RESEARCH ARTICLE

Evaluation of nerve transfer options for treating total brachial plexus avulsion injury: a retrospective study of 73 participants

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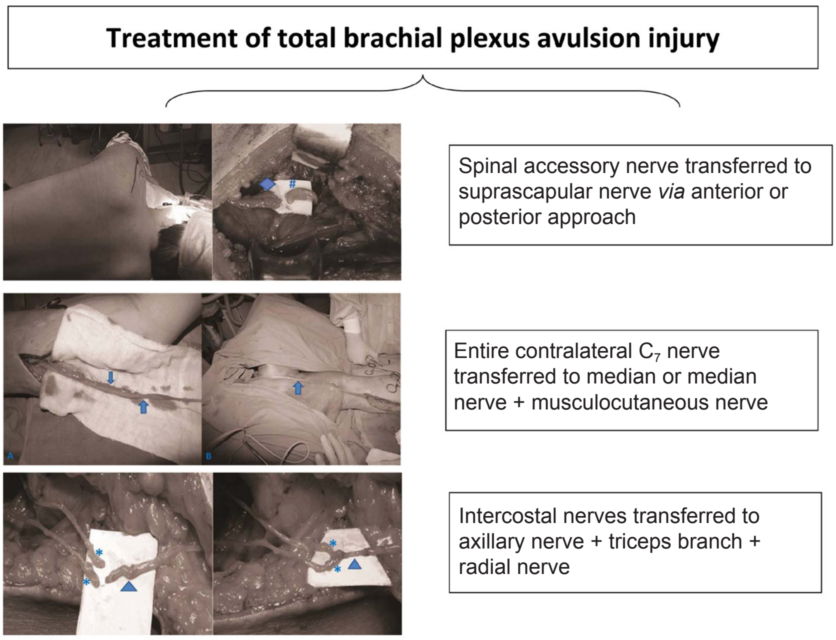
Graphical Abstract

Optimal surgical treatment of total brachial plexus avulsion injury



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Abstract

Despite recent great progress in diagnosis and microsurgical repair, the prognosis in total brachial plexus-avulsion injury remains unfavorable. Insufficient number of donors and unreasonable use of donor nerves might be key factors. To identify an optimal treatment strategy for this condition, we conducted a retrospective review. Seventy-three patients with total brachial plexus avulsion injury were followed up for an average of 7.3 years. Our analysis demonstrated no significant difference in elbow-flexion recovery between phrenic nerve-transfer (25 cases), phrenic nerve-graft (19 cases), intercostal nerve (17 cases), or contralateral C_7-transfer (12 cases) groups. Restoration of shoulder function was attempted through anterior accessory nerve (27 cases), posterior accessory nerve (10 cases), intercostal nerve (5 cases), or accessory + intercostal nerve transfer (31 cases). Accessory nerve + intercostal nerve transfer was the most effective method. A significantly greater amount of elbow extension was observed in patients with intercostal nerve transfer (25 cases) than in those with contralateral C_7 transfer (10 cases). Recovery of median nerve function was noticeably better for those who received entire contralateral C_7 transfer (33 cases) than for those who received partial contralateral C_7 transfer (40 cases). Wrist and finger extension were reconstructed by intercostal nerve transfer (31 cases). Overall, the recommended surgical treatment for total brachial plexus-avulsion injury is phrenic nerve transfer for elbow flexion, accessory nerve + intercostal nerve transfer for shoulder function, intercostal nerves transfer for elbow extension, entire contralateral C_7 transfer for median nerve function, and intercostal nerve transfer for finger extension. The trial was registered at ClinicalTrials.gov (identifier: NCT03166033).

Key Words: *nerve regeneration; brachial plexus-avulsion injury; nerve transfer; phrenic nerve; accessary nerve; contralateral C_7 nerve; intercostal nerve; shoulder function; elbow function; median nerve; radial nerve; neural regeneration*

