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End-to-Side Neurorrhaphy for Brachial Plexus Injury (A Systematic Review)

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Abstract

Background: Brachial plexus injury is one of the most challenging cases in the microsurgery field, due to complexity of its anatomy and the significance of its function. End-to-side neurorrhaphy (ETS) has lately been developed as an option for the reconstruction of this injury, due to its reported minimal donor nerve morbidity. However, its effectivity is still debatable due to varying reported outcome. This systematic review aims to investigate the efficacy of this promising technique. **Methods:** We comprehensively searched PubMed to search previous studies on end-to-side neurorrhaphy up to August 26th, 2019 which resulted in 128 articles. Review by two independent authors resulted in 5 articles for systematic review. **Results:** The efficacy of ETS varies among the included studies, with success rate ranging from 0% to 100%, with combined success rate of 43%. The most commonly attributed advantage of ETS is the minimal or absence of donor nerve morbidity. While there is one author recommended ETS for axillary nerve repair if no nerve transfer donor available, two authors do not recommend ETS, and preferred nerve transfer/grafting. One author has reported synkinesis of the muscles innervated by donor and recipient nerve. **Conclusion:** ETS is a new procedure to mitigate the risk of failed reinnervation in brachial plexus injury with minimal risk of donor nerve morbidity compared to nerve transfer. However, its efficacy is still lower than other procedures more commonly used, thus its use has not been recommended.
Level of Evidence: Level V

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Introduction

Brachial plexus injury is one of the most challenging cases in the microsurgery field, due to complexity of its anatomy and the significance of its function.[1] End-to-side neurorrhaphy (ETS) has lately been developed as an option for the reconstruction of this injury, due to its reported minimal donor nerve morbidity.[2,3] However, its effectivity is still debatable due to varying reported outcome.

Brachial plexus injury affects around 0.1-1.2% of multiple trauma patients,[4,5] and around 0.4% of all infants born.[6] This relatively rare but significant injury can affect deeply the quality of life of the patients, due to its crucial role to innervate upper limb.[7] Its management mostly consists of surgical intervention, with the main aim to restore the impaired movement of the affected segment.[8] There are various technique of surgery for this injury, which its use depends on the pattern and severity of the injury.[9] Several surgical techniques are available such as end-to-end neurorrhaphy, end-to-side neurorrhaphy, free functional muscle transfer, nerve transfer, fascicular transfer can be done to manage this injury.[1]

Among the surgical techniques, end-to-side neurorrhaphy is one of the latest to be used for the management of brachial plexus injury. This technique has its advantage of minimal to non-existent donor site morbidity.[10] However, the report of its usage on managing nerve injury is still controversial due to its various outcome.[11,12]

Due to this variance of the reported outcome, this research is aimed to systematically review previously available literature related to the outcome of end-to-side neurorrhaphy used to manage brachial plexus injury.

METHODS

We comprehensively searched PubMed to search previous studies on end-to-side neurorrhaphy on brachial plexus injury up to August 26th, 2019. We searched these databases using the following key words: “BRACHIAL PLEXUS INJURY” AND “END-TO-SIDE” AND “OUTCOME”. The PICO (Population, Intervention, Comparison, and Outcome) of this study is explained on the Table 1 below. The resulting articles are then reviewed by two independent authors manually to minimize the bias risk. The article searches and selection process are described on PRISMA flowchart on Figure 1.

Table 1. PICO Table of the study

Study Component	Inclusion	Exclusion
Population	• Brachial plexus injury patients	• Less than 6 months of follow up • Oncological pathology • Animal/cadaveric studies
Intervention and Comparison	• End-to-side neurorrhaphy • Any other surgical modality	• None
Outcome	• Any outcomes (motor strength, sensory function, range of motion, donor site morbidity)	• No measured outcome mentioned
Publication	• Primary research published in English in a peer-reviewed journal	• Abstracts, editorials, letters • Conference presentations or proceedings • Book chapter
Design	• Randomized controlled trials • Cohort studies	• Review articles • Case reports or series • Expert opinion

Abbreviations: PICO, Population, Intervention, Comparison, and Outcome.

