



Original Article

## The efficacy of wrapping the neurorrhaphy site utilizing dura substitute: A case series

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### ABSTRACT

**Background:** Different procedures have been developed to improve the surgical outcome of peripheral nerve injuries. The purpose of this study was to evaluate the efficacy of wrapping the neurorrhaphy site utilizing dura substitute graft as an alternative conduit in the management of peripheral nerve injury.

**Methods:** This retrospective clinical case series included 42 patients with a single peripheral nerve injury. The mean age was  $26.8 \pm 11$  years, and the mean duration of symptoms was  $3 \pm 1.8$  months. The visual analogue score (VAS) for pain and the Medical Research Council's (MRC) grading for motor power were used to evaluate the functional outcome among our patients. All patients were operated on for primary microscopic end-to-end repair, followed by wrapping the neurorrhaphy site with dura substitute graft as a conduit. Patients were followed in the outpatient clinic with regular visits for average of 6 months.

**Results:** Thirty-seven patients (83%), showed functional improvement in all aspects, the VAS for pain and the MRC for motor power, as well as the functional state. One patient (2.3%) developed a postoperative hematoma collection, which needed immediate evacuation. Superficial wound infection, reported in two patients (4.7%), was treated conservatively. No postoperative neuroma was observed among our patients during the follow-up period.

**Conclusion:** Wrapping the neurorrhaphy site utilizing dura substitute as conduit appears to be safe and might prove effective in managing peripheral nerve injury.

**Keywords:** Conduit, Dura substitute, Nerve injury, Neurorrhaphy

### INTRODUCTION

Peripheral nerve injury is considered one of the most common clinical problems worldwide, especially in young patients. It affects the quality of life of patients and causes significant a socioeconomic burden.<sup>[3,19]</sup>

Despite improvements in microsurgical techniques for peripheral nerve repair, including epineural neurorrhaphy and interfascicular suturing, only an estimated 50–60% of patients regain

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useful function after microsurgical repair.<sup>[7,14]</sup> In addition to the dysfunctionality of the limb and the lack of motor power, medically refractory pain is a significant concern for both the patient and the healthcare system. Chronic neuropathic pain post-peripheral nerve injury is a very devastating consequence and as it commonly affects young patients, it has a detrimental effect on the social welfare system.<sup>[4]</sup> Multiple factors can alter the recovery after surgical intervention, including the age of the patient, the type of injury, the involved nerve, the time of the surgical intervention, the level of injury, and the availability of specialized programs and clinical pathways as well as rehabilitation programs.<sup>[12]</sup>

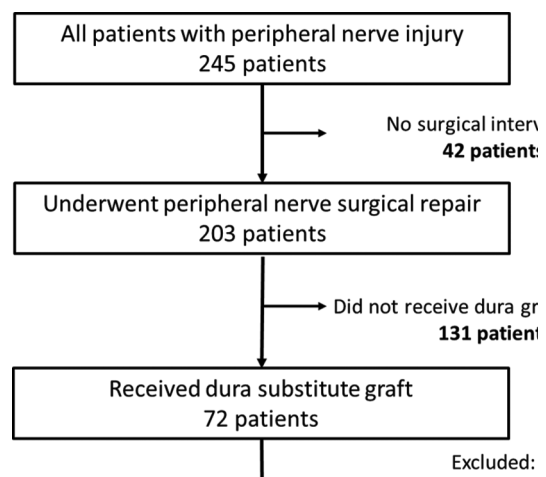
It is estimated that more than 70% of patients post-nerve injury repair will continue to experience pain for months to years.<sup>[13,17]</sup> with 20% to 30% fulfilling the criteria of intense, severe, and chronic pain.<sup>[8]</sup> Patients with nerve injury can have any type of pain or combinations of pain types, including nociceptive, neuropathic, neurogenic, avulsion pain syndromes, complex regional pain syndromes, and phantom limb pain. The clinical symptoms of neuropathic pain can be divided into two categories: (1) Negative symptoms include hypesthesia, hypoalgesia, mechanical anesthesia, thermal pain, and the loss of vibratory sense; and (2) Positive symptoms such as paresthesia, dysesthesia, hyperesthesia, and allodynia.<sup>[15]</sup> The causes of this type of pain can be numerous, the most common being abnormal regeneration processes of the nerve and adjacent tissue, formation of a painful neuroma, and adjacent fibrous tissue formation that can cause direct external or internal compression, ischemia, or traction on the nerve that may lead to the generation of the pain.<sup>8</sup> As a result, a clean and healthy environment at the injury site is essential for better pain management and functional outcome after neurorrhaphy. One of the techniques that have been utilized to achieve the desired healthy local environment for nerve regeneration is the use of conduit or tubulization.

