NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of nerve transfer to partially restore upper limb function in tetraplegia

Tetraplegia is when both the arms and legs are partly or totally paralysed because of nerve damage caused by trauma to the spinal cord in the neck. Some people with nerve damage lower in the neck can have nerve transfer to try and improve function in the upper limbs. This procedure involves connecting an undamaged, functioning, but non-essential nerve near the injury to the damaged essential nerve. The aim, with specialised physiotherapy, is to recover strength in the muscles supplied by the nerve, and restore arm and hand function.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in September 2017.

Procedure name

- Nerve transfer to partially restore upper limb function in tetraplegia

Specialist societies

- British Society for Surgery of the Hand (BSSH)
- British Orthopaedic Association (BOA)
- Spinal Injuries Association
- British Association of Spinal Cord Injury specialists (BASCIS)
- British Association of Plastic Reconstructive and Aesthetic Surgeons (BAPRAS)
- British Thoracic Society
- Royal College of Surgeons

Description of the procedure

Indications and current treatment

Tetraplegia is typically caused by cervical spinal cord injuries, with associated complete or incomplete loss of muscle strength in all 4 extremities. The exact symptoms depend on the location and extent of injury. The most common neurologic level of injury is the fifth cervical vertebra. This results in loss of upper limb function and the inability to carry out activities of daily living.

Restoring upper limb function is an important rehabilitation aim in people with tetraplegia. Conservative treatment options include a comprehensive program of physical and occupational therapy, including orthoses and functional electrical stimulation. Surgical techniques to restore function of the upper limbs (elbow, thumb and finger extension, wrist movement, hand opening and closing, and pinch and grip) include neuroprostheses, tendon transfer, nerve transfers, reconstructive surgeries or a combination of these procedures.

What the procedure involves

In this procedure, the nearest undamaged functional non-essential nerve is used as the donor nerve.

Under general anaesthesia, with the patient in a supine position and with their arm on a board, the non-functioning nerve is exposed and the degree of paralysis is defined neurophysiologically. The closest functional donor nerve is identified. It is then isolated, divided, transferred and joined to the selected damaged nerve while avoiding tension in the donor nerve. The aim of the procedure is to re-innervate the target muscles and improve limb function.

Postoperatively, the patient needs nerve and muscle rehabilitation training to recover the strength of the re-innervated muscles and improve activities of daily living.

Nerve transfers may sometimes be combined with tendon transfers.

Outcome measures

Medical Research Council (MRC) muscle scale: The muscle scale grades muscle strength in relation to the maximum expected for that muscle. The patient's effort is graded on a scale of 0 to 5 and has been widely used to assess muscle strength of the upper extremities.

0: No contraction

I: Flicker or trace of contraction

2: Active movement, with gravity eliminated

3: Active movement against gravity

4: Active movement against gravity and resistance

5: Normal power

Efficacy summary

Time to surgery post spinal cord injury

A systematic review included 13 studies (3 case series and 10 case reports) with 89 nerve transfers of various types (including 15 cases of double nerve transfer and 1 case of triple nerve transfer) in 59 patients with a mean spinal cord injury (SCI) level of C6 (range C5 to C7). The aim in the studies was to restore upper limb function in tetraplegia. The mean time to surgery post SCI was 19.9 months (range 4.1 to 156.0 months). [1]

Functional outcomes

Restoring movement of hand muscles (elbow extension, finger and thumb extension, wrist extension, pinch and grasp strength)

In the systematic review, muscle strength was reported according to the MRC muscle scale. An MRC score of 3 or 4 for recipient muscle power was reported in all of the case reports and series in the review at a mean follow-up of 18.2 months (range 3.0 to 60.0 months). In 1 of the case reports of 1 patient who had brachialis to anterior interosseous nerve (AIN) transfer, gain in both strength and functional control continued 15 months after surgery. In 2 of the case series (reporting musculocutaneous to median nerve transfer in 42 patients), results varied on a 3-point grading scale of simple hand function; they were good (functional grasp restored) in 16 patients, fair (grasp was weak) in 16 and bad (no result) in 10.[1]

In a case series of 9 patients with tetraplegia (SCI level C5 in 4 upper limbs, C6 in 10 and C7 in 3), different nerve transfers (brachialis to AIN in 3 upper limbs, brachialis to median nerve in 5, brachioradialis to AIN in 4 and extensor carpi radialis brevis [ECRB] to AIN in 5) were used to restore finger flexion. Complete finger flexion was defined as all fingertips touching the palm of the hand with the wrist at neutral. There was complete finger flexion with an MRC score of 4 in 5 upper limbs when the nerve to the ECRB was transferred to the AIN at an average follow-up of 16 months. Incomplete finger flexion range with varied strength was reported in the other types of nerve transfers. An MRC score of 3 was seen in 59% (10/17) of limbs. No functional downgrading of elbow flexion or wrist extension strength was seen in these patients.[2]