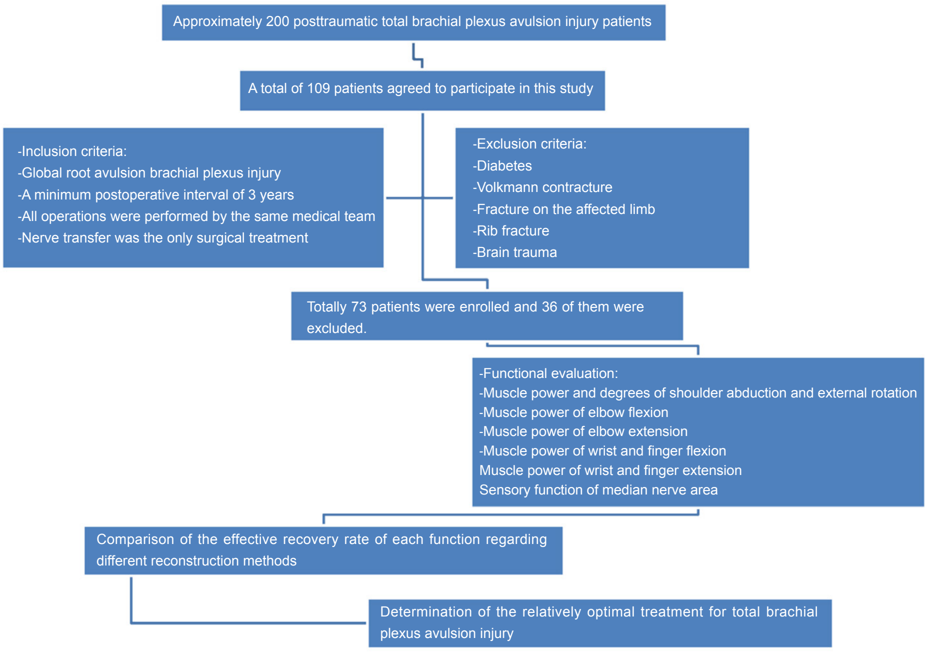

Figure 1 Trial flow chart.

Introduction

Total brachial plexus-avulsion injury (BPAI) is extremely difficult to treat in the clinic (Allieu et al., 1984; Midha, 2004; Shin et al., 2005). Nerve transfer is recognized as the most successful method for treating BPAI (Chuang, 1995; Narakas et al., 1988). The phrenic nerve (Gu et al., 1996; Hou et al., 2002), spinal accessory nerve (SAN) (Songcharoen et al., 1996; Terzis et al., 2006; Rui et al., 2013), intercostal nerve (ICN) (Malessy et al., 1998; Goubier et al., 2011; Gao et al., 2013a, b, c) and contralateral C_7 (cC_7) (Gu et al., 1992, 1998; Chuang et al., 1998, 2012; Gao et al., 2006; Chen et al., 2007) are all commonly used donors, and the surgical technique as well as the effect of treatment are well-established. As previously reported, shoulder function, elbow flexion, elbow extension, and wrist and finger functions have been restored successfully *via* spinal accessory nerve, phrenic nerve, intercostal nerve, and cC_7 transfers. Terzis et al. (2006) reported good or excellent results in 79% of patients for the supraspinatus muscle and in 55% for the infraspinatus muscle when the SAN was transferred to the suprascapular nerve (SSN). Monreal et al. (2007) reported 70% functional recovery of the biceps after phrenic nerve transfer. In another study, Gao et al. (2013a, b, c) reported 56% recovery of the triceps after ICN transfer. They also reported that functional recovery of the median nerve reached 49% for motor function and 63% for sensory function after cC_7 transferred to the median nerve. However, these studies only focused on a few elements of limb function, rather than the restoration of the entire range of limb functions. In different medical groups even within our own department, several different surgical strategies have been used for treating total BPAI, and the results have varied tremendously. Here, we investigated the effectiveness of different commonly used nerve-transfer choices to determine the best surgical strategy for treatment of total BPAI.

Participants and Methods

Participants

This was a retrospective study. The study protocol was approved by the Ethics Committee of Fudan University of China (approval number: 2015-064). From 1999 to 2006, approximately 200 patients with posttraumatic total BPAI underwent surgical exploration and nerve transfer of the brachial plexus. Phrenic nerve transfer was conducted in 115 cases, SAN transfer in 182 cases, ICN transfer in 137 cases and cC_7 transfer in 167 cases. Among these patients, 109 agreed to participate in our study and 73 were ultimately enrolled (**Figure 1**).