Multiple conduits materials have been developed and utilized in nerve repair, including biological, synthetic tubes, and more recently, tissue-engineered conduits. Some are completely biological, and others are synthetic materials in the form of tubes or conduits. The goal of all types of conduit is to facilitate neurotropic and neurotrophic communication between the proximal and distal stumps of the nerve, with or without a gap in between the stumps, to provide a protective barrier, thus reducing the risk of an impeded healing process due to external factors such as scar tissue formation as well as facilitating nerve tissue regrowth. Although proven effective in varying degrees, the availability of such conduits is generally limited in many medical centers worldwide.<sup>[20,23]</sup> In this retrospective clinical case series, we evaluate the use of an alternative material's safety, efficacy, and outcome with a novel technique of utilizing a widely available material (i.e., dura substitute graft) as a conduit by wrapping the neurorrhaphy site.

## MATERIALS AND METHODS

Over a 4 year period (February 2016 to January 2020) hospital record databases were searched for patients with peripheral nerve injuries who had undergone surgical repair at the adult Neurosurgery Department, National Neuroscience Institute, in King Fahad Medical City in Riyadh, Saudi Arabia. Records revealed that 245 patients were seen in our clinic for peripheral nerve injury. Of those 203 patients had undergone microsurgical repair or exploratory procedures related to peripheral nerve injuries including brachial plexus branches, musculocutaneous nerve, median nerve, ulnar nerve, radial nerve, and sciatic nerve branches. Out of the 203 patients, 42 (20%) patients were selected for the study who had undergone microsurgical repair of the injured nerve, utilizing dura substitute graft as a conduit to the injured site [Chart 1]. The remaining patient files were excluded from this study as they did not have a dura substitute as a conduit, had multiple nerve injuries, or nerve graft was used and direct repair was not achieved. Out of the 203 patients, 72 patients had a dura substitute graft; however, 30 patients were excluded as they had their repair after 12 months of the injury (22 patients), or because they had multiple nerve injuries (8 patients). Those patients were not included to avoid factors that might lead to difficulty in understanding or evaluating the efficacy and the safety of an alternative technique to the more expensive and less available conduit material (e.g., the conduit).

The selected 42 patients' files were reviewed carefully. The involved nerve and level of injury were primarily determined by physical examination, nerve conduction study, and a few patients also had a magnetic resonance imaging (9/42). All selected patients had a single nerve injury, surgical intervention within 6 months from the time of the injury,



**Chart 1:** The process of the patients' exclusion (date period January 2016 – December 2020).

and direct end-to-end repair was achieved. The remaining 161/203 (79.3%) patients were not included in our analysis as they had the following: (1) multiple nerve injuries; (2) injury more than 6 months' duration; (3) indirect nerve repair (nerve grafting); and (4) extensive muscle damage or skin loss.

Hospital charts were reviewed and all patients' data were collected including detailed diagnoses, and treatment outcomes in terms of pain scoring, power, and functionality of the involved limb were collected for analysis [Table 1]. More than 90% of the patients were followed up in our clinic and evaluated for more than 9 months. The patient's

postoperative, 3-month, and 6-month follow-up data were collected.

Approval from the research ethics committee was obtained. However, being a retrospective study, patient consent for participation and publication was not applicable.

### Preoperative evaluation

All patients were evaluated and subjected to a complete clinical history and general and neurological examination. Pain was evaluated by the Visual Analogue Scale (VAS).<sup>[19,21]</sup> Motor power (muscle strength) was assessed by the Medical Research Council's (MRC) grading system.<sup>[5]</sup>

The electrophysiological study included electromyography and nerve conduction velocity for all patients, to confirm the diagnosis and identify the site and degree of injury. Nine patients (21.4%) had an MRI scan.

### Operative technique

Under general anesthesia, the suspected nerve injury was explored in the usual fashion. The proximal and distal stumps were identified, in some cases after the removal of the associated neuroma, and debrided utilizing a microsurgical technique. Mobilization of both nerve segments was performed as necessary to reduce tension at the repair site [Figures 1 and 2].

