Review

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Investigation Into the Optimal Number of Intercostal Nerve Transfers for Musculocutaneous Nerve Reinnervation: A Systematic Review

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Abstract
Background: The purpose of this study was to systematically review outcomes following intercostal nerve (ICN) transfer for restoration of elbow flexion, with a focus on identifying the optimal number of nerve transfers. **Methods:** A systematic review was performed following Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines to identify studies describing ICN transfers to the musculocutaneous nerve (MCN) for traumatic brachial plexus injuries in patients 16 years or older. Demographics were recorded, including age, time to operation, and level of brachial plexus injury. Muscle strength was scored based upon the British Medical Research Council scale. **Results:** Twelve studies met inclusion criteria for a total of 196 patients. Either 2 (n = 113), 3 (n = 69), or 4 (n = 11) ICNs were transferred to the MCN in each patient. The groups were similar with regard to patient demographics. Elbow flexion ≥M3 was achieved in 71.3% (95% confidence interval [CI], 61.1%-79.7%) of patients with 2 ICNs, 67.7% (95% CI, 55.3%-78.0%) of patients with 3 ICNs, and 77.0% (95% CI, 44.9%-93.2%) of patients with 4 ICNs (*P* = .79). Elbow flexion ≥M4 was achieved in 51.1% (95% CI, 37.4%-64.6%) of patients with 2 ICNs, 42.1% (95% CI, 29.5%-55.9%) of patients with 3 ICNs, and 48.4% (95% CI, 19.2%-78.8%) of patients with 4 ICNs (*P* = .66). **Conclusions:** Previous reports have described 2.5 times increased morbidity with each additional ICN harvest. Based on the equivalent strength of elbow flexion irrespective of the number of nerves transferred, 2 ICNs are recommended to the MCN to avoid further donor-site morbidity.

Keywords: peripheral nerve, brachial plexus, nerve transfer, intercostal nerve, musculocutaneous nerve, elbow flexion

Introduction

The intercostal nerve (ICN) transfer is most frequently used in patients with polynerve trauma or in cases of pan-plexus palsy, where no other suitable donor nerves are available.[12] First described in 1963, Seddon proposed using 2 ICNs (T3 and T4) with a nerve graft extension to neurotize the musculocutaneous nerve (MCN).[24] Since then, several studies have reported on the ICN to MCN transfer as an effective means of restoring elbow flexion in patients with brachial plexus injuries.[5,15,24]

Despite the effectiveness and well-described use of the ICN to MCN transfer, the number of ICNs used as well as treatment outcomes vary greatly among different surgical center.[16] Tsuyama and colleagues[30] and Minami and Ishii[17] advocated transferring 2 ICNs, while Narakas[20] and Chuang and colleagues[6] recommended 3 ICNs to better match the diameter of the MCN. While there may be an ideal size match for the success of a nerve transfer, it is likely dependent on a combination of host, anatomic, and functional factors, and is yet to be studied in detail. However, this may explain why the transfer of 2, 3, or 4 ICNs is preferred over more. Reports also differ in the degree of injury, time from injury to surgical repair, and other aspects of the surgical technique, thereby complicating outcomes analysis. In this systematic review, we sought to answer 2 questions: (1) What are the outcomes following ICN to MCN transfer? and (2) How many nerve transfers are needed to achieve optimal elbow flexion?

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Materials and Methods

Literature Review

A systematic review of published studies was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[18] After specifying the search criteria, inclusion and exclusion criteria, and analytic methods in advance, the PubMed and Google Scholar databases were queried using 3 distinct search terms. The search terms were: (1) "intercostal nerve" AND "transfer"; (2) "musculocutaneous nerve" AND "reinnervation"; and (3) "musculocutaneous nerve" AND "transfer." Inclusion criteria were journal articles published in the English language that described the use of intercostal to MCN transfer for restoration of elbow function, with results reported using the British Medical Research Council (MRC) scale for muscle strength. Exclusion criteria were: (1) patients under the age of 16; (2) use of interposition nerve grafts; (3) inadequate reporting of number of ICNs used; (4) transfer of additional donor nerves to the MCN or its branches; (5) patients who had follow-up less than 12 months after their operation; (6) studies without any functional data for elbow flexion; and (7) review articles.