In another case series, 7 patients with SCI-related upper extremity dysfunction had peripheral nerve transfers in 8 limbs (brachialis to AIN, nerve branches to flexor carpi radialis and flexor digitorum superficialis to restore pinch) at a mean of 5 years post SCI. There was an increase in grasp strength in 2 patients and improvement in pinch activities in 1 patient. Muscle strength measured by MRC scale scores of 2 or 1 for recipient muscle power were seen in 5 patients at follow-up periods ranging from 1 to 18 months.[4]

Restoration of sensory function

In another case series, 5 patients with tetraplegia had sensory reconstruction on the ulnar side of the hand and little finger to restore sensation on the C8 to T1 dermatomes by transferring sensory nerves with afferents on C5 to C6 roots (in 10 limbs) at a mean of 10 months post SCI. Sensory thresholds were investigated using Semmes–Weinstein monofilament pressure. All patients improved and perceived 19.3 g monofilament pressure and pain on the medial sides of the little finger and hand bilaterally. Nociception was restored on the medial side of the elbow, forearm and hand.[3]

Functional improvement in activities of daily living

In the systematic review, it was reported that there was no consistent tool used to measure the overall functional improvement in activities of daily living.[1]

In the case series of 7 patients, subjective changes in activities in 3 patients were reported, including: increased use of hand for feeding, holding things and ability to self-catheterise; increased arm use for reaching out and grabbing things; and increased wrist stability when reaching a hand into a bag.[4]

Combined nerve and tendon transfers

In 1 case report (Bertelli JA, 2015) in the systematic review, upper limb function (elbow extension, finger extension, thumb extension and pinch) was restored by combining tendon and nerve transfers in 1 procedure.[1]

Mean operative time and hospital stay

In the case series of 7 patients, the mean operative time was 231 minutes and the mean length of hospital stay was 1.3 days.[4]

Safety summary

Urinary tract infection and urosepsis

Urinary tract infection needing prolonged hospital stay was reported in 1 patient in the case series of 7 patients who had peripheral nerve transfers for upper extremity dysfunction. Urosepsis (1 week postoperatively) was reported in 1 patient in the same study. The patient was readmitted and treated successfully.[4]

Thumb paraesthesia

Thumb paraesthesia was the most common perioperative complication reported in 4 patients in the case series of 7 patients. Most paraesthesias resolved or improved but 1 patient continued to have mild symptoms.[4]

Seroma

Seroma (needing percutaneous drainage) was reported in 1 patient in the case series of 7 patients.[4]

Numbness

Numbness on the radial side of the hand was reported (after proximal dissection of the AIN for connection with the nerve to the brachialis) by all patients in the case series of 9 patients (17 upper limbs) with tetraplegia who had nerve transfer to restore finger flexion. This disappeared within 3 months of surgery.[2]

Referred sensation

Referred sensation was reported by all patients in the case series of 5 patients with tetraplegia who had sensory nerve transfers. None of the patients complained that this adversely affected daily activities.[3]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: permanent or temporary donor muscle weakness, donor nerves with a low level of function unsuitable for transfer (found at surgery) and failure of the target muscle to regain useful function. They considered that the following were theoretical adverse events: no recovery because of a poor donor nerve, a denervated recipient nerve, technical failure of the nerve co-aptation, weakness in functional power of the donor nerve and compromise of other reconstructive options in future.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to nerve transfer to partially restore upper limb function in tetraplegia. The following databases were searched, covering the period from their start to 6 June 2017: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with tetraplegia.
Intervention/test	Nerve transfer to partially restore upper limb function.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 80 patients from 1 systematic review[1],3 case series[2-4] and 1 case report[5].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A. presented

Table 2 Summary of key efficacy and safety findings on nerve transfer to partially restore upper limb function in tetraplegia

Study 1 Cain SA 2015

Details

Study type	Systematic review
Country	Australia
Recruitment period	
Study population and number	n=**13 studies (3 case series and 10 case reports)** (59 patients with tetraplegia, 89 nerve transfers in upper limb) Mean spinal cord injury (SCI) level:C6 (range C5-7) Time to surgery post SCI: mean 19.9 months (range 4.1-156 months).
Age and sex	Mean 34 years; 97% (57/59) male
Study selection criteria	Studies that reported patients with cervical SCI (tetraplegia) having nerve transfer for restoration of upper limb function, English language studies, randomised controlled trials, cohort studies, case control studies and case series were included. Nerve transfers performed on patients without SCI were excluded. Search strategy: Medline, Embase (from 1950- February 2015) databases were searched, Cochrane collaboration and NHS evidence health information resources website were also searched. Additional studies were identified through manual reference check of articles.
Technique	Nerve transfers performed for restoration of upper limb function in tetraplegia 15 cases of double nerve transfer (Bertelli and Ghizoni 2015, 2013, Brown 2011) 1 case of triple nerve transfer (van Zyl 2014)
Follow-up	**Mean 18.2 months (range 3-60 months)**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: review of published literature, the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement/checklist was followed but quality assessment was not done as case series and case reports were included. Functional outcomes were extracted. The primary outcome reported in this review was strength grading according to the MRC scale. Quantitative assessments were done with descriptive data, case by case analysis was done for summary data. There was no consistent measurement tool used to report overall functional improvement in activities of daily living.