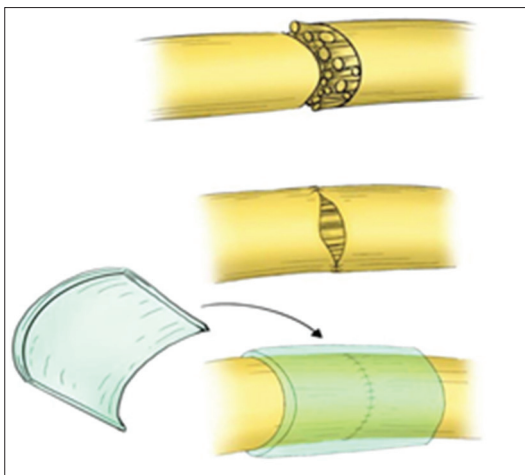
Microscopic repair by epineural sutures occurred for all injured sites, using 6-0 proline suture in most cases, followed by wrapping the repair site with one of the available dura substitute grafts as a conduit; for example., DuraGuard, Tampa, FL, USA; DuraFoam, Menlo Park, CA, USA; Integra/DuraGen, Plainsboro, NJ, USA; DuraMatrix, Oakland, CA, USA; and Hemopatch/Baxter International, Deerfield, IL, USA [Table 1]. The selection of a specific dura substitute graft was based on its availability in our operating room store at the time of the repair. After necessary hemostasis, the surgical site was typically approximated in two layers. Immobilization was recommended to all patients for a duration of 2 weeks.

### Postoperative evaluation

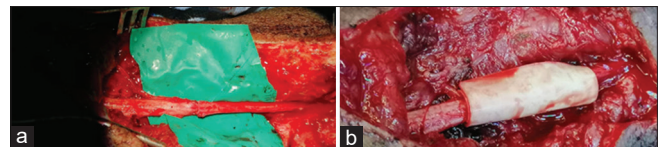
As per our standard postoperative follow-up, all patients were seen in the clinic 2 weeks postoperatively to assess the

**Table 1:** Patient demography, injured nerve and type of dura substitute used.

Gender		
Male	22	52.4%
Female	20	47.6%
Age		26.8±11.9
Injured nerve	42	100%
Lateral cord	12	28.6%
Musculocutaneous nerve	5	11.9%
Median nerve	3	7.1%
Ulnar nerve	5	11.9%
Radial nerve	5	11.9%
Sciatic nerve	7	16.7%
Common peroneal nerve	5	11.9%
Preoperative VAS scale	5.95±2.38	
Preoperative MRC grade	0.83±0.73	
Type of dura substitute	42	
DuraGuard	8	19%
DuraGen	12	28.6%
DuraFoam	7	16.7%
DuraMatrix	6	14.3%
Hemopatch	9	21.4%



**Figure 1:** Diagram of end-to-end neurorrhaphy and wrapping by dura substitute.



**Figure 2:** (a) Microsurgical repair of the radial nerve at the elbow. (b) Wrapping the neurorrhaphy site by dura substitute conduit.

wound, remove the sutures and the cast when applicable, and get a baseline post-op physical exam. The patients are then sent for an extensive rehabilitation program usually spanning 6 weeks, followed by an in-home rehabilitation program. Clinical follow-up was done regularly every 3 months afterward, for at least 12 months, to assess VAS for pain and MRC for motor power. In addition, other tests, including Tinel's sign at the repair site, were utilized to evaluate the presence of local neuroma formation.

Patient data were collected retrospectively after the 6-month follow-up. Patients were divided into three groups based on the severity of pain and the weakness they reported before the surgical intervention [Table 2].

## RESULTS

This study included 42 patients with a single peripheral nerve injury who underwent a surgical repair. The patient data were collected retrospectively and the average follow-up was found to be at least 9 months postoperatively (minimum follow-up is 6 months and maximum 12 months). Twenty-two patients (52.4%) were males and 20 patients (47.6 %) were females, with a male to female ratio of 1.1: 0.9, and a mean age of  $26.8 \pm 11$  years [Table 1].

The series included distal (lateral cord) brachial plexus injury in 12 patients (28.6%), musculocutaneous nerve injury in five patients (11.9%), median nerve injury in three patients (7.1%), radial nerve injury in five patients (11.9%), ulnar nerve injury in five patients (11.9%), sciatic nerve injury in seven patients (16.7%), and common peroneal nerve injury in five patients (11.9%).