Inclusion criteria

Patients presenting with all of the following criteria were considered for study inclusion:
- Global root-avulsion brachial plexus injury
- Postoperative interval ≥ 3 years
- All operations were performed by the same medical team
- Nerve transfer was the only reconstruction method used

Exclusion criteria

Patients with one or more of the following conditions were excluded from this study:
- Diabetes (2 cases)
- Volkmann contracture (3 cases)
- Fracture on the affected limb (humeral fracture in 7 cases, radial fracture in 5 cases, ulnar fracture in 3 cases)
- Rib fracture (11 cases)
- Brain trauma (5 cases)

Evaluation

The recovery of postoperative motor and sensory functions was evaluated by the British Medical Research Council

Table 1 Methods of reconstructing the nerves of the affected limb

	Elbow flexion (*n*)	Shoulder abduction (*n*)	Elbow extension (*n*)	Wrist and finger flexion (*n*)	Wrist and finger extension (*n*)
Phrenic nerve transfer	25				
Phrenic nerve grafted	19				
Spinal accessory nerve transfer (anterior)		27			
Spinal accessory nerve transfer (posterior)		10			
Contralateral C_7 transfer	12		10	73	
Intercostal nerve transfer	17	5	25		31
Spinal accessory nerve + intercostal nerve transfer		31			
Total	73	73	35	73	31

Table 2 Different outcomes for elbow flexion recovery using different reconstruction methods

	Elbow flexion			
Reconstruction methods	Efficient (*n*)	Non-efficient (*n*)	Total (*n*)	Efficacy (%)
Phrenic nerve transfer	21	4	25	84.0
Phrenic nerve grafted	16	3	19	84.2
Intercostal nerve transfer	13	4	17	76.5
Contralateral C_7 transfer	8	4	12	66.7
Total	58	15	73	79.5

Comparisons were performed using chi square tests. Phrenic nerve-transfer group: The phrenic nerve was transferred to upper trunk. Phrenic nerve-grafted group: The phrenic nerve was transferred to the musculocutaneous nerve grafted by the superficial branch of the radial nerve. Intercostal nerve-transfer group: The intercostal nerve was transferred to the musculocutaneous nerve. Contralateral C_7 transfer group: The contralateral C_7 nerve was transferred to the musculocutaneous nerve as well as to the median nerve.

Table 3 Different outcomes for shoulder abduction recovery using different reconstruction methods

	Shoulder abduction			
Reconstruction methods	Efficient (*n*)	Non-efficient (*n*)	Total (*n*)	Efficacy (%)
Spinal accessory nerve transfer (anterior)	21	6	27	*77.8*
Spinal accessory nerve transfer (posterior)	7	3	10	70.0
Intercostal nerve transfer	2	3	5	40.0*
Spinal accessory nerve + intercostal nerve transfer	26	5	31	83.9
Total	56	17	73	76.7

*$P < 0.05$, *vs*. other 3 groups. Comparisons were performed using chi square tests. Spinal accessory nerve-transfer groups (Anterior/Posterior): The spinal accessory nerve was transferred to the suprascapular nerve *via* the anterior or posterior approach. Intercostal nerve-transfer group: The intercostal nerve was transferred to the axillary nerve. Spinal accessory nerve + intercostal nerve-transfer group: The spinal accessory nerve was transferred to the suprascapular nerve and the intercostal nerves were transferred to the axillary nerve.

grading system (John, 1984) in all 73 patients after a minimal interval of 3 postoperative years. In the British Medical Research Council grading system, the motor and sensory function scores are divided into 6 grades from grade 0 to 5. A grade of three or above was regarded as an effective recovery of motor and sensory function. The efficacy rate of a procedure was calculated by dividing the number of effective recoveries for that procedure by the number of times that procedure was used.

Intraoperative findings of the injured brachial plexus

The injured brachial plexus was supraclavicularly explored in all patients under 2.5× magnification (Heine Surgical loupe, Dover, NH, USA). All 73 patients were confirmed to exhibit total BPAI. Using similar approaches, transfer of the phrenic nerve to the musculocutaneous nerve and transfer of the SAN to the SSN could be performed.

