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REVIEW ARTICLE

Elbow flexion in neonatal brachial plexus palsy: a meta-analysis of graft versus transfer

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Abstract

Background Functional elbow flexion recovery is one of the main goals of neonatal brachial plexus palsy (NBPP) reconstruction. The current neurosurgical treatment options include nerve grafting and nerve transfer.

Objective The present study sought to examine the literature for comparison of functional elbow flexion recovery in NBPP following nerve grafting or nerve transfer. We conducted a systematic literature review and meta-analysis according to PRISMA guidelines. A search was conducted on Pubmed/Medline and Cochrane for eligible studies published until November of 2018. Odd ratios (OR) and 95% confidence intervals (CI) were calculated to compare functional elbow flexion outcomes between nerve graft and nerve transfer. A random effects model meta-analysis was conducted. A Medical Research Council (MRC) score ≥ 3 or Active Movement Scale (AMS) ≥ 5 was considered a functional recovery of elbow flexion.

Results The present study included 194 patients from 1990 to 2015 across five observational trials. Only pediatric patients with obstetric brachial plexus injury were included. The mean patient age at surgery varied between studies from 5.7 months to 11.9 months and mean follow-up from 12 to 70 months. No complications or cases of donor site morbidity were reported. From the included studies, 118 patients were reported with MRC or AMS scoring usable for odd ratio comparison. Functional recovery occurred with nerve transfer in 95.2% of patients ($n = 59/62$) and with nerve grafting in 96.4% of patients ($n = 54/56$). Overall, the outcomes for elbow flexion between the groups appeared similar (OR 1.15, 95% CI 0.19–7.08, I^2 2.9%).

Conclusion Comparing nerve grafting and nerve transfer for NBPP, there is no statistically significant difference in functional elbow flexion recovery.

Keywords Neonatal brachial plexus palsy · Nerve graft · Nerve transfer · Elbow flexion · Erb's palsy

Introduction

Neonatal brachial plexus palsy (NBPP) is a common obstetric complication due to stretch injury of the nerves of the brachial plexus during childbirth, with an incidence of up to 3 per 1000 live births [2, 5, 6, 21]. When involving the distributions of C5 to C7, patients can experience severe or complete loss of shoulder abduction, supination, and most importantly elbow flexion which is one of the primary goals of brachial plexus reconstruction [23].

The current neurosurgical options for NBPP to restore elbow flexion include either nerve grafting or nerve transfer. Neurolysis alone was a historical option, but was significantly outperformed by nerve grafting with regard to functional outcomes in NBPP and has fallen out of practice as an isolated surgical approach [14]. Nerve grafting has been implemented in NBPP for more than three decades and involves the use of

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an autologous nerve donor, most commonly the sural nerve [3]. The nerve graft can act as a bridge across the site of a neurotmetic injury. If for example the C5 or C6 nerve roots are available following a post-ganglionic injury, a nerve graft can be used to connect the nerve roots across the neurotmetic site, following excision of the neuroma. Nerve transfers involve sacrifice of a donor nerve or fascicles by incision and subsequent coaptation to a nerve of interest. While their use is relatively new compared with nerve grafts, several studies have established their capability for restoration of elbow flexion in NBPP [4, 15, 20, 21]. For the recovery of elbow flexion, common donors include intercostal nerve [12], ulnar or median nerve transfers (Oberlin) [3], and medial pectoral nerve [24], as well as intraplexal nerve transfer following root avulsion [16].

Both nerve transfers and grafts have demonstrated functional outcomes with regard to elbow flexion, but the question of the optimal approach remains controversial [15, 18, 21]. Here, we present a meta-analysis of all the available studies comparing graft vs transfer in NBPP and subsequent elbow flexion outcomes.

Methods

The present systematic review and meta-analysis were performed according to the PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses). A systematic search was conducted in PubMed/Medline and Cochrane databases by two independent investigators (PT, MT), search terms: "Brachial Plexus," "Injury," "elbow flexion," "trauma," "traumatic," "transfer," "transfers," "graft," "grafting." Any discrepancies were resolved through consensus.