Articles were initially screened based on title and abstract. Duplicates were eliminated, and a full-text review of the remaining articles was performed. Citations were cross-referenced to ensure a complete list of potential studies. The final articles included in the study were then reviewed for study design as well as the presence of individual data points, including number of nerves transferred and general cohort characteristics (age, gender, time from injury to operation, British MRC scale postoperatively, and follow-up time). Figure 1 depicts the study attrition.

The Methodological Index for Non-randomized Studies (MINORS) criteria were applied to each study to evaluate its quality and reporting bias.[25] Each study was assigned 0, 1, or 2 points for each of the applicable MINORS criteria items, and the scores were added and reported in percentages to allow for evaluation of the quality of each study; 100% indicates a perfectly conducted study, and 0% indicates the worst possible study design.

Data Analysis

Individual data points were categorized based on the number of ICNs transferred (2, 3, or 4). Summary statistics (mean and range of study means) were calculated for age, time from injury to repair, follow-up time, and percent (95% confidence interval [CI]) male patients, for subsets of these studies that included these data. Statistical comparisons could not be made between patient age, time from injury to repair, and follow-up time across the different nerve groups, as standard deviations were inconsistently reported in the included studies. An effort was made to contact authors for this information, but usable data were unable to be obtained.

Primary endpoints are summarized as percentages and 95% CIs overall, and by subgroups defined by number of nerves (2, 3, or 4). Meta-analyses were performed for 2 binary endpoints, percentage of patients achieving ≥M3 and ≥M4 strength, using Comprehensive Meta-Analysis v3 software. This software requires studies to have n ≥ 1; therefore two 2-nerve studies were excluded from the meta-analyses. A value of $P \leq .05$ was considered significant.

Results

The primary literature search identified 210 results. When abstracts were reviewed and studies not meeting inclusion criteria excluded, 12 articles were included for analysis (Figure 1). General study characteristics can be found in Table 1. The mean MINORS criteria score of the studies was 74% (95% CI, 69%-78%).

One hundred ninety-three patients underwent intercostal to MCN transfer. Either 2 (n = 113), 3 (n = 69), or 4 (n = 11) ICNs were transferred to the MCN in each patient. The average age of the study population was 29 ± 13 years, and 93% of the patients were male. Per individual nerve group, the average ages were 26.1 (2 ICNs), 27.1 (3 ICNs), and 33.6 (4 ICNs) years. The average time to surgery for the total population was 3.5 ± 2 months. For the 2 ICN group, the average time to surgery was 5.6 months, for the 3 ICN group it was 4.5 months, and for the 4 ICN group it was 1.7 months. For the total population, the mean follow-up length was 33.7 ± 14.6 months, and the average length of follow-up per individual nerve group was as follows: 51.5 (2 ICNs), 37.5 (3 ICNs), and 42.5 (4 ICNs) months (Table 2).

Strength of elbow flexion was then evaluated following ICN transfer. Based on all evaluable studies, elbow flexion ≥M3 was found in 70.2% (95% CI, 62.8%-76.7%) of patients and elbow flexion ≥M4 was reported in 46.7% (95% CI, 37.5%-56.1%) of patients. Functional outcomes were then compared across the different ICN groups. Elbow flexion ≥M3 was achieved in 71.3% (95% CI, 61.1%-79.7%) of patients with 2 ICNs, 67.7% (95% CI, 55.3%-78.0%) of patients with 3 ICNs, and 77.0% (95% CI, 44.9%-93.2%) of patients with 4 ICNs (P = .79). Elbow flexion ≥M4 was achieved in 51.1% (95% CI, 37.4%-64.6%) of patients with 2 ICNs, 42.1% (95% CI, 29.5%-55.9%) of patients with 3 ICNs, and 48.4% (95% CI, 19.2%-78.8%) of patients with 4 ICNs (P = .66; Table 3).