Posterior approach for transferring the SAN to the SSN

This surgery was performed with the patient in a lateral position and the affected side upward. An approximately 10 cm long transverse incision was made over the scapular spine. The trapezius insertion on the scapular spine was divided. The trapezius was then retracted upwards and the SAN was exposed. The SSN located in the suprascapular notch under the transverse ligament of the scapula was then identified and isolated. The SSN was divided as far proximally as possible for transfer (**Figure 2**).

cC7 transfer

The cC_7 nerve transfer procedure was separated into two stages. The first stage was conducted by two teams simultaneously. One team explored the normal brachial plexus. The cC_7 nerve was exposed to its division level and a longitudinal epineurotomy was performed in the division to expose the constituent bundles. The other team transected the ulnar nerve at the level of the wrist on the affected limb and the full-length ulnar nerve was harvested. The ulnar nerve was vascularized by the superior ulnar collateral artery from the level of the elbow. The vascularized ulnar nerve was then passed across the chest through a subcutaneous tunnel to the normal neck. The partial or entire cC_7 nerve was coapted to the ulnar nerves at 4× magnification (Heine Surgical loupe) with 8-0 microsutures.

In the second stage, the ulnar nerve on the affected side was neurotized into different recipient nerves. A longitudinal epineurotomy was performed on the ulna if it was going to be transferred to two recipient nerves simultaneously (**Figure 3**).

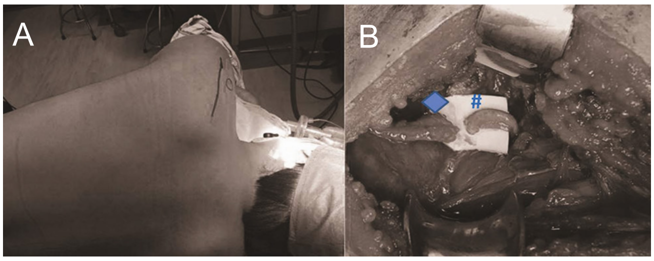

Figure 2 A patient under general anesthesia in the lateral position (A) and the skin incision superior to the scapular spine (B).
The trapezius and the supraspinatus muscle were retracted and then the spinal accessory nerve (◆) was coapted to the suprascapular nerve (#) with no tension.

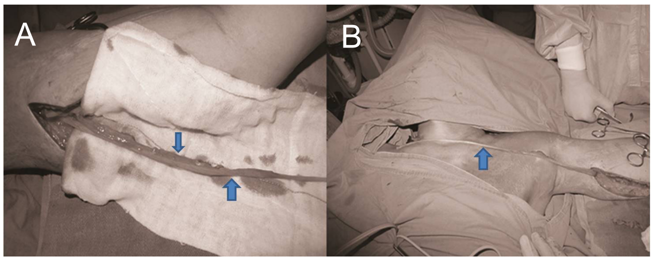

Figure 3 Preparation of the pedicled ulnar nerve graft.
(A) The ulnar nerve (↑) of the affected upper limb was transected at the wrist level and the full-length nerve pedicled by the superior ulnar collateral artery (↓) was harvested. (B) The measurement of the ulnar nerve (↑) to the contralateral neck.

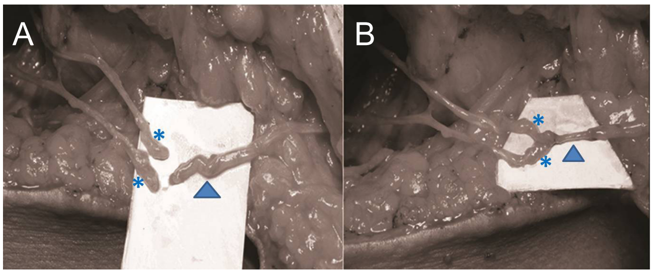

Figure 4 Intercostal nerve harvesting.
(A) Two intercostal nerves (*) and the long head of the triceps branch (▲) were harvested. (B) Two intercostal nerves (*) were directly coapted to the long head of the triceps branch (▲) with no tension in the axilla with the arm in full abduction.

Intercostal nerve harvesting

A continuous thoraco-brachial incision was performed in axilla, the lateral chest, and the arm. The thoracic part of the incision began from the inferior axilla and followed the curve of the anterior border of the latisimus dorsi muscle. The arm part of the incision was performed on the medial side of the arm.

The ICNs were exposed in the chest incision. The latisimus dorsi muscle and the serratus anterior muscle, as well as the periosteum of the ribs, were reflected and the intercostal nerves were exposed. The periosteum was detached and pulled downward to expose its posterior aspect, and the thin motor branch of each ICN was identified and harvested, while the split sensory branch was left inside (**Figure 4**). The numbers of ICNs harvested depended on the recipient nerves.