Selection criterion

Pre-determined criteria defined the following requirements for inclusion of a study: i) an included study must be randomized controlled trial or observational study, ii) the study must have reported head to head comparison of nerve graft vs transfer in NBPP; iii) the study must have been published in English by November of 2018; and iv) studies must have reported quantitative outcomes data of post-operative elbow flexion, including the Medical Research Council (MRC) score, or the Active Movement Scale (AMS) score. These inclusion criteria were used to focus only on comparative studies of graft vs transfer in NBPP and that reported relevant outcomes.

Data abstraction

Independent and blinded reviewers (NH, MT) extracted data from eligible studies. The variables of abstraction include the following: author, years of enrollment, location, study design, arms, number of patients, sex, follow-up, reported functional scores (AMS and MRC), age at surgery, complications, donor nerve for either procedure, level of injury, length of graft, and surgical details. The primary outcome was recovery of elbow flexion following a nerve transfer or graft procedure. Post-operative functional recovery of elbow flexion for NBPP was defined as ≥ 3 on the MRC scale as reported elsewhere [3]. In studies reporting AMS scales but not MRC, an AMS score of ≥ 5 was considered an equivalent functional recovery of elbow flexion against gravity [1].

Risk of bias assessment

Risk of bias was assessed by two investigators (PT, MT) with the Robins-I tool for non-randomized studies [9]. The following domains were evaluated: confounding, selection of participants, departure from intended interventions, missing data, measurement of outcomes, and selective reporting. Any discrepancies were resolved via consensus following discussion with senior authors.

Statistical analysis

Primary outcomes were compared using odd ratios (ORs) with corresponding 95% confidence intervals (CIs). A random effects model was used to account for heterogeneity among studies. Heterogeneity was assessed with the Higgins I-square statistic, where an I^2 greater than 50% indicated significant heterogeneity [10]. Forest plots were used to graphically display the effect size in each study and the pooled estimates. A p value of < 0.05 was considered significant. STATA 14.1 (StataCorp, College Station, TX) software was used for all analyses.

Results

Search results

The literature search yielded 147 records after removal of duplicates. Following the screening of titles and abstracts, seven studies were eligible for full-text evaluation. Five studies met pre-determined eligibility criteria and were included in the meta-analysis, outlined in the PRISMA Flow Diagram (Fig. 1) [1, 3, 8, 16, 18].

Study characteristics

The present study included 194 patients from 1990 to 2018 across five observational trials. Only pediatric patients with obstetric brachial plexus injury were included. The mean patient age at surgery varied between studies from 5.7 to