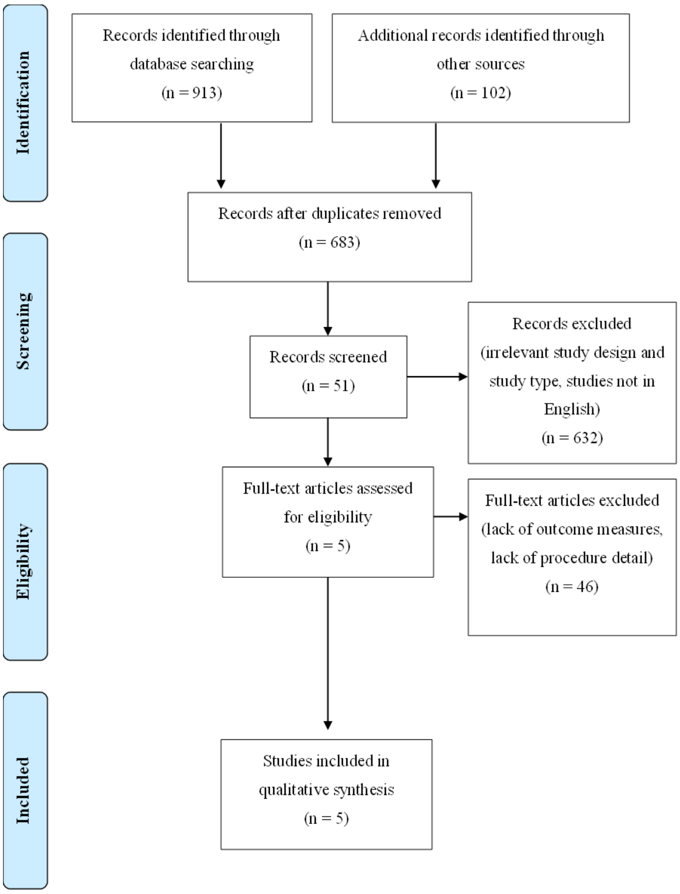

Figure 1. PRISMA flow diagram on systematic review article selection

RESULTS

The initial search resulted in 913 articles. The search of references on the articles resulted in 102 additional papers. Twenty-two papers are duplicates and then removed. Filtering through the inclusion and exclusion criteria removed 1010 articles, leaving 5 articles included for data extraction. The complete selection flow can be seen on the PRISMA flow diagram in Figure 1 below.

From the included articles, data are then extracted, such as number of samples, gender distribution, age range with its mean, type of procedure done, amount of delay before surgery, mechanism of injury, receiver and donor nerve, follow up duration range with its mean, and the functional outcome score. The extracted data can be seen in Table 2 below.

The studies included in this systematic review have gone through a strict quality assessment. The Risk of Bias in Non-Randomized Studies – of interventions (ROBINS-I) assessment tool was used to assess the quality of retrospective studies (Fig. 2 and 3). For the five cohort retrospective studies, all studies have definite selection criteria. All studies had a low to moderate risk of selection of participants, classification of intervention, incomplete outcome data, measurement of outcomes and selectively reporting results.

DISCUSSION

End-to-side neurorrhaphy has been researched nowadays as an alternative procedure for surgical treatment of peripheral nerve injury, especially brachial plexus injury.[13] This is due to the minimal or no donor site morbidity, unlike nerve transfer, which is until now still the golden standard for nerve repair with inaccessible proximal stump.[14,15] However, most of the trial done using this technique are applied to animal, therefore, more researches on human subject are needed to further analyze its efficacy.

This study has several limitations. First, the minimal amount of study that involves human subject restrict the number of samples gathered, thus reducing the significance of the outcome. The second, lack of unity on functional outcome measurement, and successful nerve recovery criteria reduced the comparability of the studies included. Third, since there is still no recommendation and guideline regarding the use of end-to-side neurorrhaphy for management of brachial plexus injury, there are discrepancy related to surgical technique and indication among studies included in this review. Lastly, the various nerve level and aspect makes the comparison between studies difficult since there is still no paper studying specifically single aspect of brachial plexus injury.

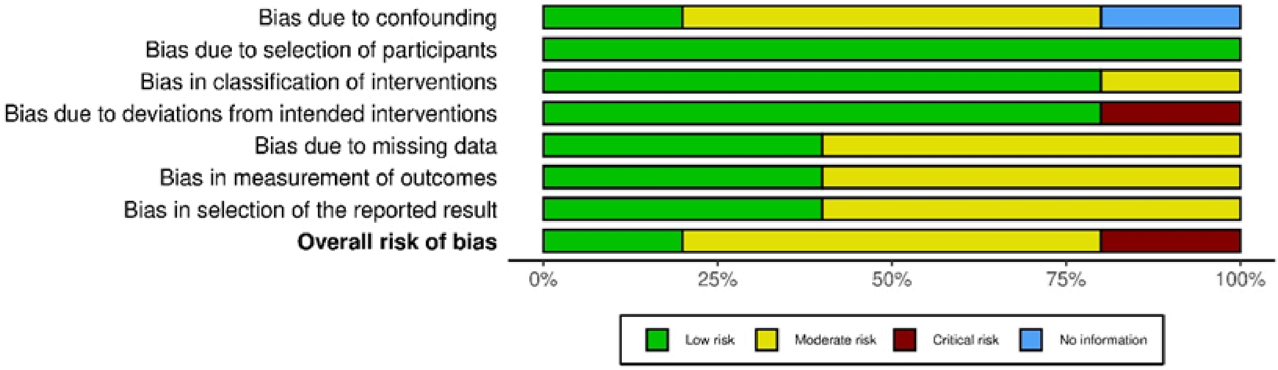

Figure 2. Risk of bias graph of all studies included.

