between the 2 groups.

In clinical factors, the transfusion rate was higher in the CCH group than the IBH group ( $P = 0.032$ ), although there was no significant difference between the 2 groups in significant decrease in hemoglobin level. No differences in length of hospital stay or

use of medical leeches were observed between the 2 groups. Five surgeons conducted replantation surgery during the study period. Operation month and operation start time, which accounted for the surgeon's condition, showed no statistically significant differences. The ratio between arterio-arterial versus arteriovenous anastomosis also showed no differences between the groups. No major bleeding complications were reported in either group. No significant decrease in patients' platelet levels was observed in either group.

The replantation success rate was 91.17% in the CCH group and 59.25% in the IBH group. The replantation success rate, as analyzed by univariate logistic regression analysis and the IPTW propensity score method, is presented in Table 4. Among the variables, continuous heparinization showed a statistically significant contribution to replantation success. Multivariable logistic regression analysis with potent univariate variables ( $P < 0.10$ ) also showed that continuous heparinization is a statistically significant variable contributing to the replantation success rate ( $P = 0.004$ , area under the curve = 0.8359).

### 4. Discussion

Venous anastomosis is known to improve the success rate of distal digital replantation surgery.<sup>[7,17,18]</sup> However, 68% of distal digital amputation cases include concomitant crushing injuries at the stump and to the amputated digit.<sup>[7]</sup> Distal digital replantation surgery requires fine microsurgical skill. Venorrhaphy, which is known to improve the success rate, is more technically demanding than arteriorrhaphy for the less-experienced surgeon, and sometimes the vein itself cannot be located in

**Table 4****Analysis of replantation success rate by univariate logistic regression analysis between normal and IPTW Propensity Score method.**

Variables	Normal		Inverse probability of treatment weights (IPTW)	
	Odds ratio	P	Odds ratio (95% CI)	P
Sex (Male)	0.32 (0.08–1.22)	0.095	<b>0.28 (0.08–1.02)</b>	<b>0.053</b>
Age	0.97 (0.92–1.01)	0.167	<b>0.96 (0.91–1.01)</b>	<b>0.083</b>
Comorbidities	N/A		N/A	
Hypertension	N/A		N/A	
Heparin (Continuous)	7.10 (1.73–29.16)	0.007*	<b>10.31 (2.16–49.15)</b>	<b>0.003*</b>
Length of stay	0.94 (0.80–1.09)	0.390	<b>0.86 (0.73–1.01)</b>	<b>0.069</b>
Transfusion	1.15 (0.27–5.00)	0.851	2.54 (0.68–9.56)	0.168
HB significance	0.31 (0.08–1.26)	0.101	0.78 (0.22–2.74)	0.704
Leech	0.22 (0.03–1.90)	0.171	<b>0.14 (0.02–1.20)</b>	<b>0.073</b>
Operation method	1.45 (0.42–5.00)	0.553	2.42 (0.64–9.24)	0.195

Five potent univariate variables ( $P < 0.10$ ) included in creating multivariable logistic regression model are listed in bold characters.

CI = confidence interval.

\*  $P < 0.05$ .

the operative field due to the crushing nature of the injury. In such cases, the amputated digit is replanted using artery-only anastomosis and alternative venous drainage, such as external exsanguination<sup>[8,19,20]</sup> or medical leech application<sup>[5,21,22]</sup> until the venous channel is re-established. In addition, systemic anticoagulation has been used for digital replantation surgery using heparin,<sup>[8,19]</sup> low molecular weight heparin,<sup>[16,23]</sup> low molecular weight dextran,<sup>[21,24]</sup> urokinase,<sup>[21,25]</sup> aspirin,<sup>[19,23]</sup> and dipyridamole.<sup>[8,22]</sup> Because digital amputation usually accompanies concomitant injuries and shows various presentations, constructing randomized controlled trials in a homogeneous patient group in a reasonable time period is difficult. Previous research consists mainly of case-series studies, and the available randomized controlled trials are limited to comparisons of the efficacy of low molecular weight heparin and unfractionated heparin in preventing microvascular occlusion after replantation of the forearm and hand, and the results yielded limited evidence.<sup>[26–28]</sup> These studies included not only digital amputations but also major limb amputations or free flaps. Therefore, the previous research is limited in providing a guideline for systemic anticoagulation after digital replantation.