The onset of injuries to the time of surgical intervention ranged from 1 to 6 months, with a mean duration of  $3.0 \pm 1.8$  months [Table 2]. Pain and motor deficits were the most common

clinical manifestations in all cases (100%). The mean preoperative VAS for pain was  $5.95 \pm 2.38$ , while the mean preoperative MRC grading for motor power was  $0.83 \pm 0.73$ . The preoperative electrophysiological studies revealed complete degeneration of the injured nerve in all patients.

The data showed that all patients were operated on for primary microscopic end-to-end repair, followed by site wrapping (neuroorrhaphy) with dura substitute conduit: DuraGuard in eight patients (19%), DuraGen in 12 patients (28.6%), DuraFoam in seven patients (16.7%), DuraMatrix in six patients (14.3%), and Hemopatch in nine (21.4%). The dura substitute grafts are made from the same basic material and they are all collagen-rich grafts.<sup>[11]</sup>

In the 3- and 6-month follow-ups, the patient record showed that all patient VAS for pain had improved. The mean postoperative VAS at 3 months was  $3.29 \pm 1.48$  and at 6 months was  $1.55 \pm 0.83$ . Statistical analysis revealed a significant improvement in VAS among patients at 6 months postoperatively compared to the situation preoperatively [Tables 3 and 4].

The MRC for motor power showed overall improvement in most patients 37 (83%); however, one patient (2.3%) had worsening of his strength, from Grade 2 to Grade 0. Four patients (9.5%) did not show any improvement in strength [Table 3]. The mean postoperative MRC grading for motor power at 3 months was  $1.26 \pm 0.79$ ; at 6 months' follow-up, it was  $3.67 \pm 0.92$ . Statistical analysis revealed a significant improvement in MRC grading of motor power postoperatively among our patients at 6 months, compared to preoperative levels [Table 5].

## Post-operative complications

Patient record showed that postoperative neuroma was not reported among our patients during the follow-up period.

**Table 2:** The pre and post-operative pain and motor improvement in three groups of patients based on the preoperative clinical exam.

Group no	No of patients	Average age	Site of injury	Interval between surgery and injury (months)	Pain		Motor	
					Preop (average)	6 months postop	Preop (average)	6 months postop
Group 1 High grade	11 (26%)	25	MC Radial Ulnar	2.7	8.4	2.1	1.1	3.8
Group 2 moderate grade	22 (52.3)	24	MC Radial Ulnar Median Peroneal	2.8	5.6	1.6	0.9	3.6
Group 3 Mild grade	9	26	MC Radial Ulnar	3.5	3.9	1	0.7	3.6

**Table 3:** List of patients that had worsening post op motor power or did not change.

No	Pre op MRC	6 months MRC	Functionality
Case 1	2	0	Worse
Case 2	2	2	Not changed
Case 3	0	0	Not changed
Case 4	0	0	Not changed
Case 5	1	1	Not changed

**Table 4:** The pre-op VAS and 6 months post-op VAS.

	Pre-op	Post-op 6 months	P-value
Mean VAS	5.95±2.38	1.55±0.83	0.001
Significant $P \leq 0.05$			

**Table 5:** The pre-op MRC and 6 months post-op MRC in the study.

	Mean Pre-op	Mean Post-op 6 months	P-value
MRC	0.83±0.73	3.67±0.92	0.001
Significant $P \leq 0.05$			

One patient developed postoperative swelling at the surgical wound due to hematoma collection, which necessitated immediate evacuation. Postoperative course was excellent.

Superficial wound infection was reported in 2 patients (4.7%) after surgery, which was treated with oral antibiotics for 10 days.

There was no report of any allergic reaction from the dura substitutes used in our study.

## DISCUSSION

The management of peripheral nerve injuries can be difficult and requires a multidisciplinary approach. The objectives of the management must be clear to the treating team and the patient, with the goal of restoring functionality in terms of power, sensation and pain relief, which is a common symptom that can be devastating. In our series, most of the patients (80%) had a neuropathic pain similar to that reported in the literature (60–90%).<sup>[16]</sup> The causes of this pain have been well investigated in the literature. At the cellular level, the injured nerve will stimulate a significant and multiple cascade that is modulated by the injured Schwann cells and their genes. This activation will lead to the synthesis and release of many cytokines, chemokines, and lymphocytes, which will release many proinflammatory factors. These factors are important in the healing of the injured nerve and to recruit leukocytes to the injured site as part of the healing process, reorganization, and repair. This complex and active process of factor interactions during healing of the surgical site can lead to

