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Phrenic nerve transfer to the musculocutaneous nerve for the repair of brachial plexus injury: electrophysiological characteristics

Ying Liu[1,*], Xun-cheng Xu[1], Yi Zou[1], Su-rong Li[1], Bin Zhang[2], Yue Wang[2]

1 Department of Neurology, Sichuan Academy of Medical Sciences and Sichuan Provincial People's Hospital, Chengdu, Sichuan Province, China
2 Department of Orthopedics, Sichuan Academy of Medical Sciences and Sichuan Provincial People's Hospital, Chengdu, Sichuan Province, China

Correspondence to:
Ying Liu, binfen_1220@163.com.

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Abstract

Phrenic nerve transfer is a major dynamic treatment used to repair brachial plexus root avulsion. We analyzed 72 relevant articles on phrenic nerve transfer to repair injured brachial plexus that were indexed by Science Citation Index. The keywords searched were brachial plexus injury, phrenic nerve, repair, surgery, protection, nerve transfer, and nerve graft. In addition, we performed neurophysiological analysis of the preoperative condition and prognosis of 10 patients undergoing ipsilateral phrenic nerve transfer to the musculocutaneous nerve in our hospital from 2008 to 201 3 and observed the electromyograms of the biceps brachii and motor conduction function of the musculocutaneous nerve. Clinically, approximately 28% of patients had brachial plexus injury combined with phrenic nerve injury, and injured phrenic nerve cannot be used as a nerve graft. After phrenic nerve transfer to the musculocutaneous nerve, the regenerated potentials first appeared at 3 months. Recovery of motor unit action potential occurred 6 months later and became more apparent at 12 months. The percent of patients recovering 'excellent' and 'good' muscle strength in the biceps brachii was 80% after 18 months. At 12 months after surgery, motor nerve conduction potential appeared in the musculocutaneous nerve in seven cases. These data suggest that preoperative evaluation of phrenic nerve function may help identify the most appropriate nerve graft in patients with an injured brachial plexus. The functional recovery of a transplanted nerve can be dynamically observed after the surgery.

Key Words: *nerve regeneration; phrenic nerve; brachial plexus injury; nerve transfer; nerve repair; musculocutaneous nerve; nerve function test; bibliometrics; neural regeneration*

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Introduction

The brachial plexus is composed of anterior branches of the fifth, sixth, seventh, and eighth cervical nerves and the anterior branch of the first thoracic nerve. The brachial plexus is the origin of the upper extremity nerve and shows a very high rate of disability after injury. Since Smeeiil described an injured brachial plexus in 1765, its repair after injury has been a problem for the medical profession (Stirrat and Taylor, 2002). The avulsion of the brachial plexus root always occurs in the intervertebral foramina on the surface of spinal cord, and no stump is available for involution. Moreover, the avulsion site is in close proximity to the spinal neurons and frequently results in the loss of many spinal neurons. The remaining impaired spinal neurons cannot synthesize adequate nutrients for axonal regeneration. The transfer of a healthy nerve is a feasible method for repairing an injured brachial plexus. Currently, the nerves used to repair elbow flexion contain the C_7, intercostal nerves, accessory nerve, phrenic nerve, and motor branch of the cervical plexus on the uninjured side. Compared with these many nerves, the phrenic nerve has thick motor nerve fibers and the unique advantage of showing high-frequency large-amplitude spontaneous electrophysiological activity (Pamphlett et al., 1996; Banneheka, 2008). Monreal (2008) reported that the phrenic nerve contains adequate power fibers and at least 800 neurons. For these reasons, it is recognized as the best power nerve for transfer by the academic community. Moreover, supraclavicular phrenic nerve transposition did not adversely impact pulmonary function (Zhang and Gu, 1994; Deng et al., 2002). Therefore, phrenic nerve transposition is widely considered the best method for nerve transfer (Samardzic, 1992). Gu (2001) from the Chinese Academy of Engineering has used phrenic nerve transposition on the clavicle to treat brachial plexus injury since 1970 with an effective rate of

84.6% after follow-up in 164 patients. Dong et al. (2007) followed 42 patients undergoing phrenic nerve transposition to restore elbow flexion for a long time, showing a total effective rate of 82.5%. Thus, phrenic nerve transplantation is an effective method for restoring elbow flexion. Xu and Gu (2000) reported performing a full-length phrenic nerve transposition to repair the musculocutaneous nerve using thoracoscopy, effectively using the phrenic nerve in the thoracic cavity, which greatly reduced the distance between the nerve regeneration and biceps brachii. Moreover, the time for neurological recovery was shortened after the transplantation.