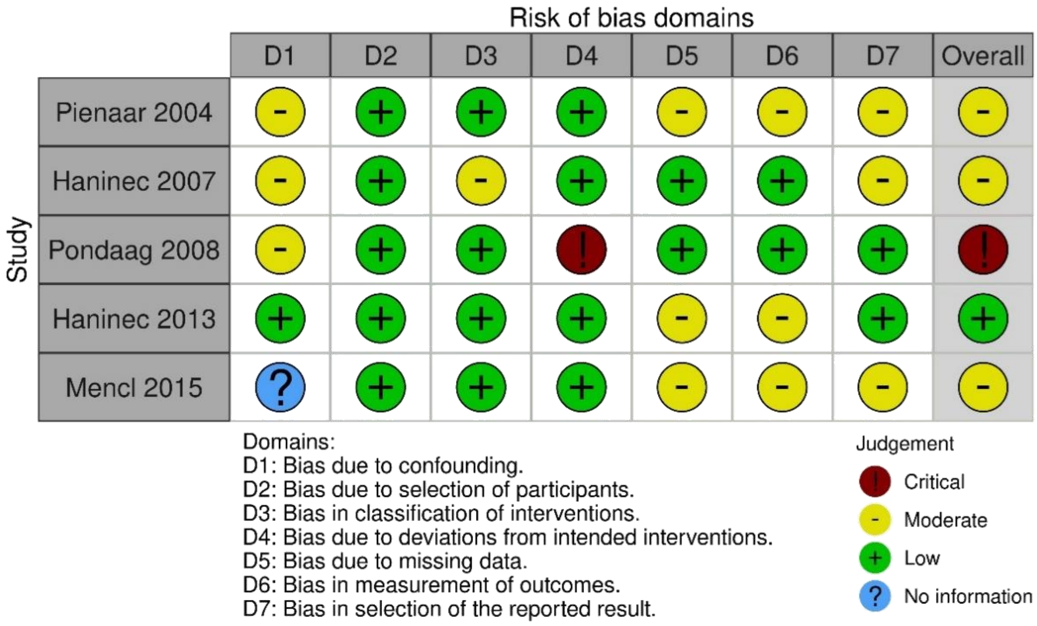

Figure 3. Risk of bias summary of all studies included.

The efficacy of ETS varies among the included studies, with success rate ranging from 0% to 100%, with combined success rate of 43%. This variability is due to wide range of severity of the brachial plexus injury, and different aspect of plexus is affected.[8,11,12,16] In the research of Haninec et al., the end-to-side neurorrhaphy resulted in the same or better success rate compared to extraplexal end-to-end neurorrhaphy, however it still lags behind the intraplexal end-to-end neurorrhaphy.[8] With this variable success rate, four of five paper included in this study have not suggested the use of this technique,[8,11,16,17] while on one paper, this technique is recommended as an option if the nerve transfer procedure is not possible.[12]

Minimal donor nerve morbidity is one of the advantages of end-to-side neurorrhaphy. This advantages however, is inconsistently reported. Research by Haninec et al. has shown this advantage with 0% donor nerve morbidity assessed by the motoric and sensory function.[8,12] However, Pienaar et al. reported a 20% donor nerve morbidity but with little to none functional impairment.[16] With this number, end-to-side neurorrhaphy is still proven superior in term of donor site morbidity compared with currently golden standard nerve transfer.[16,18]

Unlike the reported effectivity of perineurial window creation coupled with perineurial suturing of end-to-side neurorrhaphy in peripheral nerve injury on increasing the number of axonal sprouting to the recipient nerve, this technique in the setting of brachial plexus injury yields less sprouting. This is due to the thickness of the perineurium on the plexus level, thus reducing the trauma to the donor axon, therefore reducing the effectiveness of this procedure to stimulate collateral sprouting on the donor nerve. This infectivity is shown to be reduced for the more distal peripheral nerve, such as axillary nerve, with success rate of 78.6% reported by the same paper.[12]