Other issues: there is an overlap of patients between 2 studies included in the systematic review (Kiwerski 1982, Krasuski and Kiwerski 1991).

Key efficacy and safety findings

Efficacy	Safety

Number of patients analysed: **59 with 89 nerve transfers**

Study	N	Nerve transfer	Follow-up	Outcome
Kiwerski 1982	20	Musculocutaneous-median (unilateral)	60 months	Good (9), satisfactory (6), bad(5)
Krasuski and Kiwerski 1991	42*	Musculocutaneous-median (unilateral)	Not reported	Good (16), fair(16), bad (10)
Bertelli and Ghizoni 2015	7	Posterior division of axillary –triceps (n=9) Anterior division of axillary –triceps (n=2) Posterior division of axillary and middle deltoid branch –triceps (n=2) Supinator –PIN (n=13)	Mean 19 months	Elbow extension M4 (n=12), M3 (n=1) Finger extension M4 (n=12), M3 (n=1) Thumb extension M4 (n=8), M3 (n=4), M2 (n=1).
Benassy 1965	1	Musculocutaneous-median (unilateral)	29 months	M3 to FCR, FDP, M2 FPL
Bertelli and Ghizoni 2015	1	Posterior division of axillary –triceps (bilateral) Supinator –PIN	22 months	Elbow extension: right-M3, 1 kg triceps strength; left M4, 2 kg triceps strength Finger extension: right M4, left M4 Thumb extension: right M3, left M4
Brown 2011	1	Musculocutaneous-median (unilateral) Posterior division of axillary-Radial (unilateral)	3 months	-
Van Zyl 2014	1	Teres minor-triceps (unilateral) Supinator-PIN (bilateral) Brachialis-AIN (bilateral)	19 months (left) 17 months (right)	Elbow extension: left M4, 2 kgx10 reps Finger extension: right M4, left M4 Thumb extension: right M3, left M3 Finger flexion: right M4, left M4 Thumb flexion: right M4, left M4
Bertelli and Ghizoni 2012	1	Brachialis –triceps (unilateral)	13 months	Elbow extension: M4, 5 kg
Bertelli 2012	1	Distal ECRB-FPL	14 months	Thumb flexion:M4
Bertelli 2010	1	Supinator-PIN (bilateral)	6 months	Finger extension: right M4, left M4
Bertelli 2011	1	Teres minor-triceps (bilateral)	14 months	Elbow extension: right-M4, left M4
Mackinnon 2012	1	Brachialis-AIN (bilateral)	15 months	Finger flexion/thumb flexion: right M3, left M3
Friden 2012	1	Brachialis-ECRL (unilateral)	5 months	Wrist extension: M3

*includes 20 cases from Kiwerski 1982.Results were reported on a 3 point grading scale: 'good' if functional grasp restored, 'satisfactory' if grasp was weak and 'bad' if no result.

All case reports reported a MRC score of 3 to 4 for recipient muscle power but 2 case series (Kiwerski 1982, Krasuski and Kiwerski 1991) reported more variable results.

Summary of total nerve transfers performed

Donor nerve/branch	Recipient nerve/branch	Number of transfers
Posterior/middle deltoid branch	Triceps	3
Posterior division of axillary	Radial	1
Posterior division of axillary	Triceps	10
Anterior division of axillary	Triceps	2
Supinator	PIN	19
Distal ECRB	FPL portion to AIN	1
Brachialis	AIN	4
Brachialis	ECRL	1
Musculocutaneous	Median	44

Teres minor	Triceps	3
Brachialis	Triceps	1
Total		**89**

Nerve transfers in relation to function in tetraplegia

Elbow extension		**Thumb/finger extension**		**Pinch and grasp**		**Wrist extension**	
Donor	**Recipient**	**Donor**	**Recipient**	**Donor**	**Recipient**	**Donor**	**Recipient**
Teres minor	Triceps	Supinator	PIN	Distal ECRB	FPL	Brachialis	ECRL
Posterior deltoid	Triceps			Brachialis	AIN		
Brachialis	Triceps						

Abbreviations used: AIN, anterior interosseous nerve; ECRB, extensor carpi radialis brevis; ECRL, extensor carpi radialis longus; FPL, flexor pollicis longus; PIN, posterior interosseous nerve.

