Repair of recalcitrant Neuroma surgery with use of nerve allograft conduit: A Literature Review and Meta-analysis of Clinical Trials

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Introduction

Neuroma is a progressive, degenerative, enlargement of a nerve that is often associated with severe pain, numbness, cramping, and loss of function (2). Interdigital neuromas are one of the most common peripheral neuropathies of the foot. Possible etiologies can be trauma, pedal morphology, repetitive biomechanical stress. The treatment for interdigital neuroma includes initial conservative treatment, ranging from wider shoe gear, NSAIDs, corticosteroid injections, to accommodative orthotics. If the conservative treatments fails, then the surgical intervention is indicated. The surgical approach is resection of the pathological nerve tissue, however there are other modalities such as cryotherapy, implantation of the resected proximal nerve to bone or muscle that have been referenced in the literature(2)(3).

Stump neuromas recur at its resected margin, a common complication attributed to nerve sheath disruption. Initial resection of neuromas often times fail with formation of a stump neuroma and recurrence of symptoms, often times progressing to further morbidity. According to Caporusso et al, there is a 20% failure rate of surgical neuroma resections, resulting in either no relief of symptoms or worsening of the condition (12).

Patients with recalcitrant neuromas are often frustrated and exhausted by the failure of conservative and surgical treatments, there is a substantial negative impact on there normal daily living. There is a paucity in the medical literature on the use and effectiveness of nerve grafting in the treatment of neuroma formation. These patients have often undergone multiple surgical attempts of peripheral nerve decompressions, external neurolysis, and nerve resections with or without burying into the bone or muscle. Consequently the authors of this paper have recognized there has yet to be a comprehensive literature review and analysis of the studies on use of nerve allografts for this particular subset of patients.

Materials and Methods

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The authors performed a standard systematic review to evaluate patients undergoing revisional surgery for stump neuroma formation with the use of nerve allograft. A prospective protocol regarding the study objectives, study outcome measures, inclusion criteria, exclusion criteria, search strategy and data are carefully constructed. Thereafter, electronic data bases were systematically searched and are listed as follows: MEDLINE (pubmed), GOOGLE SCHOLAR, Cochrane Library, clinicaltrials.gov and JFAS website.

The Inclusion criteria for the studies include: (1)Use of a nerve allograft/ collagen graft conduit, (2) Revisional peripheral nerve surgery in the lower extremity, (3) Level IV and above studies. All studies must have utilized nerve allograft for revisional procedures. Exclusion criteria were as follows: (1) Studies and patients were excluded if there was use of an autograft, (2) animal study models, (3) location of neuromas elsewhere in the body other than the lower extremity, and lastly (4) studies that were not in English.

Search Strategy and Data Extraction

The following electronic databases were searched: Google scholar, Medline(Pubmed), Cochrane library , clinicaltrials.gov and www.ifas.org for articles. Keywords and terms searched included: nerve graft, collagen nerve conduit, allograft nerve conduit, neuroma surgery, neuroma surgery with nerve allograft, neuroma surgery with nerve graft conduit, neuroma surgery of the lower extremity, revisional neuroma surgery of the foot and ankle. In addition to articles found via electronic search engines, the authors also hand searched through foot and ankle related journals. Data was analyzed based on preoperative and postoperative as the amount of improvement recorded.

Table 1: Summary of Search Results

Search Engine	Keywords	Results
Google Scholar	"Neuroma repair with nerve allograft foot and ankle"	1
Google Scholar	"Collagen nerve conduit"	1
Medline(Pubmed)	"Neuroma repair with nerve allograft foot and ankle"	1

Figure 1: End to end nerve graft

Primary Search (refer to Table 1)
-Google Scholar
-Medline(Pubmed)
-Clinicaltrials.gov

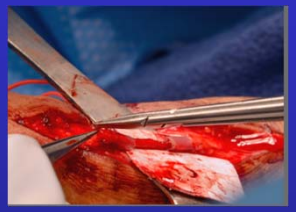
Total citations retrieved
(n = 2,150)

Title Review
(n=12)

Article Review
(n=9)

nerve graft articles included
(n=3)

Figure 2: End to End Nerve graft



Study	Year	Design	n(cases)	mean f/u time	Outcome measure	Type of graft
Gould et al	2013	retrospective case series	50 pts, 69 nerves	36 months	VAS	collagen conduit
Souza et al	2016	Case study, retrospective	26 pts	15.5 months	PROMIS	Nerve Allograft
C.Bibbo/Rodrigues- Colazzo et al	2017	Case study	4pts	26 months	VAS	Nerve Allograft

Table 2: Summary of Included studies for Nerve repair with graft

Results

•There were a total of 2,150 results from the aforementioned searches. Citations (titles, abstracts) were reviewed systematically by the authors and 3 articles were found to meet the inclusion criteria. Table 2 summarizes the selected studies that met the inclusion criteria. The results demonstrate the use of nerve allograft in recalcitrant neuroma surgery in the foot and ankle. Although the authors maintain that there is limited literature available using nerve allograft in revisional neuroma surgery. Patient age, follow up, outcome measure were documented and appeared to vary between the studies. There was only one prospective study, of which was not randomized. All three studies measured the patient outcome measures, after recalcitrant neuroma surgery of the foot. The studies included were of peripheral nerve pathologies of the lower extremity, and the final studies included in the analysis pertained to the foot and ankle.

Figure 5: Nerve Allograft

Discussion

Peripheral nerve pathologies are ubiquitous throughout medical literature, however the treatment of such conditions appear to be limited and not well studied, particularly as it pertains to the lower extremity. The authors have found a more expansive armentarium when researching the upper extremity. Historically, nerve resection, external neurolysis (decompressions) and implantation of nerves into adjacent muscle or bone appear to be the sole tools of addressing peripheral nerve pathologies in the lower extremity.

There appears to be little to no literature on use of peripheral nerve allografts in the treatment of nerve pathologies (i.e. stump neuromas) in the lower extremity.

According to Kim and Dellon, a literature search of the last 30 years does not reveal a single series of nerve repairs in the foot distal to the ankle (8). In the current study, the authors found the limited number of studies to be consistent with the hypothesis that there is little to no literature on use of nerve allograft in the lower extremity (particularly the foot or ankle) in treatment of revisional nerve surgery.

The primary limitation of the current study is the limited number of cases included in the final analysis. The authors acknowledge with such a small sample size, it is difficult to draw any substantial inferences; however the study served its purpose in identifying the clear lack of medical literature on the topic. Therefore, the authors propose more Type I through type III studies on the topic so that the foot and ankle community may potentially identify a worthy treatment alternative for patients suffering from recalcitrant neuroma symptoms and prevent unnecessary multiple surgical interventions.

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