However, after the more detailed review of the literature on using systemic anticoagulation in distal digital replantation surgery, the authors were able to extract the success rate of the artery-only anastomosis cases from each study and compared this with the current study results (See Table, Supplemental Content, <http://links.lww.com/MD/B68>, which summarizes and compares the systemic anticoagulation regimens and their outcomes after digital replantation surgery). Although direct comparison between the studies was limited due to the variety of anticoagulation regimens applied, we could observe a few gross trends as follows: CCH showed the second-best artery-only replantation success rate among studies utilizing systemic anticoagulation regimens with more than 10 cases of artery-only replantation. Increasing the number of combined systemic anticoagulation regimens did not always increase the overall success rate or the artery-only replantation success rate. The overall success rate for cases that included venous anastomosis was usually higher than the artery-only replantation success rate. Most of the regimens administered the heparin in an intermittent manner in a routine schedule. However, a few studies used the heparin with feedback dosage adjustment, continuous intravenous dripping, or monitoring of aPTT level. Although these studies used different anticoagulation regimens, their artery-only replantation success rates were higher than other studies in which

heparin was administered intermittently (86.6% by Matsuzaki et al,<sup>[15]</sup> 91.0% by Shi et al,<sup>[29]</sup> 100% by Buntic et al,<sup>[30]</sup> 71.4% by Gordon et al<sup>[19]</sup>).

The authors hypothesized that systemic anticoagulation after artery-only anastomosis distal digital replantation surgery was as important as fine arterial anastomosis. Because external bleeding served as a venous drainage after artery-only anastomosis replantation surgery, coagulation-induced cessation of the external bleeding caused severe venous congestion and resulting replantation failure. The commonly adopted heparinization dose of 5000U intravenous bolus did not enable us to maintain an adequate level of anticoagulation.<sup>[31]</sup> Therefore, to improve the success rate of the artery-only anastomosis distal digital replantation surgery with objectives of safety, reliability, and a longer duration and higher level of anticoagulation, we established an anticoagulation regimen with the Department of Internal Medicine. The IBH dose of 12,500U was based on the interventional cardiology regimen that was safely used during percutaneous transluminal coronary angioplasty in a bolus manner.<sup>[32]</sup> This amount of systemic heparin has also been used in head and neck cancer reconstruction surgery with free flaps.<sup>[33]</sup> Surveys of vascular surgeons have shown that a high dose of heparinization has been safely used to prevent thrombosis at the vessel clamping area.<sup>[34]</sup> Clinically, this regimen increased the blood flow for flushing inside the replanted digit by thinning the blood without complications. However, in our study, we could sometimes observe a venous congestion and hemostasis at the fingertip fish-mouth incision even though it was covered with heparin-soaked gauze. We suspected that this hemostasis at the fingertip was due to the thrombogenic effect caused by an abrupt decrease in blood heparin concentration after intermittent bolus heparinization.<sup>[35,36]</sup> Therefore, we changed our heparinization method from intermittent bolus to continuous infusion and adopted a tapering method for ending the heparinization. Our CCH regimen was adopted from the heparin nomogram used for patients with acute coronary syndromes and revised for our institution (Table 2).<sup>[37]</sup> Because we needed to flush out the thrombogenic debris from the crushed amputated part after arterial anastomosis, we used a higher loading dose of 12,500U instead of 5000U in the original heparin nomogram. Instead, the starting rate was decreased from 1000U per hour to 500U per hour. Because the heparin dose for rate change was consistent with the original heparin nomogram, we could control the level of anticoagulation by following up the aPTT level and adjusting the heparin infusion dose. Of note, heparin showed a variable

response to different aPTT systems as compared with the international normalized ratio (INR) for prothrombin time; these nomograms showed variability among the institution and might be transferable to other institution after modifications.<sup>[38,39]</sup> This change in the heparinization method resulted in an increased replantation success rate, as shown in this study (from 59.25% to 91.17%). Statistical analysis indicated that CCH was the key factor in the increased success rate after artery-only anastomosis distal digital replantation.