Study 2 Bertelli JA 2017

Details

Study type	Case series
Country	Brazil
Recruitment period	2011-2013
Study population and number	n=**9 patients (17 upper limbs) with tetraplegia** Mean spinal cord injury (SCI) level (according to international standards for neurological classification of SCI): C5 in 4 upper limbs, C6 in 10, and C7 in 3 Time to surgery post SCI: 7.6±4 months
Age and sex	Mean 28 years; 89% (8/9) male
Patient selection criteria	All patients had complete spinal cord lesions as a result of road traffic accidents, and all had had surgery for spine stabilisation, or spinal cord decompression during the 1st week after the accident. None had traumatic brain injury or cognitive impairment after the accident.
Technique	Nerve transfer surgery was done for restoration of finger flexion under general anaesthesia. Intraoperative electric stimulation was used to identify healthy donor and recipient nerves. Patients had bilateral surgery, in 17 upper limbs, elbow, thumb, and finger extension together with finger flexion were restored via nerve transfers. In 3 upper limbs the nerve to the brachialis was transferred to the anterior interosseous nerve (AIN), which was separated from the median nerve from the antecubital fossa to the mid-arm. In 5 upper limbs, the nerve to the brachialis was transferred to the median nerve motor fascicles innervating finger flexion muscles in the mid-arm. In 4 upper limbs, the nerve to the brachioradialis was transferred to the AIN. In the remaining 5 upper limbs, the nerve to the extensor carpi radialis brevis (ECRB) was transferred to the AIN. Nerve co-aptation was done using a microscope and microfilament sutures. After surgery an arm sling was used for 10 days, and 4 cycles of 5 does of nandrolone given every 15 days with an interval of 30 days between cycles.
Follow-up	**Average 16±6 months (range 9-24 months)**
Conflict of interest/source of funding	None

Analysis

Study design issues: small number of patients, clinical examination based on tendon palpation was done to determine the status of wrist extensors. Patients had different surgical procedures and at final follow-up, the range of finger flexion and strength were estimated by manual muscle testing according to the British Medical Research Council scale.

Study population issues: in 1 patient finger flexion was not restored because of poor donor nerves. Reconstruction was done by tendon transfer. Only elbow, and thumb, and finger extension were restored via nerve transfers.

Other issues: authors conclude that ECRB is a better donor than the nerve to the brachialis or the nerve to the brachioradialis.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 9 patients (17 upper limbs)
Restoration of finger flexion
Complete finger flexion (defined as all fingertips touching the palm of the hand with the wrist at neutral to avoid any tendinosis effect promoted by wrist extension)
• Full finger flexion with M4 strength was demonstrated when the nerve to the ECRB was transferred to the AIN (in all 5 upper limbs).

Failure (defined as strength of at least M3 not achieved)
Incomplete finger flexion range and strength were associated when
• the nerve to brachialis was transferred to the proximally dissected AIN (in 3 limbs, 2 had M3 strength, 1 had M4 strength)
• the nerve to the brachialis was transferred to motor fascicles of the AIN at the proximal arm (in 5 limbs, 1 had M3 strength, 4 did not show recovery)
• the nerve to the brachioradialis was transferred to the AIN (in 4 limbs: 3 did not show any recovery, but partial finger flexion with M4 strength was restored in 1)

Recovery of M3 or better finger flexion strength was seen in 59% (10/17) limbs.
Proximal retrograde dissection of the AIN was associated with better outcomes than transfer of the nerve to the brachialis to median nerve motor fascicles in the arm.

No functional downgrading of elbow flexion or wrist extension strength was observed.</td><td>After proximal dissection of the AIN for connection with the nerve to the brachialis, all patients complained about numbness on the radial side of the hand, this disappeared within 3 months of surgery.</td></tr>
<tr><td colspan="2">Abbreviations used: AIN, anterior interosseous nerve; ECRB, extensor carpi radialis brevis;</td></tr>
</table>

Study 3 Bertelli JA & Ghizoni MF 2016

Details

Study type	Case series
Country	Brazil
Recruitment period	2013-2015
Study population and number	n=**5 patients (10 upper limbs) with tetraplegia** Mean spinal cord injury (SCI) level :C6 Time to surgery post SCI: mean 10 months
Age and sex	Average 23 years; 80% (4/5) male
Patient selection criteria	Patients with complete cervical spinal cord injury, all had wrist extension preserved, indicating preservation of the C6 spinal cord level. Protective sensation (perception of 19.3g Semmes-Weinstein monofilaments) was preserved at the pulp of the index and thumb and in the centre of the palm,
Technique	Sensory reconstruction on the ulnar side of the hand: in C8-T1 dermatomes by transferring sensory nerves with afferents at C5-C6 roots. Cutaneous branches of the median nerve (MB) in the palm were transferred to the skin just distal to the carpal tunnel to the ulnar proper palmer digital nerve of the little finger (V). In 2 patients the lateral antebrachial cutaneous nerve (LAC) was also transferred to the medial antebrachial cutaneous nerve (MAC). All patients had surgery bilaterally. Nerve co-aptation was done using a microscope and microfilament sutures.
Follow-up	**Mean 20 months (range 12 -24 months)**
Conflict of interest/source of funding	Study did not receive any financial support.