Reconstruction methods

The phrenic nerve was transferred to upper trunk in 25 patients and grafted to the musculocutaneous nerve in 19 patients. The SAN was transferred to the SSN *via* an anterior approach in 49 patients and *via* a posterior approach in 19 patients. The cC_7 was transferred to the median nerve in 51 patients, to the median + musculocutaneous nerves in 12 patients, and to the median nerve + the triceps branch in 10 patients. Two ICNs were transferred to the musculocutaneous nerve in 19 patients, to the axillary nerve in 36 patients, and to the radial nerve in 31 patients. Two or three ICNs were transferred to the triceps branch in 25 patients (**Table 1**).

Postoperative rehabilitation

Immediately after the operation, the affected limb was immobilized for 4 weeks. Physiotherapy began at 5 weeks to prevent joint contractures. Patients were also asked to breathe deeply, raise their shoulders, and to adduct their shoulders against resistance since contraction of the latissimus dorsi muscle of the healthy side.

Statistical analysis

All data were analyzed with Stata 13.0 software (Stata Corp, Baltimore, MD, USA). Data are expressed as percentages. Comparisons among postoperative groups were performed using chi-square tests. *P* values less than 0.05 were considered statistically significant.

Results

Changes in the rates of functional recovery after surgery

Among the 73 patients, 79.45% (58/73) exhibited effective recovery for elbow flexion, 76.71% (56/73) for shoulder abduction, 45.71% (16/35) for elbow extension, 38.71% (12/31) for wrist and finger extension, 54.79% (40/73) for wrist and finger flexion, and 57.53% (42/73) for the sensation around the median nerve. No complications were found in any patient.

Postoperative functional recovery

Patients were divided into groups according to the reconstruction method and rates of functional recovery for each category were determined for each group.

For elbow-flexion function, the efficacy rate was 84% (21/25) in phrenic nerve-transfer group, 84.21% (16/19) in phrenic nerve-grafted group, 76.47% (13/17) in the ICN transfer group, and 66.67% (8/12) in the cC_7 transfer group. There was no statistically significant difference in efficacy between the groups ($P > 0.05$; **Table 2**).

For shoulder-abduction function, the efficacy rate was 77.78% (21/27) in the anterior SAN-transfer group, 70% (7/10) in the posterior SAN-transfer group, 40% (2/5) in the group of ICNs transferred to the axillary nerve, and 83.87% (26/31) in the SAN + ICNs transfer group. Analysis showed that the efficacy rate for the group of ICNs transferred to the axillary nerve was significantly worse than that for the other groups ($P < 0.05$; **Table 3**).

Table 4 Different outcomes for median nerve functional recovery using different donor nerves

	Entire cC_7					
	One recipient		Two recipients		Partial cC_7	
	Motor (*n*)	Sensory (*n*)	Motor (*n*)	Sensory (*n*)	Motor (*n*)	Sensory (*n*)
Efficient	9	9	15	10	16	23
Non-efficient	2	2	7	12	24	17
Total	33				40	

Comparisons were performed using chi square tests. One-recipient group: The entire cC_7 nerve was transferred to the median nerve. Two-recipient group: The entire cC_7 nerve was simultaneously transferred to the median nerve and to an additional nerve. Partial cC_7 group: a portion of the cC_7 nerve was transferred to the median nerve. cC_7: Contralateral C_7.

Table 5 Different outcomes for elbow extension recovery using different reconstruction methods

	ICNs transfer			
	Two ICNs (*n*)	Three ICNs (*n*)	cC_7 transfer (*n*)	Total (*n*)
Efficient	10	4	2*	16
Non-efficient	8	3	8	21
Total	25		10	35

*$P < 0.05$, *vs.* the two-ICNs and three-ICNs groups. Comparisons were performed using chi square tests. Two/Three-ICNs groups: Two or Three ICNs were transferred to the triceps branch. cC_7-transfer group: The cC_7 nerve was transferred to the triceps branch in addition to the median nerve. ICNs: Intercostal nerves; cC_7: contralateral C_7.