The normal functioning of the phrenic nerve plays a key role in the therapeutic effect of phrenic nerve transposition. If injury to the brachial plexus involves damage to the phrenic nerve, its function is damaged and should not be used. Thus, preoperative evaluation of the phrenic nerve is very important. The following functions should be evaluated: diaphragmatic elevation, diaphragm height index (Pornrattanamaneewong et al., 2012), diaphragmatic activity observed by X-ray fluoroscopy, pulmonary function test, and phrenic nerve contraction after electrical stimulation during transplantation. In addition, ultrasonic imaging can also clearly show the phrenic nerve and the adjacent structures (Kessler et al., 2008; Canella et al., 2010). The goal of the present article was to analyze in detail the relevant articles indexed by Science Citation Index (SCI) that address phrenic nerve transposition for the repair of brachial plexus injury. In addition, we performed neurophysiological analysis of the preoperative condition and prognosis of 10 patients undergoing ipsilateral phrenic nerve transfer to the musculocutaneous nerve from 2008 to 2013 in our hospital by investigating the electrophysiological characteristics of the phrenic nerve transfer to the musculocutaneous nerve after brachial plexus injury.

Data and Methods

Data source

Retrieval database: SCI.

Retrieval keywords: Brachial plexus injury, phrenic nerve, repair, surgery, protection, nerve transfer, nerve graft.

Number of retrieved articles: 72.

Selection criteria

Inclusion criteria: Peer-reviewed articles on brachial plexus injury; articles on phrenic nerve transfer for the repair of brachial plexus injury.

Exclusion criteria: Irrelevant articles; unpublished articles; obsolete research; articles that are only available by phone tracking and manual searches.

Indexes

Analyses were performed for: (1) citations of articles on phrenic nerve transfer for the repair of injured brachial plexus; (2) the countries and regions where many relevant articles were published; (3) the institutions that issued many of the articles; (4) the journals that published many of the articles; (5) the foundations that supported many of the studies; and (6) the clinical cases in our own hospital.

Results

Analysis of articles indexed by SCI concerning phrenic nerve transfer for the repair of injured brachial plexus

Citations for the nine individual articles retrieved on phrenic nerve transfer for the repair of injured brachial plexus are listed in **Table 1**.

From these nine articles, we determined that the height of interest in nerve transfer for the repair of injured brachial plexus occurred around the year 2000. An article titled *Restoration of shoulder abduction by nerve transfer in avulsed brachial-plexus injury: evaluation of 99 patients with various nerve transfers* was published by *Plastic and Reconstructive Surgery* in 1995 and has been cited 100 times (Chuang et al., 1995). In this article, the authors described the use of donor nerves (intercostal nerve, phrenic nerve, accessory nerve, and C_7 on the affected side) for rebuilding the C_5, C_6, and C_7; the recovery of elbow flexion, shoulder abduction, and external rotation induced by brachial plexus injury; and solved the problem that the proximal end cannot be used for transplantation. Chuang et al. (1993) published an article titled *Functional restoration of elbow flexion in brachial plexus* injuries: *results in 167 patients* (excluding obstetric brachial-plexus injury) in the *Journal of Hand Surgery-American Volume* in 1993 that has been cited 77 times. In this article, the authors compared the transfer of intercostal nerve, phrenic nerve, accessory nerve, muscle, or tendon for the repair of injured brachial plexus. The results suggested that reconstruction with nerves is better than with tendon transfers, direct suture is better than nerve grafts, short nerve grafts (< 10 cm) are better than longer nerve grafts (> 10 cm), vascularized ulnar nerve grafts are better than conventional long nerve grafts, and the recovery after ruptured nerve injury is better than that after root avulsion. Gu and Ma (1996) published an article titled *Use of the phrenic nerve for brachial plexus reconstruction in Clinical Orthopaedics and Related Research* in 1996 that has been cited 71 times.

