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Original Article

Electrophysiological outcomes analysis in peripheral nerve injury patients treated with biodegradable conduit small-gap (2 mm) tubulization

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Abstract: Nerve repair and functional reconstruction after peripheral nerve injury (PNI) is a crucial and challenging topic. In this prospective study, we investigated 14 PNI patients with complete median or ulnar nerve injury treated with biodegradable small-gap (2-mm) tubulization. We aim to investigate the change tendency of electrophysiological index during nerve repair and evaluate the effect of the biodegradable small-gap tubulization. Nerve regeneration was evaluated at 1, 2, 4, 6 months and 5 years after surgery according to electromyography examination and combined functional evaluation. The mean SCV restoration ratios of these patients were 25.6%, 39.4%, 38.6%, 60.1% and 82.0% at 1, 2, 4, 6 months and 5 years after surgery. The mean MCV restoration ratios were 1.4%, 10.4%, 15.4%, 25.1% and 78.0% at the same follow-up time points respectively. The combined functional recovery excellent and good rates were 50.0%, 78.6% and 85.7% at 4, 6 months and 5 years after surgery. No complication was observed in these patients. Our results demonstrated that the SCV and MCV restoration ratios were both continual increased as time went on after nerve repair operation. The mean restoration ratio of SCV was increased much faster than MCV within 6 months after surgery. However, the mean restoration ratios of SCV and MCV were closed at 5 years after surgery. The recovery of nerve conduction velocity was slower than functional evaluation at each time point. Owing to the good functional outcomes in the majority of cases, biodegradable small-gap tubulization is an effective procedure for PNI management.

Keywords: Peripheral nerve injury, bioabsorbable conduit, nerve repair, re-innervation, nerve electrophysiology

Introduction

Peripheral nerve injury (PNI) has always been a significant clinical problem in human history. Peripheral nerves are susceptible to various mechanisms of injury, such as crush, stretch, cutting, and penetrating traumas. Each year, about 1 million people in the world suffer from PNI, accounting for 2.8% of trauma patients approximately. PNI typically leads to life-long loss or disturbances in functions mediated by the injured nerve. Thus, PNI greatly reduces the life quality of affected individuals and has a significant socioeconomic impact [1, 2].

Peripheral nerves have the ability to regenerate after incomplete transection or crush [3]. Surgical intervention should be performed to establish continuity of the transected peripheral nerve, with proper rotational alignment and without tension. The traditional repair method for peripheral nerve transection without deficits is epineurial repair of injured nerve segments. However, the functional outcomes of this nerve repair method are unsatisfactory, even by using microsurgical techniques, the motor and sensory function recoveries were less than satisfactory because of failure in the correct formation of the sensory and motor nerve fiber connections [4].

Aligning the motor and sensory nerve fiber in acorrect orientation not only ensure good nerve regeneration but also optimise the functional recovery for any nerve repair. Functional recovery is dependent on the number of motor and sensory neurons correctly connected [5].

Based on the phenomenon of peripheral nerve selective regeneration [6], we used a new type of biodegradable conduit to repair PNI, in which a small gap was remained between the stumps