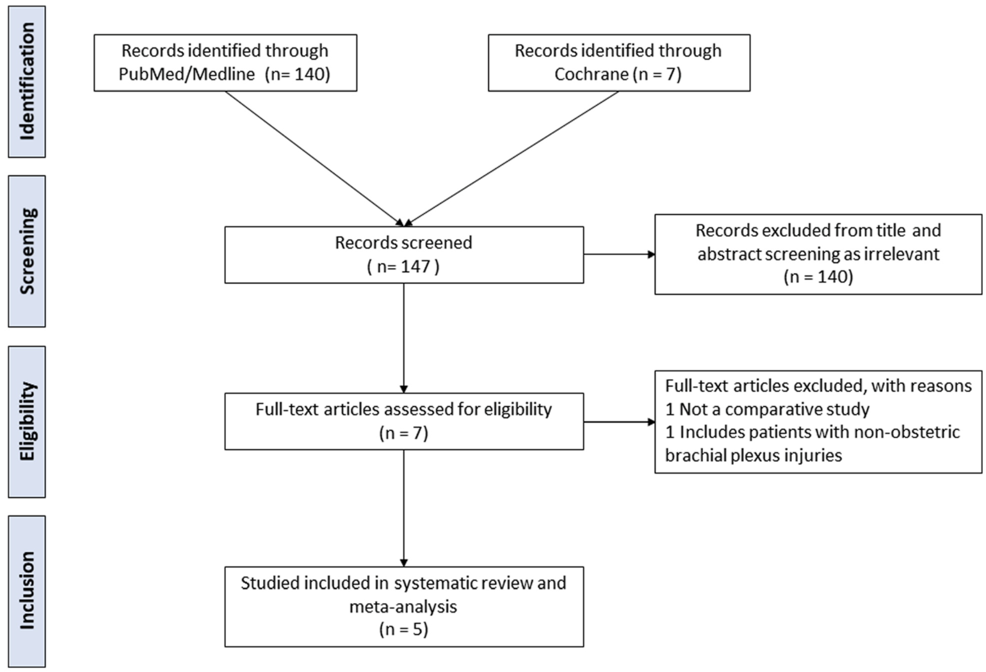

Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flow diagram

11.9 months [16, 18]; 46% of patients were male, and mean follow-up among the studies was between 12 to 70 months [3, 16]. Study characteristics are detailed in Table 1. From the included studies, 118 patients were reported with MRC or AMS scoring usable for odds ratio comparison [1, 8, 16]. A detailed assessment of risk of bias utilizing the Robins-I Tool for non-randomized studies is available in the Supplemental Table 1.

Few studies reported quantitative information regarding complications, need for secondary reconstructive or orthopedic procedures, rehabilitative practice, or donor site morbidity. O'Grady et al. reported no donor site morbidity following sural nerve graft harvesting [18]. In addition, they reported the need for secondary procedures in each treatment arm, with 58% of graft patients and 14% of transfer patients requiring secondary orthopedic procedures [18]. Malessy et al. reported the need for secondary reconstructive procedures for shoulder function, but not elbow flexion [16]. With regard to the degree of injury, three studies included injuries involving C5-C7 [1, 8, 16] and one study included injuries involving C5-C6 [18]. Only one study reported the severity of injury using the Narakas Grade I-IV, including patients with C5-T1 injuries [3]. Specific patient data in each treatment arm with root involvement, injury type (neurotmesis or avulsion), and electrodiagnostic findings were inconsistent.

Regarding donors for nerve transfer, two studies transferred the ulnar or median nerves [1, 8], two studies transferred the ulnar nerve [3, 18], and one study performed intraplexal nerve transfer of C6 [16]. Regarding donors for nerve grafting, the sural nerve was used in three studies with available data [8, 16, 18]. Only one study reported graft length, ranging from 2 to 4 cm [16]. Method of coaptation was reported in only two studies, including Fibrin sealant [18] and micro-suture followed by tissue glue [3].

The surgical approach for the restoration of elbow flexion varied between the included studies and was described as follows. Patients in Chang et al. received sural nerve grafting to complete reconstruction if both C5 and C6 nerve roots were available. However, if only a single nerve root was available, either C5 or C6, then a sural nerve graft was coapted to the nerve root proximally and to the anterior division of the upper trunk distally. All patients in Chang et al. with upper root avulsions received a distal nerve transfer of the ulnar nerve to the musculocutaneous nerve [3]. Patients in Al-Qattan et al. who underwent grafting received three "cable grafts" from the ruptured root to the anterior division of the superior trunk. Patients in Al-Qattan et al. who received nerve transfers underwent Oberlin nerve transfer using either the ulnar or median nerve to the biceps nerve [1]. O'Grady et al. performed sural nerve grafting to complete reconstruction in case of neurotmetic injury to C5 or C6. Transfers performed by O'Grady et al. involved transfer of the ulnar nerve to the musculocutaneous nerve [18]. Malessy et al. performed intraplexal transfers using the entire C6 nerve or anterior C6 filaments to the C5 stump in cases of C5 neurotmesis and C6 avulsion. Patients with C5 neurotmesis received sural nerve grafting of C5 to the anterior division of the superior trunk [16]. Heise et al. performed distal nerve transfers using either the ulnar or median nerve to the musculocutaneous nerve. No double Oberlin nerve transfers were performed in their study. Lastly, Heise et al. performed nerve grafting depending on intraoperative identification of viable nerve fascicles. One approach utilized sural nerve grafting either from C5 or both C5 and C6 roots to the superior trunk. The other approach utilized sural nerve grafting from C5, C6, or both C5 and C6 to the anterior division of the superior trunk [8].