Analysis

Study design issues: small number of patients, sensory thresholds were investigated using Semmes-Weinstein 4 sets of monofilaments. The skin of the ulnar border of the hand was grasped with a flat Adson forceps for nociceptive assessment. Referred sensation corresponding to the donor nerve primary zone of innervation was considered as a guideline for innervation. The skin on the ulnar side of the hand was grasped with a flat Adson forceps with increasing firmness until pain was perceived, either in the central part of the palm or in the thenar region. This denoted that re-innervation stemmed from the nerve transfer rather than the spontaneous regeneration of adjacent nerves. This was repeated all over the medial side of the elbow and forearm in 2 patients with transfer of LAC to the MAC.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>
Number of patients analysed: 5 patients (10 upper limbs)
Sensation recovery along the medial side of the elbow, forearm and hand
<table>
<tr><th>Patient number</th><th>Surgery</th><th>Hand/monofilament thresholds</th><th>Forearm nociception</th></tr>
<tr><td>1</td><td>MB-V</td><td>19.3g</td><td>NA</td></tr>
<tr><td>2</td><td>MB-V</td><td>19.3g</td><td>NA</td></tr>
<tr><td>3</td><td>MB-V</td><td>19.3g</td><td>NA</td></tr>
<tr><td>4</td><td>MB-V+LAC-MAC</td><td>19.3g</td><td>+</td></tr>
<tr><td>5</td><td>MB-V+LAC-MAC</td><td>19.3g</td><td>+</td></tr>
</table>
+indicates perception of painful stimuli inflicted by a flat Adson forceps by grasping the skin of the ulnar border of the hand and medial forearm. There were no differences on the right and left side recovery.
All patients improved from baseline and perceived the 19.3 g monofilament pressure and pain on the medial side of the little finger and hand bilaterally. In the 2 patients in whom MAC was re-innervated via an LAC transfer, protective sensation (perception of 19.3g monofilaments) was restored in the medial side of the elbow and forearm. Sensation was preserved along the forearm and radial side of the hand after a musculocutaneous nerve block before LAC transfer.
Assessment for nociceptive recovery
Nociception was restored on the medial side of the elbow, forearm and hand. There were no deficits in the cutaneous branches of the median nerve in the palm or LAC when harvested.
</td><td>Referred sensation was demonstrated in all patients, but none complained that it adversely affected daily activities.</td></tr>
<tr><td colspan="2">Abbreviations used: LAC, lateral antebrachial cutaneous nerve; MAC, medial antebrachial cutaneous nerve; MB, median nerve branches to the palm; NA, not applicable because sensation was not surgically reconstructed; V, ulnar proper palmar digital nerve of the little finger.</td></tr>
</table>

Study 4 Fox IK 2015

Details

Study type	Case series
Country	USA
Recruitment period	2012-2013
Study population and number	n=**7 patients (8 upper limbs) with spinal cord injury related upper extremity dysfunction** Mean spinal cord injury (SCI) level :C6 Time to surgery post SCI: mean 5.4±5.4 years (range 0.9 to 12.6 years)
Age and sex	Mean 28±9.9 years; 86%(6/7) male
Patient selection criteria	Patients with cervical spinal cord injury presenting for consideration of surgery to restore upper extremity dysfunction, all needed volatile elbow flexion (Medical Research Council [MRC]>4) so that the brachialis can be used as a donor nerve, and no volatile hand function. 6 extremities had brachioradialis function and some use of hand and wrist function.
Technique	Nerve transfer from brachialis to AIN for restoration of pinch 4 had transfer from brachialis to flexor carpi radialis (FCR) and flexor digitorum superficialis (FDS) 1 patient had supinator to extensor carpi ulnaris transfer 1 patient had deltoid to triceps transfer When wrist extension was absent, the exterior carpi radialis or extensor carpi ulnaris nerves were targeted as recipients. When wrist extension was present, the anterior interosseous nerve (AIN) was used as recipient nerve for restoration of pinch. Patients were discharged next day with instructions to avoid full weight bearing until oedema and pain had resolved. Light activities including elbow flexion were allowed after surgery. No casts were needed and a simple airstrip dressing was done and removed on day 2.
Follow-up	**Range 1 to 18 months**
Conflict of interest/source of funding	Study did not receive any financial support. 2 authors received travel/accommodation reimbursement from the paralysed veterans of America organisation for lectures.

Analysis

Follow-up issues: postoperative evaluation done at 2, 4 and 12 weeks.