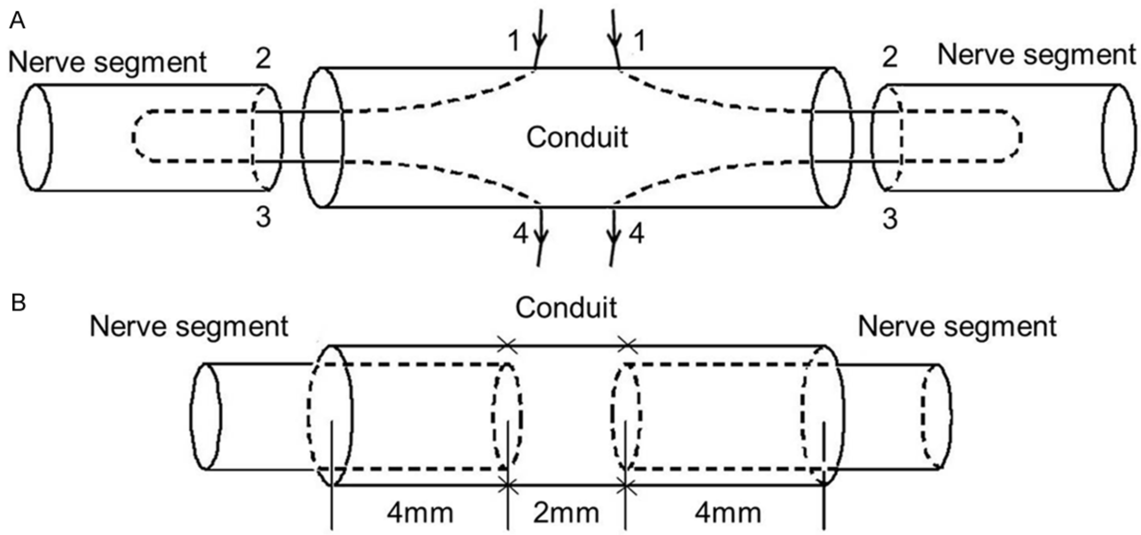

Figure 1. View of the small gap tubulization method. Both nerve ends were pulled 4 mm into the nerve guide by a horizontal U-stitch with 6-0 nylon suture, in which a 2-mm small gap existed between the two ruptured stumps. A. The needle insertion sequence; B. Schematic diagram of injured nerve after tubulization and suture.

Table 1. The combined excellent and good evaluation criteria

Grading	Mixed nerve	
	Middle and lower segment of forearm and wrist	Upper of forearm and other nerve
Excellent	M5 S3A3	M5 S3A3 above
Good	M4 S3A2 above	M3 S3A2 above
Common	M3 S2A1 above	M2 S2A1 above
Poor	M2 S1A0 above	M2 S1A0

for selective regeneration. By providing a conduit to guide nerve connection, this method was used to maximize re-innervation of the regenerating proximal stump to the degenerating distal stump. The conduit used in our study contains de-acetyl chitin, which was invented by Peking University People's Hospital (China) and Chinese Textile Academy (State Patent No. 01136314.2). Our previous experiments in rats and rhesus monkeys showed that a 2-mm small gap between two ruptured stumps exhibited the most satisfactory selective regeneration [6-9]. After confirming the effectiveness and safety of the conduit through a series of animal experiments, we performed a prospective clinical experiment to further confirm the superiority of biodegradable conduit small-gap tubulization in PNI repair.

In this study, we followed-up and evaluated the electrophysiological and functional outcomes of patients with PNI treated with biodegradable small-gap tubulization. We aim to assess the long-term clinical application of small-gap tubulization techniques and observe the change tendency of SCV and MCV restoration ratios after nerve repair surgery.

Methods

Patients

Before the start of the clinical study, informed consent was obtained from the patients. This study was approved by the Medical Ethics Committee of Peking University People's Hospital. All data of this study were analyzed anonymously. From November 2008 to February 2010, 14 patients (8 females and 6 males) with complete median or ulnar nerve transections (11 median nerves, 3 ulnar nerves) were recruited in this study. The mean age of these 14 patients was 28.0 (24.8, 31.3) years old when performed surgery.

All 14 patients were suffered from simple nerve transection without deficits. Clean transection, skeletal stability and adequate soft-tissue coverage were necessary to avoid the influence of these known factors on outcomes.

Biodegradable conduit

The hollow cylindrical de-acetyl chitin conduit was invented by Peking University People's Hospital and Chinese Textile Academy (State Patent No. 01136314.2). The conduit is 10 mm length, 1 mm thickness and 4-6 mm inner