Functional recovery of elbow flexion

From the included studies, 118 patients were reported with MRC or AMS scoring usable for odds ratio comparison [1, 8, 16]. Functional recovery occurred with nerve transfer in 95.2% of patients ($n = 59/62$) and with nerve grafting in 96.4% of patients ($n = 54/56$) (Fig. 2). Overall, the outcomes for elbow flexion between the groups appeared similar (OR 1.15, 95% CI 0.19–7.08, I^2 2.9%). The two studies that reported mean functional recovery of elbow flexion did not demonstrate any statistically significant differences between transfer vs graft [3, 18].

Discussion

Functional recovery of elbow flexion with either graft or transfer was achieved in greater than 95% of the pooled patients with NBPP. The results from this meta-analysis demonstrate no statistically significant differences in elbow flexion recovery between the two treatment approaches. These findings are consistent with the fact that none of the included studies demonstrated a statistically significant difference in elbow flexion, with the exception of Heise et al. at 12 months but not at 24 months. The results in Heise et al. in the shorter-term follow-up can be reasonably explained by the fact that nerve transfers are expected to confer a more rapid recovery, as the repair is performed much closer to the muscle of interest [8, 18]. Indeed, the authors state that distal nerve transfers were not superior when compared with grafting.

While elbow flexion is one of the main goals of reconstruction in NBPP, other limb functions including shoulder abduction, forearm supination, wrist extension, and finger flexion and extension are critical to improving overall function and thus a patient's quality of life. The specific functions measured at follow-up varied between included studies. Chang et al. reported no significant differences between graft vs transfer groups in shoulder, wrist, or hand functions, but reported statistically significant difference in forearm supination (Transfer 100° vs Graft 19° range of motion) at 12-month follow-up [3]. O'Grady et al. found significantly better outcomes with triple nerve transfer for shoulder external rotation, forearm supination, and faster recovery compared with nerve grafting. Elbow flexion, shoulder abduction, and shoulder flexion did not show any statistically significant differences [18]. Heise, Al-Qattan, and Malessy et al. did not compare graft vs transfer for shoulder, wrist, or hand function or used mixed approaches for reconstruction [1, 16]. A retrospective study by Seruya et al.

Table 1 Study characteristics

Study	Country	Years of enrollment	Design	Injuries	TF: mean age at surgery	GF: mean age at surgery	% Male	N TF	N GF	Mean follow-up	TF donor nerve	GF donor nerve
Chang (2017)	USA	2005–2015	Observational	C5-T1	7 months	6 months	0.38	19	31	12 months	Oberlin (Ulnar)	NR
Al-Qattan (2017)	Saudi Arabia	1995–2013	Observational	C5-C7	NR	NR	NR	26	29	36 months	Oberlin (Ulnar or Median)	NR
Heise (2017)	Brazil	2005–2015	Observational	C5-C7	8.3 months (4–22)	6.2 months (4–10)	0.58	19	10	24 months	Oberlin (Ulnar or Median)	Sural
O'Grady (2017)	Canada	NR	Observational	C5-C6	11.4 months (± 6.1)	11.9 months (± 2.3)	0.50	14	12	24 months	Oberlin (Ulnar)	Sural
Malessy (2014)	Netherlands	1990–2008	Observational	C5-C7	5.7 (4.1–2.8)	5.7 (4.1–2.8)	0.44	17	17	70 Months	Intraplexal C6 to C5 Stump	Sural