The countries where many of the articles on phrenic nerve transfer for the repair of brachial plexus injury were published are shown in **Figure 1**.

The institutions that have published articles on phrenic nerve transfer for the repair of brachial plexus injury that are indexed by SCI are shown in **Figure 2**.

The journals that have published articles on phrenic nerve transfer for the repair of brachial plexus injury that are indexed by SCI are shown in **Table 2**.

The largest number of related articles were published in *Microsurgery* (14 articles, 19.44%), followed by the *Journal of Neurosurgery* (10 articles, 13.89%) and *Neurosurgery* (seven articles, 9.72%). Other journals each published fewer than five articles each.

The foundations that have supported many of the articles on phrenic nerve transfer for the repair of brachial plexus injury that are indexed by SCI are listed in **Table 3**.

Among the articles on phrenic nerve transfer for the repair of brachial plexus injury that are indexed by SCI, 17 articles were funded by foundations. Most funds were from China, including the National Program on Key Basic Research Project of China (973 Program), National Natural Science Foundation of China, Program for New Century Excellent Talents in Universities of China, Shanghai Municipal Education Commission of China, Shanghai Scientific and Technological Commission of China, Hand Function Research Center in Fudan University, China, Hand Surgery Department in Huashan Hospital, China, Chang Gung Medical Research Program, China, and Military Medicine and Health Research Foundation of China. The other two articles were funded by foundations in Saudi Arabia and Spain. The remaining 55 articles did not report the funding source.

Clinical cases of phrenic nerve transfer for the repair of injured brachial plexus

From June 2008 to August 2013, phrenic nerve function was assessed in 50 patients suffering from brachial plexus injury in our hospital. The patients included 46 males and four females aged 15–63 years, with an average age of 35.5 years. Of the patients, 36 were injured in traffic accidents, 12 were injured by falling (six cases in an earthquake), and two were bruised. The types of brachial plexus injury were complete brachial plexus avulsion in 17 cases, partial brachial plexus avulsion in 13 cases, and postganglionic injury of the brachial plexus roots in 20 cases. A control group consisted of 20 healthy people from the Health Management Center of the Hospital. No significant differences in gender or age were found between the two groups. A Danish Keypoint electromyography was used to assess the phrenic nerve. Surface electrodes were used to record the potentials on the anterior axillary line between the seventh and eighth ribs. Stimulation was conducted at the junction of the trailing edge of the sternocleidomastoid and the clavicle with a pulse length of 0.2 ms and a frequency of 1 Hz. The stimulation current was strong. The results of the phrenic nerve motor function were recorded, and the latent period and the amplitude of the movement were measured.

For phrenic nerve transplantation, free phrenic nerves were isolated and removed. End-to-end anastomosis was performed to connect the phrenic nerves to the trunk or branches of the musculocutaneous nerves. In this way, the elbow bending function of the biceps can only be restored using the transfer of phrenic nerves. Postoperative follow-up observations were made for 18–75 months, with an average follow-up time of 45.5 months. Electromyography at 3 months after the operation using concentric needle electrodes for recording showed for the first time the insertion potential of the biceps on the affected side, *i.e.*, the regenerative potential under resting conditions; the time limit and the amplitude of the motor nerve under slight contraction; and the motor unit number under strong movement. One follow-up observation was made with electromyography every 3 months for 1 year, then every 6 months for 3 years, and finally once per year.

The musculocutaneous nerves were measured with electromyography at 12 months after the operation. Surface electrodes were placed on the center of the biceps to record the electromyography while the stimulating electrode was placed 20 cm away from the recording point on the brachial plexus at Erb's point. The latent period and the amplitude of the movement of the musculocutaneous nerves were recorded during stimulation. A follow-up observation was made once at 6 months or at 1 year.