For the transfer of the cC_7 to the median nerve, the entire cC_7 root was used in 33 patients (22 underwent the transfer of the cC_7 to two recipient nerves simultaneously) and a partial cC_7 root was used in 40 patients. The motor function recovery for the entire-C_7 group was significantly better than that for the partial C_7 group ($P < 0.05$; **Table 4**). However, we found no statistically significant difference in the recovery of sensory function between the groups ($P > 0.05$; **Table 4**).

For elbow-extension function, the efficacy rate was 56% (14/25) in the ICNs-transfer group and 20% (2/10) in the cC_7-transfer group (cC_7 transfer to the median nerve + triceps branch). Analysis showed that these efficacy rates were significantly different ($P < 0.05$; **Table 5**).

For wrist- and finger-extension function, ICN transfer was conducted in 31 patients and the efficacy rate was 51.61% (16/31).

Discussion

At present, the most successful method of restoring affected limb function in patients with total BPAI is nerve transfer (Seddon, 1963; Panupan, 1995). In our department, the surgical order for function restoration in patients with BPAI is elbow flexion, shoulder abduction and external rotation, elbow extension, wrist and finger flexion, and wrist and finger extension (Gu et al., 1984).

The commonly used reconstruction methods for restoring elbow flexion are phrenic nerve transfer (with or without grafting the nerve) (El-Gammal et al., 2002), ICN transfer (Ploncard, 1982; Nagano, 2001) and cC_7 nerve transfer (Gu et al., 2002; Wang et al., 2012; Gao et al., 2013a,b,c; Hu et al., 2014; Yang et al., 2015). In the current study, all four reconstruction methods were used and no statistically significant difference was found in the rates of effective recovery. However, the cC_7 group was special in that the cC_7 was transferred simultaneously to the median nerve and the musculocutaneous nerve. In this group (12 patients), the effective recovery rates for the two recipient nerves were both acceptable (66.67% for elbow flexion and 75% for wrist and finger flexion). This suggests that simultaneous transfer of the entire root of the cC_7 nerve to the musculocutaneous and median nerves could be a good option for treating total BPAI because the median nerve and biceps branch are collaborative in motor functions (Terzis et al., 2009; Zou et al., 2010; Gao et al., 2013a, b, c).

For shoulder function, the most commonly used donor nerves are the SAN (Terzis et al., 2006) and ICNs (Terzis et al., 2006). In the current study, four different methods were used to reconstruct the shoulder and restore function, including anterior transfer of the SAN to the SSN, posterior transfer of the SAN to the SSN, transfer of ICNs to the axillary nerve, and transfer of the SAN to the SSN combined with transfer of ICNs to axillary nerve. According to the British Medical Research Council scale, the efficacy of ICN transfer to the axillary nerve was only 40%, which was significantly worse than the other groups. This unsatisfactory result might have occurred because restoration of deltoid function alone could not provide enough stability for the glenohumeral joint, which is important for shoulder abduction. No statistically significant difference in efficacy was found between anterior and posterior transfers of the SAN to the SSN. Rui et al. (2013) conducted an electrophysiological study to compare the effectiveness of anterior and posterior approaches of SAN transfer to the SSN. Similar to the current study, they found no significant difference between approaches in the time it took for the infraspinatus to show low-incidence motor unit action potentials and an incomplete interference pattern. Additionally, the final percentage of patients that showed potential regeneration of the infraspinatus did not significantly differ between the approaches. Our experience is that the anterior approach is more commonly used because it can be performed at the same time as brachial plexus exploration. Nevertheless, if a scapular fracture occurs, the posterior approach is recommended because the SSN might be injured by the fracture and need a surgical exploration. In this study, we found no difference between the recovery in SAN-transfer (anterior and posterior) group and the SAN + ICNs group. However, the efficacy of shoulder abduction regarding the power of the target muscle does not accurately reflect the recovery of shoulder function. Using the degrees of abduction and external rotation might be better criteria. In the anterior and posterior SAN-transfer groups, patients achieved an average shoulder abduction of 45° and an average external rotation of 10°. Recovery in the SAN + ICNs transfer group was markedly better, with the average shoulder abduction reaching 70° and the average external rotation reaching 30°. Cardenas-Mejia et al. (2008) reported that the average degree of shoulder abduction was 160° following triple-nerve transfers, 85° following double-nerve transfers, and 65° following single-nerve transfers. Average shoulder abduction following either double-nerve or triple-nerve transfer was significantly greater than that achieved by single-nerve transfer. Thus, increasing the number of donor nerves appears to improve shoulder function and using the method that combines SSN and ICNs transfer is recommended for reconstructing the shoulder and restoring function.