When systemic heparinization is used, bleeding complications such as intracranial or gastrointestinal tract bleeding and heparin-induced thrombocytopenia (HIT) should be monitored. Although the probability of HIT is estimated by the scoring system,<sup>[40]</sup> HIT can be suspected when there is an unexplained fall in platelet count of more than 50% from the baseline and median nadir of  $55 \times 10^9/L$ , or when skin lesions at heparin injection sites are present clinically.<sup>[41]</sup> In the current study, no major bleeding complications were observed. The authors also traced the patient's platelet counts during the treatment period; however, no patients had a fall in platelet count of more than 50% from the baseline. Although incidences of internal bleeding and falls in platelet counts are low, careful observation is required.

Previous reports showed that the transfusion rate was up to 88% among patients with intermittent heparinization without aPTT monitoring.<sup>[12]</sup> In reports documenting continuous heparinization, studies targeting therapeutic aPTT levels, including the current study, showed a lower transfusion rate than the study with targeting subtherapeutic aPTT levels (21.4%,<sup>[19]</sup> 29.4% in current study vs 65%).<sup>[30]</sup> These results imply that monitoring of aPTT levels in distal digital replantation surgery may play a role in avoiding unnecessary transfusions. To improve the surgical results, surgeons were prone to let the fingertip bleed more and give a preemptive transfusion as a further decrease in hemoglobin levels was anticipated. We observed this tendency in the current study, as there was an increased chance of receiving a transfusion in patients with CCH; however, the significant decrease in hemoglobin levels did not show any significant differences between the 2 heparinization methods. Therefore, to minimize unnecessary transfusions in patients undergoing systemic heparinization, monitoring of the aPTT at a therapeutic level, adoption of the strict transfusion indications based on the hemoglobin level, and avoidance of CCH in patients with bleeding diathesis or multiple trauma should be considered.

This retrospective cohort study has meaningful implications for future practice. This is the first study to compare the conventionally administered IBH with CCH based on the heparin nomogram after distal digital artery only anastomosis replantation surgery. With the sparsity of the randomized controlled trial in digital replantation surgery, we adopted IPTW propensity score methods to improve the reliability of our study and focused the study for the Zone I and II single digit distal amputation patients excluding confounding factors. To reflect the changes in hemoglobin levels more specifically to single digit amputation, we excluded patients with concomitant traumatic injuries, in whom excess bleeding was expected after systemic heparinization. We excluded the surgeon's first 5 cases to minimize bias from the surgeon's experience. The patients who underwent revision surgeries more than 24 hours after the initial surgery were also excluded because the surgeon's intervention may have deviated the success rate.

We believe that our study may provide a guideline for use of the anticoagulation method in artery-only anastomosis distal digital

replantation surgery. Moreover, our CCH method could serve as a bridging technique for surgeons who are able to perform arterial anastomosis but may be inexperienced in venous anastomosis. By improving the success rate of the replantation surgery, the CCH method may encourage surgeons to perform more complicated replantation surgery.

## 5. Conclusion

CCH improved the success rate after artery-only anastomosis replantation surgery in Zone I and II single distal digital amputation patients without any major bleeding complications. Despite the increased transfusion rate in the CCH group, the significant decrease in hemoglobin level did not differ statistically between the CCH and IBH groups.

Our study suggests that CCH after artery-only anastomosis distal digital replantation is a safe method to improve the replantation success rate and may provide a guideline for use of the anticoagulation method following artery-only anastomosis distal digital replantation surgery.