Study design issues: prospective cohort study, small number of patients, nerve transfer procedures were selected based on available donor nerves, and preoperative functional and electro diagnostic assessment of the upper extremity. Data were entered into a SCI database. The main outcomes were the proportion of patients with a postoperative complication and the proportion of patients with functional loss related to nerve transfer.

Population issues: all patients had comorbidities including pulmonary or urinary infections and pressure sores. Patients had varying degrees of spasticity that was managed with medication, botulinum toxin type A injection, or baclofen bump.

Other issues: authors state that careful patient selection, evaluation, treatment and management by skilled microsurgery/nerve surgeons are important as patients have limited treatment options and any downgrade of function is unacceptable.

Key efficacy and safety findings

Efficacy

Number of patients analysed: 7 **patients (8 upper limbs)**

Mean operative time: 231±95 minutes

Mean length of hospital stay: 1.3±0.5 days

Functional outcomes

No patient had any loss of baseline upper extremity function.

Patient	Follow-up(months)	Nerve transfer	Time since SCI (years)	MRC for muscle strength	Functional outcomes
1 left 1 right	1	Brachialis to AIN &FCR Brachialis to AIN, FCR/FDS	0.9	Not measured	Increase in grasp strength
2 right hand	18	Brachialis to AIN, Brachialis to FCR Supinator to PIN	10.4	FCR-2, FPL-2, FDP IF/LF 2	Increase use of hand for feeding, holding things, ability to self-catheterize
4 left hand	11	Brachialis to AIN/FCR, deltoid to triceps	0.6	FPL 2, FDP IF/LF 2, TRICEPS 2+	Improved pinch activities, increased arm use for reaching out and grabbing files.
5 right hand	10	Brachialis to AIN Supinator to ECU	1.7	ECU 2, ECR 2 to3, FPL, FDP IF 1+	Increased wrist stability when reaching hand into snack bag, better tenodesis grip
6 right hand	9	Brachialis to AIN Brachialis to FCR	12.4	FDP IF 1	No appreciable subjective changes reported
7 right hand	11	Brachialis to AIN/FDS	12.6	FPL 2, FDP IF 2, FDS 2	Increased grasp strength, able to self-catheterize without use of clip assist device.

Presence of distal muscle function (assessed by intraoperative stimulation)

7 nerve specimens had preserved micro architecture and all intraoperative stimulation of recipient muscular units was successful further supporting feasibility.

safety

Perioperative complications

	n
Thumb paraesthesia (resolved or improved in 3, 1 had mild symptoms)	4
Urinary tract infection (prolonged stay)	1
Seroma (drained percutaneously in hospital)	1
Urosepsis (1 week after surgery; readmitted and treated)	1

Abbreviations used: AIN, anterior interosseous nerve; ECRL, extensor carpi radialis longus; ECU, extensor carpi ulnaris; FCR, flexor carpi radialis; FDS, flexor digitorum superficialis.

Study 5 Hawasli AH 2015

Details

Study type	Case report
Country	USA
Recruitment period	
Study population and number	n=**1 patient with complete C7 spinal cord injury and failure of any hand motor recovery** Mean spinal cord injury (SCI) level :C7 Time to surgery post SCI: 8 months
Age and sex	21 years; 86%(6/7) male
Patient selection criteria	
Technique	Nerve transfer from brachialis to anterior interosseous nerve (AIN) The brachialis nerve and AIN fascicles were isolated using visual inspection and motor mapping. Careful dissection and microsurgical co-aptation was done. Bilateral surgery performed and regular outpatient hand physical therapy provided through a specialised SCI rehabilitation program. Traditional therapy has been enriched by advanced technologies. In addition, goal directed exercises to improve activities of daily living were provided.
Follow-up	**3 months**
Conflict of interest/source of funding	None Study supported by the Department of Neurosurgery at Washington University and funded by the National Institutes of Health.

Analysis

Population issues: Preoperatively patient had full strength in biceps, triceps and wrist extension but only minimal finger movements in hands and required assistance with basic tasks. A preoperative electromyogram and nerve conduction study showed normal motor activity above C7, no muscle action at the wrist and no motor potentials to the FDP and FPL.

Key efficacy and safety findings

Efficacy
Number of patients analysed: 1 **patient** Recovery from surgery was uncomplicated. After 3 months of outpatient physical therapy, the patient demonstrated improvement in left hand function with MRC scale for muscle strength 2 to 3/5 function on the first and second digit FDP AND FPL. Recovery on the right side was more modest.
Abbreviations used: FDP, flexor digitorum profundus; FPL, flexor pollicis longus; MRC, Medical Research Council.