abnormal nerve regeneration, formation of painful neuroma, and adjacent fibrous tissue formation that can cause direct compression, ischemia, or traction on the nerve that may lead to the generation of pain and unsatisfactory outcome. For example, secondary to the sustainability of the expression of phospholipase A2 fragmentation, an uncontrolled growth of the myelin at the injured side can lead to the formation of neuroma, which might lead to chronic neuropathic pain.<sup>[9]</sup> Many other genes and growth factors have been suggested as the cause of an uncontrolled regeneration of the nerve that can lead to unsatisfactory results. Many studies showed that the outcome of these injuries and the uncontrolled regeneration can be influenced by microsurgical repair of the peripheral nerve. To improve the outcome the surgical team should focus on achieving early, tension-free repair of the nerve and take all necessary action to reduce any intra-nerve or extra-nerve factors that can lead to scar/fibrous tissue formation, one of the important elements that can lead to an unsatisfactory outcome. To achieve that goal, interfascicular nerve grafting as a tube (conduit) made an advancement in the 1970s, nearly 100 years after it was first attempted by Glück in 1880.<sup>[2]</sup> Subsequently, many materials have been utilized in nerve repair, including biological material such as blood vessels or muscle fibers and synthetic tubes from silicon or more advanced technology such as tissue engineering.<sup>[1,14]</sup> Initially the main goal of these tubelizations (conduits) was to fill the gap between the two nerve stumps when approximation was not possible and a local nerve donor was not available.<sup>[7]</sup>

It was noticed that isolating that covering the nerve with the conduits from the external adjacent environment at the repair site can help with the healing process and slow down the diffusion of trophic and modified growth factors. It showed a more promising outcome by potentially reducing the scar formation around the injured site. It also provides a proper environment for regeneration of the injured nerve and acts as a scaffold for cell adhesions and axonal regeneration.<sup>[6,10,22,23]</sup>

In Zhang *et al.*'s 2013 study,<sup>[24]</sup> they used a conduit to manage peripheral nerve injury and reported significant improvement in VAS for pain and MCR grading for motor power among patients of the study 6 months post-surgery. Their outcomes were similar to our study results; however, we believe our study utilized a more cost-effective and widely available, and less expensive material and gives the equivalent outcomes.

In 2018, Zhu *et al.*<sup>[25]</sup> evaluated collagen conduits to wrap the neuroorrhaphy site after end-to-end repair: They found significant improvement in degree of pain, as well. In a different study, collagen conduits were found to absorb completely in 3 months, with a low incidence of scar formation, in turn providing a good environment for nerve regeneration.<sup>[18]</sup>

In this work, we used a collagen dura substitute as a conduit to cover the neurorrhaphy site in 42 patients, which resulted in acceptable functional outcomes, including pain and motor power, which denotes proper nerve regeneration [Table 4]. We used the dura substitutes as an alternative to the conduit to wrap the repair site in all patients (100%). No deep postoperative infection or allergic reactions were reported, which indicates acceptable biocompatibility and safety. We believe the motor improvement in this study was related to the selection of patients with a specific type of injury, the interval of <6 months between the injury and the surgical intervention, the type of repair (direct end-to-end tension-free repair), and the dura graft just optimizing the local environment. However, we suggest that the significant pain relief is directly related to the provided protection to the injured site from the unwanted scars tissue by the dura graft.

Neuroma was not seen among our patients during follow-up physical examination. As such, we agree with the results of Thirumalai *et al.*, as they reported that the use of a biologically inert barrier to protect the repair site from surrounding tissues is essential in preventing nerve tether, axonal escape, and neuroma formation.<sup>[20]</sup>

### Limitations

This is a retrospective study with a limited number of patients and experience of dura substitute graft in peripheral nerve injury. Although this study found that covering the injured nerve postrepair significantly reduced the severity of the pain, we acknowledge that the improvement in strength and overall functionality is not necessarily related to the covering of the nerve but to the selectivity of patients with fresh single nerve injuries.

### CONCLUSION

Wrapping the neurorrhaphy site with dura substitute as an alternative conduit can be effective and safe in the management of peripheral nerve injury. We noticed better pain relief with its use, and a similar complication profile to the standard procedure.

### Acknowledgments

None.

### Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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