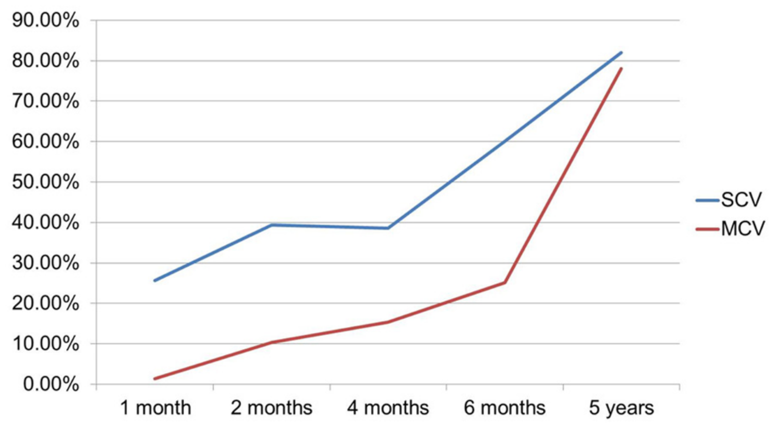

Figure 2. The change tendency of SCV and MCV restoration ratios at 1, 2, 4, 6 months and 5 years after surgery.

Table 2. Detailed condition of the 14 patients' combined functional evaluation

Case	Sex	Age	Injured nerve	4th month	6th month	5th year
1	M	69	LM*	M2S2A1	M3S2A1	M4 S3A2
2	M	23	LU**	M2S2A1	M2S2A1	M3S3A2
3	F	46	L U	M4S3A2	M4S3A2	M5S4A2
4	F	30	L U	M4S3A2	M4S3+A2	M4S3+A2
5	F	30	L M	M3S2A2	M4S3A2	M5S3+A2
6	M	28	RM	M3S2A1	M3S2A1	M3S3A2
7	F	25	RM	M4S3+A2	M4S3+A2	M4S4A3
8	M	27	L M	M3S2A1	M4S3A2	M5S3+A2
9	M	24	L M	M4S3A2	M4S3+A2	M5S3+A2
10	F	35	L M	M3S3A1	M4S3A2	M4S3A2
11	M	28	L M	M4S3+A2	M4S3+A2	M5S4A2
12	F	22	RM	M4S3A2	M4S3A2	M4S3+A3
13	F	28	L M	M4S3A2	M4S3+A2	M5S4A2
14	F	27	RM	M3S3A1	M4S3A2	M4S3A2

*M for median nerve; **U for ulnar nerve.

diameter. The half-quality degradation time of this biodegradable conduit material is 3 months in rhesus monkeys and 6 months in SD rats based on our previous experiments.

Technique

Figure 1 described the suture technique used for biodegradable conduit small-gap tubulization. Both nerve ends were pulled 4 mm into the nerve guide by a horizontal U-stitch with 6-0 nylon suture, in which a 2-mm small gap existed between the two ruptured stumps. The surgical site was immobilized after nerve repaired to protect the repair area until ten days after wound healing.

Follow-up and criterion evaluation

The wound and drainage conditions were observed at 1, 3, 7 and 14 days after operation. The follow-up time points of this study were 1, 2, 4, 6 months and 5 years after surgery. Electrophysiological examination and combined functional evaluation of the peripheral nerve were performed at these time points. The ratio of measured SCV and normal SCV was defined as the SCV restoration ratio. The MCV restoration ratio was calculated by the same method as SCV restoration ratio.

We used the combined excellent and good evaluation criteria (**Table 1**) to evaluate the motor and sensory recovery. This criteria is a modified version of the British Medical Research Council (BMRC)'s System [10] established by Zhu Jiakai and Shen Ningjiang. BMRC motor function evaluation grading (M), sensory function evaluation grading (S) and autonomic nerve function evaluation grading (A) were involved in this system.

Statistics analysis

SPSS 20.0 software (SPSS, Chicago, IL, USA) was used for data analysis. The median was treated as mean, and the distribution was indicated by 25th and 75th percentiles.

Results

General results

The wound healing of all 14 patients were as scheduled during the 5-years follow-up period. No inflammation, infection, suspicious allergic complication or abnormal drainage was observed.