Validity and generalisability of the studies

- Multiple small case series and case reports have reported several types of nerve transfer to partially restore upper extremity function in selected patients with tetraplegia.
- Triceps function (elbow extension) has been restored by transfer of the axillary nerve, teres minor nerve or brachialis nerve to the triceps nerve in patients with C6 SCI; hand (finger and thumb extension, pinch and grasp) and wrist function has been restored by a handful of methods, including: transfers of the supinator to posterior interosseous nerve (PIN), the distal extensor carp radialis brevis (ECRB) to the flexor pollicis longus (FPL), the brachialis nerve to anterior interosseous nerve (the AIN) in patients with C7 SCI and the axillary to the radial nerve in patients with C6 SCI; and transfers of the brachialis to the extensor carpi radialis longus (ECRL) in patients with C5 SCI and the musculocutaneous nerve to median nerve in patients with C5-7 SCI.
- Time to nerve transfer surgery post SCI varied across studies and patients.
- Only 1 case report included tendon and nerve transfer technique in 1 procedure.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Phrenic nerve transfer in brachial plexus injury. NICE interventional procedure guidance IPG468 (2013). Available from https://www.nice.org.uk/guidance/ipg468

NCE guidelines

- Spinal injury: assessment and initial management (2016) NICE guideline 41

Available from http://www.nice.org.uk/guidance/NG41

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Four Specialist Advisor Questionnaires for nerve transfer to partially restore upper limb function in tetraplegia were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 10 questionnaires to 2 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 3 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Company engagement

No structured information requests were sent to companies who manufacture a potentially relevant device for use in this procedure.

Issues for consideration by IPAC

- Ongoing studies
  - **NCT01714349:** Restoring hand function using nerve transfers in persons with spinal cord injury- an interventional study; estimated enrolment: 20; intervention: single nerve transfer- brachialis branch to AIN; primary outcome: change in upper motor function; study start date: October 2012; completion date: October 2019; location: USA; status: currently recruiting.

- **NCT01579604:** early nerve reconstruction approach in tetraplegic patients with dysfunctional upper extremity-a randomised controlled trial; estimated enrolment: 10; surgical arm-nerve reconstruction (supinator to PIN transfer in 5 patients) compared with standard care (observation in 5 patients); primary outcome: hand function recovery (MRC grading system testing the strength of muscles ranging from grade 0 to 5); study start date: June 2012. Completion date: December 2017; location: Canada; status: currently recruiting.
- **NCT01899664.** Upper Extremity Surgery in Spinal Cord Injury. Study is currently recruiting participants. Estimated enrolment: 50. Study start date: June 2012. Estimated study completion date: December 2018
- **NCT02861612** Nerve Transfers to Restore Hand Function in Spinal Cord Injury. This study is not yet open for participant recruitment. Estimated enrolment: 5. Study start date: August 2016. Estimated study completion date: July 2021

References

1. Cain SA, Gohritz A, Friden J and van Zyl N (2015). Review of Upper Extremity Nerve Transfer in Cervical Spinal Cord Injury. Journal of Brachial Plexus & Peripheral Nerve Injury (10) 1 e34-e42.
2. Bertelli JA and Ghizoni MF (2017). Nerve transfers for restoration of finger flexion in patients with tetraplegia. Journal of Neurosurgery Spine (26) 1 55-61.
3. Bertelli JA and Ghizoni MF (2016). Nerve transfer for sensory reconstruction of C8-T1 dermatomes in tetraplegia. Microsurgery (36) 8 637-641.
4. Fox IK, Davidge KM et al (2015). Use of peripheral nerve transfers in tetraplegia: evaluation of feasibility and morbidity. Hand 10: 60-67.
5. Hawasli AH, Chang J et al (2015). Transfer of the Brachialis to the Anterior Interosseous Nerve as a Treatment Strategy for Cervical Spinal Cord Injury: Technical Note. Global Spine Journal. 5:110-7.

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	15/12/2017	Issue 12 of 12, December 2017
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	15/12/2017	Issue 11 of 12, November 2017
HTA database (Cochrane Library)	15/12/2017	Issue 4 of 4, October 2016
MEDLINE (Ovid)	15/12/2017	1946 to December 13, 2017
MEDLINE In-Process (Ovid)	15/12/2017	December 13, 2017
MEDLINE E-pub ahead of print (OVID)	15/12/2017	December 13, 2017
EMBASE (Ovid)	15/12/2017	1974 to 2017 Week 50

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	exp Spinal Cord Injuries/
2	exp spinal injuries/
3	spinal cord compression/
4	exp neck injuries/
5	Spinal Nerves/
6	((spine or spinal or vertebr* or neck or cervical or lumbar or sacral or thoracic or cord or whiplash) adj4 (injur* or damag* or trauma* or fracture* or compress* or contus* or lacerat* or transect* or lesion*)).tw.
7	SCI.tw.
8	Peripheral Nerve Injuries/
9	(peripher* adj4 nerv* adj4 (injur* or damag* or trauma* or fracture* or compress* or contus* or lacerat* or transect* or lesion*)).tw.
10	(brachial adj4 plexus adj4 (diaprares* or plexopath* or injur* or damag* or trauma* or fracture* or compress* or contus* or lacerat* or transect* or lesion*)).tw.
11	avulsion*.tw.
12	or/1-11
13	Quadriplegia/