## References

- [1] Brown JD. Amputations: A Continuing Workplace Hazard. Services DolaM, ed. NE Washington, DC: U.S. Bureau of Labor Statistics; 2003.
- [2] Barmparas G, Inaba K, Teixeira PG, et al. Epidemiology of post-traumatic limb amputation: a National Trauma Databank Analysis. *Am Surg* 2010;76:1214–22.
- [3] Copuroglu C, Ozcan M, Yilmaz B, et al. Acute stress disorder and post-traumatic stress disorder following traumatic amputation. *Acta Orthop Belg* 2010;76:90–3.
- [4] Fukunishi I. Relationship of cosmetic disfigurement to the severity of posttraumatic stress disorder in burn injury or digital amputation. *Psychother Psychosom* 1999;68:82–6.
- [5] Foucher G, Norris RW. Distal and very distal digital replantations. *Br J Plast Surg* 1992;45:199–203.
- [6] Weiland AJ, Villarreal-Rios A, Kleinert HE, et al. Replantation of digits and hands: analysis of surgical techniques and functional results in 71 patients with 86 replantations. *J Hand Surg Am* 1977;2:1–2.
- [7] Sebastian SJ, Chung KC. A systematic review of the outcomes of replantation of distal digital amputation. *Plast Reconstr Surg* 2011;128:723–37.
- [8] Kim WK, Lim JH, Han SK. Fingertip replantations: clinical evaluation of 135 digits. *Plast Reconstr Surg* 1996;98:470–6.
- [9] Goldner RD, Stevanovic MV, Nunley JA, et al. Digital replantation at the level of the distal interphalangeal joint and the distal phalanx. *J Hand Surg Am* 1989;14(2 Pt 1):214–20.
- [10] Yamano Y. Replantation of the amputated distal part of the fingers. *J Hand Surg Am* 1985;10:211–8.
- [11] Littler JW. *The Hand and Upper Extremity*. Vol 6. 2nd ed. Philadelphia, PA:Saunders; 1977.
- [12] Han S-K, Lee B-I, Kim W-K. Topical and systemic anticoagulation in the treatment of absent or compromised venous outflow in replanted fingertips. *J Hand Surg* 2000;25:659–67.
- [13] Hirsh J. Heparin. *N Engl J Med* 1991;324:1565–74.
- [14] Tamai S. Twenty years' experience of limb replantation—review of 293 upper extremity replants. *J Hand Surg Am* 1982;7:549–56.
- [15] Matsuzaki H, Yoshizu T, Maki Y, et al. Functional and cosmetic results of fingertip replantation: anastomosing only the digital artery. *Ann Plast Surg* 2004;53:353–9.
- [16] Ozcelik IB, Tuncer S, Purisa H, et al. Sensory outcome of fingertip replantations without nerve repair. *Microsurgery* 2008;28:524–30.
- [17] Matsuda M, Chikamatsu E, Shimizu Y. Correlation between number of anastomosed vessels and survival rate in finger replantation. *J Reconstr Microsurg* 1993;9:1–4.
- [18] Lee BI, Chung HY, Kim WK, et al. The effects of the number and ratio of repaired arteries and veins on the survival rate in digital replantation. *Ann Plast Surg* 2000;44:288–94.
- [19] Gordon L, Leitner DW, Buncke HJ, et al. Partial nail plate removal after digital replantation as an alternative method of venous drainage. *J Hand Surg Am* 1985;10:360–4.