Discussion

In 2001, a meta-analysis conducted by Merrell et al was unable to demonstrate any significant functional differences when comparing 2 ICNs versus 3 or 4 ICNs to restore elbow flexion to ≥M3 (75% vs 66%) or ≥M4 (42% vs 38%).[16]

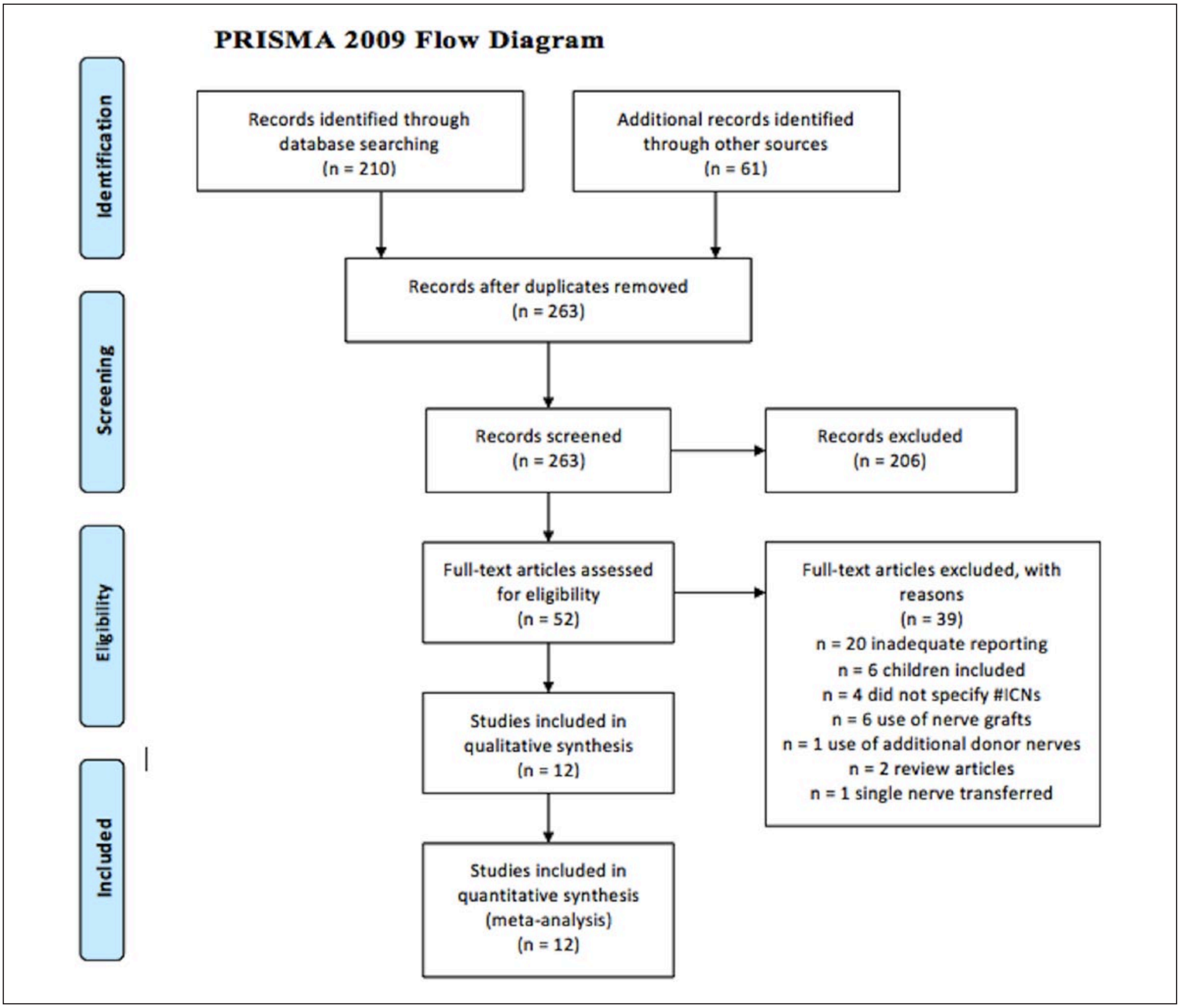

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).
Note. #ICNs = number of intercostal nerves.

While that report was based on a large number of patients, totaling 418, it contained a number of confounding variables. It included both pediatric and adult patients, relied on qualitative results that were translated into the corresponding British MRC scale, and did not exclude 7% of patients who did not have outcomes stratified by the number of ICNs transferred.

The current systematic review aimed to build on the work of Merrell and colleagues by tightening the study inclusion and exclusion criteria. It focused on the adult population, as younger patients tend to demonstrate a higher regenerative capacity.[1,13,29] Studies were excluded if they did not explicitly score elbow flexion using the British MRC scale, as conversion of qualitative results into such a format could be viewed as arbitrary. Reports were also excluded if functional outcomes were not stratified by the distribution of ICNs, as it prohibited identifying the optimal number for nerve transfer.

Based on the findings of this systematic review, the strength of elbow flexion did not improve with increasing number of ICNs transferred. This is in agreement with the aforementioned meta-analysis performed by Merrell et al.[16] It also matches the individual results reported by Chuang and colleagues, which found no significant functional differences when comparing 2 ICNs versus 3 ICNs to restore elbow flexion to ≥M4 (59% vs 73%, $P \geq .05$),[6] as well as those reported by Xiao et al, which found no statistical difference in ≥M3 recovery regardless of number of ICNs