Electromyography

The mean SCV restoration ratios of the 14 patients were 25.6%, 39.4%, 38.6%, 60.1% and 82.0% at 1, 2, 4, 6 months and 5 years after surgery. The mean MCV restoration ratios were 1.4%, 10.4%, 15.4%, 25.1% and 78.0% at the same time points. **Figure 2** demonstrated the change tendency of SCV and MCV restoration ratio at 1, 2, 4, 6 months and 5 years after surgery. The SCV and MCV restoration ratios were both continual increased as time went on after nerve repair operation. The mean restoration ratio of SCV was increased much faster than MCV within 6 months after surgery. However, the mean restoration ratios of SCV and MCV were closed at 5 years after surgery.

Functional evaluation

The combined functional recovery excellent and good rates were 50.0% (7/14), 78.6% (11/14) and 85.7% (12/14) at 4, 6 months and 5 years after surgery. A summary of the 14 patients' combined functional evaluation was shown in **Table 2**. No patients exhibited severe neuropathic pain.

Discussion

In this prospective study, we followed-up 14 patients with complete median or ulnar nerves injury treated with biodegradable small-gap tubulization. The study showed acceptable results in terms of final functional outcomes.

We analyzed the change tendency of SCV and MCV restoration ratio of 14 patients at 1, 2, 4, 6 months and 5 years after nerve repair operation. The SCV and MCV restoration ratios were both continual increased as time went on after nerve repair operation. The mean restoration ratio of SCV was increased much faster than MCV within 6 months after surgery. However, the mean restoration ratios of SCV and MCV were closed at 5 years after surgery. These results can be explained according to the classification of the peripheral nerve fibers which was put forward by Erlanger and Gasser [11]. In this classification method, nerve fibers are classified into three categories as A, B and C according to their thickness. Motor nerve fibers are all belong to the A categories with a diameter range of 4-22 um, while parts of sensory nerve fibers are belong to the C categories with a diameter range of 0.4-1.2 um. These parts of sensory nerve fibers are unmyelinated. The injury tolerance and recovery capability of this kind of sensory nerve fibers are better than motor nerve fibers. This might be why we observed that the restoration ratio of SCV was increased faster than MCV.

We used the combined excellent and good evaluation criteria to assess the functional outcomes of the 14 patients at the follow-up time points after operation. The combined functional recovery excellent and good rates were 50%, 78.6% and 85.7% at 4, 6 months and 5 years after surgery. Finally, most of the patients got satisfied functional outcomes.

Functional recovery is dependent on the number of motor and sensory neurons correctly connected. Degradable biological conduit small-gap tubulization for PNI provides a relatively secluded microenvironment. The small gap provided a relatively closed space, retained the neurotrophic factors and prevented the external invasion of fibrous connective tissue. According to the theory of peripheral nerve selective regeneration phenomenon [6, 8], it maximized the effectiveness of re-innervation of the regenerating proximal stump to the degenerating distal stump.

Animal experiments to evaluate the effect of nerve regeneration have a variety of methods, such as histologic, electrophysiology and functional evaluation. However, clinical experiments only have the choice of electrophysiology and functional evaluation. The recovery of nerve conduction velocity was slower than functional evaluation at the same time points. Namely, good recovery of nerve conduction velocity does not necessarily represent an ideal recovery of function. The degree of comprehensive functional recovery is the main measure of nerve function recovery after repair [6].

In our previous animal experiments of PNI models in Sprague-Dawley rats and rhesus monkeys, tubulization with a 2 mm gap between two ruptured stumps exhibited the most satisfactory results, and was better than that with traditional epineurial repair of injured nerve segments [6, 7, 12, 13].

Conclusion

The SCV and MCV restoration ratios were both continual increased as time went on after nerve repair operation. The mean restoration ratio of SCV was increased much faster than MCV within 6 months after surgery. However, the mean restoration ratios of SCV and MCV were closed at 5 years after surgery. Our study found that the recovery of nerve conduction velocity was slower than functional evaluation at the same time points. Namely, good recovery of nerve conduction velocity does not necessarily represent an ideal recovery of function. The degree of comprehensive functional recovery is the main measure of nerve function recovery after repair. Owing to the good functional outcomes in the majority of cases, biodegradable small-gap tubulization is an effective procedure for PNI management.

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Disclosure of conflict of interest

None.

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