- [20] Suzuki K, Matsuda M. Digital replantations distal to the distal interphalangeal joint. *J Reconstr Microsurg* 1987;3:291–5.
- [21] Hirase Y. Salvage of fingertip amputated at nail level: new surgical principles and treatments. *Ann Plast Surg* 1997;38:151–7.
- [22] Hahn HO, Jung SG. Results of replantation of amputated fingertips in 450 patients. *J Reconstr Microsurg* 2006;22:407–13.
- [23] De Smet L. Digital reimplantation at the level of the distal interphalangeal joint and the distal phalanx: a good indication. *Acta Orthop Belg* 1990;56:583–6.
- [24] Pomerance J, Truppa K, Bilos ZJ, et al. Replantation and revascularization of the digits in a community microsurgical practice. *J Reconstr Microsurg* 1997;13:163–70.
- [25] Maeda M, Fukui A, Tamai S, et al. Continuous local intra-arterial infusion of antithrombotic agents for replantation (comparison with intravenous infusion). *Br J Plast Surg* 1991;44:520–5.
- [26] Chen YC, Chi CC, Chan FC, Wen YW. Low molecular weight heparin for prevention of microvascular occlusion in digital replantation. *Cochrane Database Syst Rev* 2013:CD009894.
- [27] C P, Z GH, Z XK. The Livaracine digital replantation. *Anhui Med* 2001;22:53–4.
- [28] L JX, L CH, S HJ. The application of low molecular heparin and heparin after digital replantations. *Chinese Community Doctors* 2012; 205–6.
- [29] Shi D, Qi J, Li D, et al. Fingertip replantation at or beyond the nail base in children. *Microsurgery* 2010;30:380–5.
- [30] Buntic RF, Brooks D. Standardized protocol for artery-only fingertip replantation. *J Hand Surg* 2010;35:1491–6.
- [31] Martin P, Greenstein D, Gupta NK, et al. Systemic heparinization during peripheral vascular surgery: thromboelastographic, activated coagulation time, and heparin titration monitoring. *J Cardiothorac Vasc Anesth* 1994;8:150–2.
- [32] Schachinger V, Kasper W, Zeiher AM. Adjunctive intracoronary urokinase therapy during percutaneous transluminal coronary angioplasty. *Am J Cardiol* 1996;77:1174–8.
- [33] Gerressen M, Pastaschek CI, Riediger D, et al. Microsurgical free flap reconstructions of head and neck region in 406 cases: a 13-year experience. *J Oral Maxillofac Surg* 2013;71:628–35.
- [34] Wakefield TW, Lindblad B, Stanley TJ, et al. Heparin and protamine use in peripheral vascular surgery: a comparison between surgeons of the Society for Vascular Surgery and the European Society for Vascular Surgery. *Eur J Vasc Surg* 1994;8:193–8.
- [35] Smith AJC, Holt RE, Fitzpatrick K, et al. Transient thrombotic state after abrupt discontinuation of heparin in percutaneous coronary angioplasty. *Am Heart J* 1996;131:434–9.
- [36] Granger CB, Miller JM, Bovill EG, et al. Rebound increase in thrombin generation and activity after cessation of intravenous heparin in patients with acute coronary syndromes. *Circulation* 1995;91:1929–35.
- [37] Zimmermann AT, Jeffries WS, McElroy H, et al. Utility of a weight-based heparin nomogram for patients with acute coronary syndromes. *Intern Med J* 2003;33:18–25.
- [38] Hirsh J, Dalen JE, Deykin D, et al. Heparin: mechanism of action, pharmacokinetics, dosing considerations, monitoring, efficacy, and safety. *Chest* 1992;102(4 suppl):337S–51S.
- [39] Reilly B, Raschke R, Srinivas S, et al. Intravenous heparin dosing. *J Gen Intern Med* 1993;8:536–42.
- [40] Warkentin TE, Heddle NM. Laboratory diagnosis of immune heparin-induced thrombocytopenia. *Curr Hematol Rep* 2003;2:148–57.
- [41] Warkentin TE. Heparin-induced thrombocytopenia: pathogenesis and management. *Brit J Haematol* 2003;121:535–55.
- [42] Akyurek M, Safak T, Kecik A. Fingertip replantation at or distal to the nail base: use of the technique of artery-only anastomosis. *Ann Plast Surg* 2001;46:605–12.
- [43] Hasuo T, Nishi G, Tsuchiya D, et al. Fingertip replantations: importance of venous anastomosis and the clinical results. *Hand Surg* 2009;14:1–6.
- [44] Hattori Y, Doi K, Ikeda K, et al. Significance of venous anastomosis in fingertip replantation. *Plast Reconstr Surg* 2003;111:1151–8.
- [45] Li J, Guo Z, Zhu Q, et al. Fingertip replantation: determinants of survival. *Plast Reconstr Surg* 2008;122:833–9.
- [46] Patradul A, Ngarmukos C, Parkpian V. Distal digital replantations and revascularizations. 237 digits in 192 patients. *J Hand Surg* 1998;23: 578–82.
- [47] Ito H, Sasaki K, Morioka K, et al. Fingertip amputation salvage on arterial anastomosis alone: an investigation of its limitations. *Ann Plast Surg* 2010;65:302–5.