Table 1. Outcomes Data of Studies Meeting Inclusion Criteria.

Study (year)	Number of nerves	Number of cases	Mean age	% male	Mean time from injury (mo)	Mean follow-up time (mo)	% ≥M4	% ≥M3	MINORS criteria score (%)
Minami and Ishii (1987)[17]	2	17	23	94	7	67	71 (12)	100 (17)	75
Kawai et al (1988)[10]	2	13					46 (6)	46 (6)	69
Ogino and Naito (1995)[22]	2	9	18.6	80		57.3	67 (6)	89 (8)	69
Songcharoen (1995)[26]	2	17	23	94	2.6			65 (11)	69
Malessy and Thomeer (1998)[15]	2	2	22.1	0			50 (1)	50 (1)	75
Malessy et al (2003)[14]	2	1	16	100	2.3		100 (1)	100 (1)	75
Songcharoen et al (2005)[27]	2	22						63.6 (14)	56
Kakinoki et al (2010)[10]	2	8	38.4	88	4.9	32.7	75 (6)	100 (8)	75
Xiao et al (2014)[31]	2	9	33	100	7.2	59.9	22 (2)	67 (6)	83
Cho et al (2015)[4]	2	15	28.3		6.8	38.6	27 (4)	67 (10)	69
Kawai et al (1988)[10]	3	6					33 (2)	33 (2)	69
Malessy and Thomeer (1998)[15]	3	17					47 (8)	59 (10)	75
Malessy et al (2003)[14]	3	8	20.8	63	2		63 (5)	63 (5)	75
Bhandari et al (2009)[2]	3	4	22.5	100	3.5	23.8	25 (1)	75 (3)	75
Coulet et al (2010)[7]	3	17	25	88	5.7	32	41 (7)	71 (12)	94
Xiao et al (2014)[31]	3	17	33.12	88	4.76		35 (6)	82 (14)	83
Kawai et al (1988)[10]	4	4					50 (2)	50 (2)	69
Malessy and Thomeer (1998)[15]	4	2					100 (2)	100 (2)	75
Malessy et al (2003)[14]	4	1	16	100	2		100 (1)	100 (1)	75
Xiao et al (2014)[31]	4	4	38	100	1.63		25 (1)	75 (3)	83

Note. Value in parentheses refers to the raw number of patients. MINORS = Methodological Index for Non-randomized Studies.