The phrenic nerve function was determined bilaterally in the group of patients suffering from brachial plexus injury, showing that there were 11 cases of conduction abnormality, three cases of conduction loss, and 28% of the patients suffered from both brachial plexus nerve injury and phrenic nerve injury.

The 10 patients with normal phrenic nerve function in this group were treated with transplantation operations in which the ipsilateral phrenic nerves were transplanted in place of the musculocutaneous nerves. The evaluation of the patients was performed as described in a previous study (Gu, 1990).

The 10 patients were examined by muscle electromyography for the first time at 3 months after the transplantation of phrenic nerves in place of the musculocutaneous nerves, and then every 3 months. The electromyographies from the first three examinations (at 3, 6, and 9 months after the operation) showed extended latent period of the insertion potential in five patients and a regenerated potential in two patients, which appeared as early as 3 months after the operation. In addition, positive sharp waves and fibrillation potentials were found in five cases, with only a few showing motor unit potential under slight contraction with a motor unit number of about 3–10 under slight autonomic contraction during each frequency window (3 seconds). The electromyographies from the fourth and fifth reexaminations (at 12 and 18 months after the operation) showed regenerated potentials and a significant increase in the number of motor unit potentials under slight contraction in five patients, with the number of motor units increased to about 20–50 under slight autonomic contraction during each frequency window (3 seconds). Further, a normal time limit was found in three cases, an extended time limit in seven cases, decreased amplitudes in five cases, mixed phases in five cases, four cases were monophase, and no motor unit potential under strong contraction was found in one case. The musculocutaneous nerve motor conduction function was determined at 12 months after the surgery to avoid the influence of the measurement on the transplanted nerves because of the strong stimulation and short time interval used. Seven cases showed motor nerve potential; six of these showed extended latent periods of movement and all seven showed decreased amplitudes. A significant improvement was found when comparing the cases after the operation with beforehand, when they showed no motor compound potentials, but a statistically significant difference compared with the healthy side remained.

Discussion

The goal of this study was to explore the published articles on phrenic nerve transfer for the repair of injured brachial plexus using bibliometrics. Nerve transposition remains the

Table 1 Articles cited at least 30 times on nerve transfer for the repair of injured brachial plexus indexed by Science Citation Index

Author	Title	Journal	Publication year	Total citation
Chuang et al. (1995)	Restoration of shoulder abduction by nerve transfer in avulsed brachial-plexus injury: evaluation of 99 patients with various nerve transfers	*Plastic and Reconstructive Surgery*	1995	100
Chuang et al. (1993)	Functional restoration of elbow flexion in brachial-plexus injuries: results in 167 patients (excluding obstetric brachial-plexus injury)	*Journal of Hand Surgery-American Volume*	1993	77
Gu and Ma (1996)	Use of the phrenic nerve for brachial plexus reconstruction	*Clinical Orthopaedics and Related Research*	1996	71
Songcharoen (1995)	Brachial-plexus injury in Thailand: a report of 520 cases	*Microsurgery*	1995	55
El-Gammal et al. (2002)	Outcomes of surgical treatment of brachial plexus injuries using nerve grafting and nerve transfers	*Journal of Reconstructive Microsurgery*	2002	51
Waikakul et al. (1999)	Clinical results of contralateral C_7 root neurotization to the median nerve in brachial plexus injuries with total root avulsions	*Journal of Hand Surgery-British and European Volume*	1999	51
Amr and Moharram (2005)	Repair of brachial plexus lesions by end-to-side side-to-side grafting neurorrhaphy: experience based on 11 cases	*Microsurgery*	2005	33
Xu et al. (2002)	Full-length phrenic nerve transfer by means of video-assisted thoracic surgery in treating brachial plexus avulsion injury	*Plastic and Reconstructive Surgery*	2002	30
Luedemann et al. (2002)	Brachial plexus neurotization with donor phrenic nerves and its effect on pulmonary function	*Journal of Neurosurgery*	2002	30