End-to-side neurorrhaphy is also proven can be used to reconstruct root avulsion on brachial plexus injury. This successful attempt has been reported by Pondaag et al, where he successfully repaired upper brachial plexus avulsion (C5-C6) with full functional recovery of biceps and deltoid function using end-to-side technique of C6 with C7 trunk as donor nerve.[11] Mencl et al. also reported successful repair of obstetric brachial plexus injury using end-to-side neurorrhaphy in 2 of the sample in his research. This high level of success is credited to the regenerative potential of infants compared to adult.[17]

Table 2. Data extracted from the included papers

Author	Sample Age (mean)	Procedure done	Delay (mean)	MOI	Coaptation	Follow-up	Outcome
Pondaag et al. (2008)	12 pax Infants	20 ETS 4 NG 1 NT	3-9 months (5 months)	12 OBS	C5→C7 C6→C5 C6→C7 2 C6→C8 3 C7→C8 C7→T1 ST→C8 PD→C8 C5-C6→C8-T1 C5-C7→C8-T1	24-54 m (33)	**Biceps recovery:** 5 full 5 partial 8 failure **Shoulder abduction recovery:** 1 pax No donor nerve morbidity
Pienaar et al. (2004)	8 pax (6M) 2-44 y (27.5)	13 ETS 4 ETE	1-395 days (105 days)	5 stab 1 fall 1 MVA 1 OBS	2 U→M 4 A→R 3 MC→M 2 MC→U 3 M→U 4 SS→SA (ETE)	10-18 m (14.5)	**ETS** No motoric recovery 2 MRC S1 2 minor donor nerve morbidity **ETE** 2 MRC M4 - SS 1 MRC M4+ - SS
Mencl et al. (2015)	20 pax (14M) Infants	2 ETS 3 ETE 5 NT	3 months	20 OBS	C7→C8 C5→C7-C8	55-104 m (79.5)	**Active movement scale:** 0→5-7 (6.5) 0→1-7 (5.3)
Haninec et al. (2013)	23 pax (20M) 12-63 y (32)	23 ETS	2-9 months (4.9 months)	23 trauma	10 A→U 10 A→M 1 A→R 1 MC→U 1 MC→M	24-69 m (39.1)	**Axillary nerve:** 10 MRC M3-4 1 MRC M2 6 MRC M1 4 MRC M0 **Musculocutaneous nerve:** 2 MRC M0
Haninec et al. (2007)	95 pax (85M) 13-75 y (29)	14 ETS 48 NG 106 NT	4 d-14 months (6.1 days)	Trauma	8 A→U 5 A→M 1 A→R	≥ 2 y	**ETS**: 9 /14 MRC M3-5 **NG**: 38/48 MRC M3-5 **NT**: 24/46 SA MRC M3-5 35/54 FaF MRC M3-5

M: male; y: year-old; ETS: end-to-side neurorrhaphy; NG: nerve graft; NT: nerve transfer; ETE: ent-to-end neurorrhaphy; OBS: obstetrical brachial plexus injury; MVA: motor vehicle accident; ST: superior trunk; PD: posterior division of superior trunk; U: ulnar nerve; M: median nerve; A: axillary nerve; R: radial nerve; MC: musculocutaneous nerve; SS: suprascapular nerve; SA: spinal accessory nerve; MRC: medical research council grade

As same as the other peripheral nerve injury repair, time from injury to repair has a role in the success of reinnervation in end-to-side neurorrhaphy. Several studies has reported the delay of more than 1 year after injury will result in poor outcome compared to those whose nerve repaired within 6 months after injury.[11,12] This also applies to pediatric patients, while high neural regenerative capability of infants, the contracture and atrophy accompanying the denervation complicate the restoration of function, thus requiring additional surgery to address those complications.[17]

This study is one of the first systematic reviews exploring the efficacy and outcome of end-to-side neurorrhaphy in brachial plexus injury cases. Although it has limited number of samples gathered, it has shown a generally good outcomes for end-to-side neurorrhaphy and is comparable to the gold standard end-to-end neurorrhaphy. Further research on the outcomes of end-to-side neurorrhaphy, especially the randomized controlled trial in comparison to the gold standard end-to-end neurorrhaphy and other surgical modalities is needed to further establish the outcome and possible complications regarding this relatively new technique.

CONCLUSIONS

ETS is a new procedure to mitigate the risk of failed reinnervation in brachial plexus injury with minimal risk of donor nerve morbidity compared to nerve transfer, and has successfully shown a promising result compared to the gold standard end-to-end neurorrhaphy. However, the number of research related to the outcome of this procedure is still scarce, and further studies is required to establish a place for this treatment modality in the management of brachial plexus injury.

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