Table 2. Patient Information by Number of ICNs Transferred.

Number of intercostal nerve transfers	2 ICNs	3 ICNs	4 ICNs
Mean age (years)	26.1 (16-38.4)	27.1 (20.8-33.12)	33.6 (16-38)
Mean time to operation (months)	5.6 (2.6-7.2)	3.3 (2.3-5.7)	1.7 (1.63-3.35)
Mean length of follow-up (months)	51.5 (31-59.9)	37.5 (31-46.1)	42.5 (31-48.3)

Note. Values in parentheses are minimum and maximum averages for each study group and are not values describing individual patients. ICN = intercostal nerve.

Table 3. Average Outcomes by Number of ICNs Transferred.

Number of intercostal nerve transfers	2 ICNs	3 ICNs	4 ICNs	*P* value
Postoperative MRC ≥ 3 (%)	71.3 (95% CI, 61.1-79.7)	67.7 (95% CI, 55.3-78.0)	77.0 (95% CI, 44.9-93.2)	.79
Postoperative MRC ≥ 4 (%)	51.1 (95% CI, 37.4-64.6)	42.1 (95% CI, 29.5-55.9)	48.4 (95% CI, 19.2-78.7)	.66

Note. ICN = intercostal nerve; MRC = Medical Research Council; CI = confidence interval.

transferred (77% with 2 ICNs vs 67% with 3 ICNs vs 82% with 4 ICNs, $P = .832$).[31]

The question becomes, "Why doesn't increased number of ICN transfers result in stronger elbow flexion?" As the ICN is a mixed nerve composed of 1200 to 1300 myelinated fibers, 4 to 5 ICNs would have been predicted to maximally power the roughly 6000 fibers within the MCN.[20] The importance of an appropriate size match between donor and recipient nerves as well as an appropriate donor-to-recipient axon count ratio has been suggested to determine clinical success.[23] It is possible that the present systematic review simply did not include a sufficient number of studies, with too few patients included within each individual study, and was thus unable to identify functional differences across the various nerve transfer groups. On the contrary, there may be a biological mechanism to explain the functional parity. Single motor units have been shown to enlarge up to 5 times their original size following denervation, resulting in the ability to compensate nearly 80% of motor neuron loss.[8,22] In addition, in a rabbit model, Spector and Lee found that only 12% of the original motor axon population of the facial nerve is required to evoke muscle activity.[28] Although these studies imply that a perfect axonal ratio is not necessary for muscle reinnervation, a clear explanation remains elusive at this time.

As the strength of elbow flexion did not improve with increasing number of ICNs transferred, 2 ICNs are recommended for their equivalent efficacy yet improved safety profile. In a study by Kovachevich et al, a direct correlation was found between complication rates and increased number of ICNs transferred.[11] Specifically, each additional ICN harvest was associated with a 2.49 times increase in the odds ratio of having a complication ($P < .001$). The most common complication was an iatrogenic pleural tear during nerve elevation, which was reported in 14 of 153 patients.

The findings of this systematic review must be interpreted in the context of several limitations. Functional analysis strictly focused on the strength of elbow flexion, as based upon the British MRC scale. The use of the British MRC as a quantification of strength after intervention is somewhat subjective and may introduce a degree of interrater variability.[3] The discrepancy in length of follow-up may have also confounded the functional analysis. Two ICN transfers were followed for longer periods of time on average and may have benefited from the positive effects of time on degree and strength of neurotization. It is possible that the strength of elbow flexion reported for 3 ICN transfers may have further improved if more follow-up time was allotted.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

No participants were included in this study, and thus informed consent did not need to be obtained.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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