Table 2 Seven journals that have published at least three articles on phrenic nerve transfer for the repair of brachial plexus injury indexed by Science Citation Index

Journal	Number of articles	Percentage of all articles (%)
Microsurgery	14	19.44
Journal of Neurosurgery	10	13.89
Neurosurgery	7	9.72
Journal of Hand Surgery-American Volume	4	5.56
Journal of Hand Surgery-British and European Volume	4	5.56
Plastic and Reconstructive Surgery	4	5.56
Journal of Reconstructive Microsurgery	3	4.17

best choice for the repair of brachial plexus injury up to now. The studies reviewed mainly focused on transposition after C_5–C_6 brachial plexus evulsion. In the last 10 years, the number of articles published concerning phrenic nerve transfer for the repair of injured brachial plexus has been stable and not very high. The highly cited articles were published earlier, in the 1990s. More papers are published on this topic from China, and supported by Chinese institutions, than anywhere else in the world. The large number of publications in China has played an important role in guiding the research in this field. Fudan University and its affiliated Huashan Hospital in China are key institutions related to this research field. Because the Chinese government and certain academic institutions pay more attention to this work, the number of Chinese foundations working in this area is large.

The analysis of clinical cases in the present study showed the significance of preoperative determination of the phrenic nerve conduction function in patients suffering from brachial plexus injuries. As shown in **Table 1**, brachial plexus injury may simultaneously damage the phrenic nerve. Among the 50 patients with unilateral brachial plexus injuries, 14 (28%) had related phrenic nerve injuries, and the brachial plexus injuries of these patients were more severe. Phrenic nerves are fibers of the anterior branch of the $C_{3–5}$ spinal nerves, and the brachial plexus consists of C_5–T_1 nerves. Because they do not derive from the same level of innervation, they are not normally injured at the same time during trauma, unless the injury is very severe. The most common form of brachial plexus injury is nerve root avulsion. For neural transplantation, the contralateral C_7, accessory nerves, and other nerves should be chosen as motor nerves instead of the ipsilateral phrenic nerve. Functional examination of the phrenic nerves can determine the extent of injury and help in selecting the operation method and choice of motor nerves for transplantation.

After phrenic nerve transplantation, electrophysiological tracking was conducted for 18–75 months, with an average follow-up time of 38 months. The biceps were observed at 3 months after muscle transplantation, and muscle electromyography was taken once every 3 months. Seven patients continued to lose nerve potential during the first three sessions of muscle electromyography, and the first regenerated potential in a patient occurred at 3 months after the surgery, but only a small amount of motor unit potential was generated. The fourth and the fifth muscle electromyograms taken at 12 and 18 months after the surgery showed an increase in the

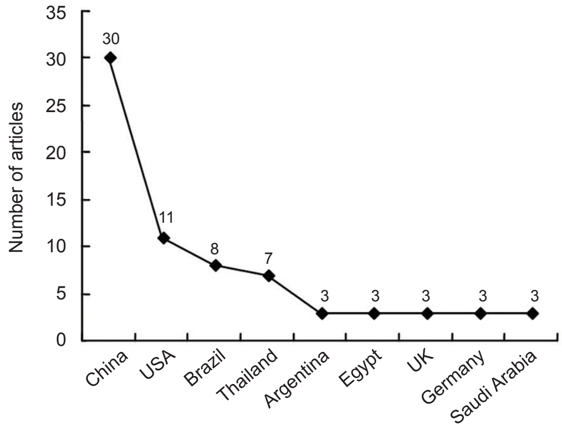

Figure 1 Countries that have published more than two papers on phrenic nerve transfer for the repair of brachial plexus injury indexed by Science Citation Index.
The greatest number of related articles was from China (30 articles, 41.66%), followed by the USA and Brazil.