Abbreviations: *NR* not reported, *TF* transfer, *GF* graft

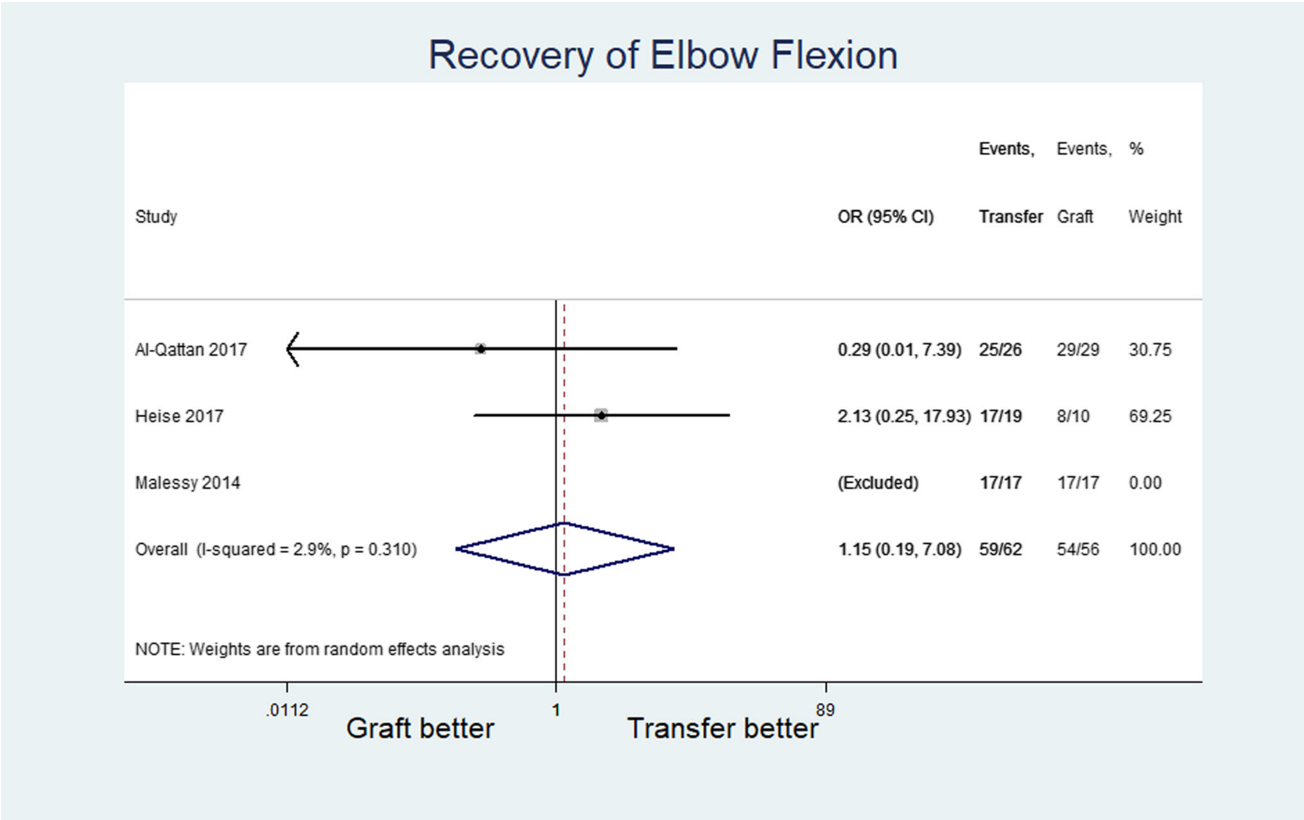

Fig. 2 Forest plot comparing elbow flexion outcomes in NBBP following nerve graft vs nerve transfer. OR, odds ratio; CI, confidence interval

reported a statistically significant increase in additional operations for patients undergoing graft, compared with transfer [19]. Overall, these findings may appear to suggest a few points of superiority of nerve transfer for supination or shoulder external rotation, but we caution the reader from making such conclusions. For one, the method of reconstruction varied widely between studies. In addition, the length of follow-up must account for the likelihood that recovery after nerve grafting simply takes longer than recovery after nerve transfer—whether or not this confers any long-term clinical benefit is unknown. The necessity of appropriately designed trials, with matched patients and surgical approaches, cannot be understated.