For elbow extension, the usual treatment plan is to use the ICNs for direct transfer to the nerve of the long head of the triceps (Gao et al., 2013a, b, c), while in some special cases, the cC_7 nerve is transferred simultaneously to the median nerve and triceps branch (Gao et al., 2013a, b, c). In the current study, the efficacy was 56% (14/25) in the ICNs-transfer group, but only 20% (2/10) in the cC_7-transfer group (cC_7transfer to the median nerve + triceps branch), which was a statistically significant difference. The median nerve and triceps branch were not collaborative for motor function, which might lead to poor recovery of triceps. In the ICNs group, two ICNs were used in 18 patients, and three ICNs in 7 patients. The recovery rate for the long head of the triceps was 55.56% in the two-ICNs group and 57.14% in the three-ICNs group, which was not a statistically significant difference. According to previous studies, the number of nerve fibers in the ICN is relatively small at approximately 500–700; however, the use of all motor fibers guaranteed the quality of the donor.

Wrist- and finger-extension function was restored by ICNs with an efficacy reaching 51.61%. Most surgeons chose the ICN as the donor because wrist- and finger-extension functions are collaborative with elbow extension and because they are both innervated by the radial nerve. The ICN seems to be the relatively optimal donor for the triceps and using the same donor nerve to reconstruct these two functions is reasonable.

cC_7 nerve transfer is the most commonly used method for restoring function to the median nerve (Wang et al., 2011, 2013; Gao et al., 2013a, b, c) because it contains many axons (Gu, 1994). However, some surgeons have recommended using only a portion of the cC_7 nerve (not the entire root) as the donor nerve to conserve more of the healthy limb's sensory function (Sungpet et al., 1999; Gao et al., 2010). In the present study, three different ways were used to harvest cC_7, including the entire root, 3/4 root, and half root. As shown in **Table 4**, functional recovery for the whole-root cC_7-transfer group was much better than that for the partial cC_7-transfer group. Previous studies also reported similar results, indicating that transferring the entire cC_7 nerve results in dramatically better recovery of median nerve function than transferring a partially harvested cC_7 nerve (Waikakul et al., 1999; Panupan et al., 2001; Sammer et al., 2012; Tu et al., 2014). Using the entire cC_7 nerve provides a large number of donor nerve fibers and thus promotes recovery. Anatomic variation in the C_7 nerve root might erroneously lead a surgeon to use more sensory fascicles as donors than motor fascicles (Hierner et al., 2007). The functional reorganization of the cerebral cortex should be another important factor for consideration, especially the postoperative transhemispheric functional reorganization of the motor cortex (Sanes et al., 1997; Lou et al., 2006; Pan et al., 2012; Yang et al., 2017). However, this topic is still being actively researched. Despite the unknown mechanism, we strongly emphasize using the entire root as the donor rather than the partial fascicles. Our results showed that the cC_7 was also used to repair an additional recipient nerve together with the median nerve, without adversely affecting the recovery of the median nerve.

Although this study has a few limitations, such as being a retrospective study and having relatively low sample sizes, we can still preliminarily conclude that for total BPAI, optimal surgical treatment is phrenic nerve transfer for elbow flexion, SAN combined with ICNs transfer for shoulder function, ICNs transfer for elbow extension, entire cC_7 transfer for median nerve function and ICNs transfer for finger extension. For older people or those whose phrenic nerve is unfit to be the donor, we recommend SAN combined with ICNs transfer for shoulder function, entire cC_7 transfer for elbow flexion and median nerve function, and ICNs transfer for elbow extension and wrist and finger extension.

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Research ethics: *The study protocol was approved by the Ethics Committee of Fudan University of China (approval number: 2015-064). The trial was registered at ClinicalTrials.gov (identifier: NCT03166033).*
Declaration of participant consent: *The authors certify that they have obtained all appropriate patient consent forms. In the form, participants have given their consent for their images and other clinical information to be reported in the journal. Participants understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.*
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