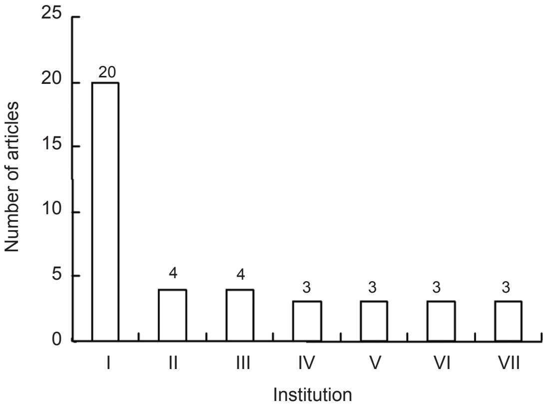

Figure 2 Institutions that have published articles on phrenic nerve transfer for the repair of brachial plexus injury indexed by Science Citation Index.
The greatest number of related articles was from Fudan University in China (20 articles), followed by Chang Gung Memorial Hospital in Taiwan of China (four articles) and Mahidol University in Thailand (four articles). I: Fudan University; II: Chang Gung Memorial Hospital; III: Mahidol University; IV: Governador Celso Ramos Hospital; V: King Saud University; VI: Second Military Medical University; VII: University of Buenos Aires.

regenerated potentials and a significant increase in the number of motor units. In this group, 80% of patients had good recovery of the musculocutaneous nerve functions in an assessment taken 48 months after the surgery, with only two cases being not ideal or satisfactory. During observation after the transplantation of phrenic nerves onto musculocutaneous nerves and elbow flexion function restoration, myodynamia was restored slowly, taking 10 to 12 months to reach level 2. However, the time required to restore myodynamia to levels 3 or 4 from level 2 was shorter, generally requiring 2–3 months. This difference is likely because more regenerative nerve fibers had reached the recipient area. At 18 months after transplantation, the recovery of myodynamia had not significantly improved further. The relatively small number of phrenic nerve fibers and limited number of regenerative nerve fibers may explain this result. The electrophysiological assessment of nerves was conducted at 12 months after the surgery, and nerve latency was highly associated with amplitude and myodynamia. Patients showing good recovery had shorter latent periods and higher amplitudes, while those with poor recovery had longer latent periods and lower amplitudes or could not even generate nerve action potentials. The recovery of muscle function was found to depend on the time between injury and surgery. For example, the patients whose operations were performed within 3 months after the injury had better recovery than those whose operations were performed more than 6 months after the injury, and the recovery of the latter cases was unsatisfactory (Samii et al., 2003). Because younger patients had better recovery, it is believed that age significantly affects nerve regeneration and functional recovery (Verdu et al., 2000; Chen et al., 2007). Active postoperative exercise of the brachial plexus is also conducive to better nerve recovery (Bahm et al., 2009). In addition, the functional recovery of the injured brachial plexus is closely related to the type of injury. Cases of full brachial plexus injury and root avulsion had a poor prognosis (Kirjavainen et al., 2008). The failure of neural transplantation for brachial plexus injury to achieve an ideal recovery is likely caused by many factors. Therefore, neural electrophysiologists should actively cooperate with clinicians, accumulate more experience, create favorable conditions, and closely observe nerve repair to improve the effective rate of

Table 3 Foundations that have supported articles on phrenic nerve transfer for the repair of brachial plexus injury indexed by Science Citation Index

Funding	Number of articles	Percentage of all articles (%)
National Program of Key Basic Research Program China (973 Program)	3	4.17
Program for New Century Excellent Talents in University of China	3	4.17
Shanghai Municipal Education Commission of China	3	4.17
Chang Gung Medical Research Program, China	1	1.39
College of Medicine Research Centre, Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia	1	1.39
Pedro Barrié de la Maza Foundation of Spain	1	1.39
Hand Function Research Center in Fudan University, China	1	1.39
Hand Surgery Department in Huashan Hospital, China	1	1.39
Military Medicine and Health Research Foundation of China	1	1.39
National Natural Science Foundation of China	1	1.39
Shanghai Scientific and Technological Commission of China	1	1.39

neural transplantation.

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