The comparative safety of these procedures would also be a reasonable consideration in the question of graft vs transfer. However, nerve grafting is considered a relatively safe and routine procedure. One study by La Scala et al. of 173 patients reported no mortality and minimal morbidity not directly related to the reconstruction [13]. While nerve transfers were cautioned against at first in NBPP due to the perceived risk of donor site morbidity (e.g., to the ulnar or median nerve), this has not been seen to be an issue in the included studies and numerous others [1, 3, 7, 8, 16–18]. Overall, the questions of donor site morbidity and complications are important to keep in mind for future study design in comparing graft vs transfer, but they are not major points of contention as both surgical approaches are considered routine and similarly safe.

The timing of surgical specialist referral and timeframe of "watchful waiting" is of interest especially in recent NBPP literature. While many patients can improve spontaneously with conservative management and physical therapy [11, 21], between 10 and 40% of patients with NBPP develop permanent deficits without surgery [20]. Consequently, the importance of early surgical care in these patients has become emphasized in recent years. While many surgical algorithms propose evaluation of NBPP patients by 6 or 9 months, a recently proposed management algorithm suggests initial referral at 1 month, with subsequent strength testing at 3 and 9 months for surgical intervention [21]. A notable study by Wilson et al. developed a decision tree prediction algorithm shortly after birth, with a sensitivity of 0.71 and specificity of 0.96 in determining a patient's ultimate surgical candidacy. The algorithm proposed by Wilson et al. also recommended that initial evaluations begin as early as 1 month, continuing at 3 months and 6 months [25]. We emphasize that future trials should consider timing in their study design and these recently proposed surgical decision-making algorithms.

Even if the neurosurgical approach to brachial plexus is optimized, this critical intervention is likely, and unfortunately, underutilized. Squitieri et al. performed a national study including 21,758 births with NBPP, with only 721 admissions for nerve surgery identified. Approximately, 3.3% of children with NBPP underwent surgical intervention for NBPP, highlighting a major underutilization of this approach [22]. This may be due to hesitance to pursue surgical options by parents or caregivers who espouse erroneous paradigms such as "all neonatal brachial plexus palsy recovers" or "wait a year to see if recovery occurs," as noted by Smith et al. [21] In addition, while this does not entirely explain these findings, Squitieri et al. also reported that patients with private insurance were much more likely to receive surgical intervention [22].

This highlights an important distinction between nerve grafting and nerve transfers with regard to clinical practice and financial burden. On this matter, the Canadian study by O'Grady et al. evaluated the healthcare costs, operative time, and length of stay. They reported statistically significant lower mean costs (Transfer $7036, Graft $15,236), shorter mean operative time (Transfer 2 h, 21 min, Graft 8 h, 39 min), and shorter mean length of stay (Transfer 1.1 days, Graft 3.3 days) all for transfers compared with grafting [18]. While clinical decision-making must rely on the most efficacious procedure available, institutions and individual surgeons should consider these factors in their practice as it plays a direct impact on access to care and practical efficiency.

Limitations

This is the first meta-analysis of comparative studies reporting elbow flexion in NBPP following graft vs transfer. The results of the present study should be examined in the context of several limitations. First, inherent to the designs, all included studies were retrospective and non-randomized studies providing limited patient-level data. Secondly, the data in each treatment arm regarding root involvement, injury type (neurotmesis or avulsion), electrodiagnostic findings, Narakas grade, graft length, and mechanism of coaptation were inconsistent. Critically, the surgical approach, donor nerves, and follow-up varied between studies. Future prospective, blinded, and randomized studies should be conducted to validate the results of the present study.

Conclusion

The optimal approach to brachial plexus reconstruction in NBPP continues to be the subject of debate. As one of the most important outcomes, the present meta-analysis finds that functional recovery of elbow flexion does not appear to differ between nerve grafting and nerve transfer.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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