14	(tetraplegi* or quadriplegi* or quadripares*).tw.
15	((limb* or extremit* or torso*) adj4 (paralys* or denervat* or "motor impair* function*" or "sens* impair* function*" or "physiological* impair* function*")).tw.
16	or/13-15
17	Nerve Transfer/
18	Nerve Regeneration/
19	(nerve* adj4 (transfer* or crossover* or regenerat* or repair* or recover* or transplant* or graft* or allotransplant*)).tw.
20	(neur* adj4 regenerat*).tw.
21	neuroregeneration.tw.
22	neuroti*.tw.
23	(re-innervat* or reinnervat*).tw.
24	Reconstructive Surgical Procedures/
25	(reconstruct* adj4 (neurosurg* or surg*)).tw.
26	Recovery of Function/
27	(recover* adj4 funct*).tw.
28	or/17-27
29	12 and 16 and 28
30	animals/ not humans/
31	29 not 30
32	limit 31 to ed=20170606-20171231

Additional relevant papers

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bertelli JA and Ghizoni MF (2015). Nerve transfers for elbow and finger extension reconstruction in midcervical spinal cord injuries. Journal of Neurosurgery (122) 1 121-7.	Case series n=13 upper limbs from 7 patients with tetraplegia (mid cervical injury, spinal level C6) average age 26 years Time to surgery: average 7 months after spinal cord injury. Intervention: Elbow, thumb, and finger extension reconstruction via nerve transfer (the posterior division of the axillary nerve was used to re-innervate the triceps long and upper medial head motor branches in 9 upper limbs. Both the posterior division and the branch to the middle deltoid were used in 2 upper limbs, and the anterior division of the axillary nerve in the final 2 limbs. For thumb and finger extension reconstruction, the nerve to the supinator was transferred to the posterior interosseous nerve in 13 limbs). Follow-up: average 19 months	In 22 of the 27 recipient nerves, a peripheral type of palsy with muscle denervation was identified. At an average of 19 months follow-up, elbow strength scored M4 in 11 upper limbs and M3 in 2, according to the British Medical Research Council scale. Thumb extension scored M4 in 8 upper limbs and scored M3 in 4. Finger extension scored M4 in 12 hands. No donor-site deficits were reported or observed. Nerve transfers are effective at restoring elbow, thumb, and finger extension in patients with a midcervical spinal cord injury.	Study included in Cain SA 2015 included in table 2.
Krasuski M and Kiwerski J (1991). An analysis of the results of transferring the musculocutaneous nerve onto the median nerve in tetraplegics. Archives of Orthopaedic & Trauma Surgery (111) 1 32-3.	Case series N=42 patients with traumatic tetraplegia (spinal level C6-7). Average age 42 years Time to surgery 4.1 months after injury Nerve transfer: anastomosis of the musculocutaneous nerve to the median nerve. Follow-up: not reported	In 32 patients this has restored simple grasping function of the hand, increasing the patients' independence. The operation is particularly indicated in cases of complete lesion of the spinal cord at the C6-C7 level in young people, and for best results should be performed with in the first few months after trauma.	Study included in Cain SA 2015 included in table 2.

Loch-Wilkinson T, McNeil S et al (2018). Nerve Transfers in Patients with Brown-Sequard Pattern of Spinal Cord Injury: Report of 2 Cases. World Neurosurgery (110) 152-157.	Case report N=2 cases of combined Brown-Sequard injury and unilateral brachial amyotrophy	Case description: patient 1, a 43-year-old woman, was involved in a motor vehicle accident and sustained left-side C5-7 level hemicord injury causing ipsilateral proximal arm weakness and sensory loss with contralateral hemisensory changes, neuropathic pain, and spasms. At 6 months after injury, she had a spinal accessory to suprascapular nerve, radial nerve triceps branch to axillary nerve, and ulnar fascicle to biceps transfer. At 2-year follow-up, she had improved function with Medical Research Council grade 4 power of shoulder abduction, elbow flexion, and internal and external rotation. Patient 2, a 38-year-old man, sustained a C4-5 fracture-dislocation in a motor vehicle accident and associated right-side hemicord injury involving the C5 and C6 myotomes with relatively preserved distal function. At 9 months after injury, he had radial nerve triceps branch to axillary nerve division and ulnar nerve fascicle to musculocutaneous nerve brachialis branch transfer. At 8 months after surgery, electromyography showed evidence of further re-innervation of the deltoid muscle. Our early experience of nerve transfer with 2 patients with combined Brown-Sequard cord injury and brachial amyotrophy indicated acceptable surgical safety and showed encouraging results.	More relevant studies included in table 2.

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