INCIDENCE, RISK FACTORS, AND RELIEF INTERVENTIONS OF DISTANT NEUROPATHIC PAIN FOLLOWING FOOT AND ANKLE SURGERY: A SYSTEMATIC LITERATURE REVIEW

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Abstract

Background: Neuropathic pain is a phenomenon that is oftentimes experienced post-operatively. Unlike nociceptive pain, neuropathic pain is not derived from direct physical damage to the tissue but rather is consistent with a malfunctioning nervous system or nerve damage. It is often characterized as a chronic shooting or burning pain with the possibility of never going away. Moreover, the causes of this seemingly random nervous system malfunction have not yet clearly been identified, and the potential risk factors for the possibility of experiencing this pain are largely unexplored. **Methods:** A systematic review was conducted through PubMed. The initial search yielded 628 articles, from which 601 were excluded and 27 were included after the initial screening of the titles and abstracts. Eight articles were then eliminated, yielding 19 articles. The 19 articles that were chosen involved patients who experienced symptoms consistent with chronic neuropathic pain that underwent surgical intervention of the foot or ankle. **Results:** The incidence rates of patients experiencing neuropathic pain symptoms post-operatively varied from study to study, including 3%, 12.4%, 13.3%, 23%, and 24%. Risk factors included smoking, age (40-60 years old), psychological distress/negative mood, obesity, tourniquet pressure, prior surgery, and acute postoperative pain. One study found a higher correlation between ankle surgeries and neuropathic pain versus forefoot surgeries and neuropathic pain. There appeared to be no correlation between neuropathic pain and tourniquet placement, time the tourniquet was on, prophylactic antibiotics, type of anesthesia, level of anesthesiology training, diabetes, hypertension, or dislocation. Types of treatment that provided promising results included ultrasound-guided radiofrequency ablation, sural nerve neurectomy, popliteal nerve blocks, peroneal nerve blocks, neurolysis, peripheral nerve stimulation, spinal cord stimulation, and VR (virtual reality). **Conclusion:** There is no definite answer as to whether a patient will or will not develop neuropathic symptoms. Patients should always be made aware of the possibility as well as their chances of developing neuralgia subsequent to foot or ankle surgery by their surgeon.

Introduction

Neuropathic pain (NP) is a health condition that affects the nerves of the body and is otherwise commonly known as neuralgia or simply nerve pain. Neuropathic pain can be commonly expressed in the foot and ankle, and can oftentimes arise postoperatively. This type of phantom pain is characterized by a shooting, burning, stabbing, tingling, or numbness sort of pain, and the duration of neuropathic pain varies from person to person. In some individuals, neuropathic pain will only appear acutely postoperatively, while for other individuals it may persist for a lifetime. The risk factors for neuropathic pain have been largely undefined in a surgical context, and there has been no consensus as to the incidence rates in relation to foot or ankle surgery. While there are a couple of non-operative treatments for neuropathic pain such as over-the-counter medication or physical therapy, there has not been a clearly defined surgical intervention that is commonly recommended to relieve this post-operative pain.

Research Questions

1) What is the incidence rate of distant neuropathic pain after foot and ankle surgery?

2) What are the associated risk factors of distant neuropathic pain after foot and ankle surgery?

3) Are there any interventions following surgery that provide relief and show promising results?

Methods and Materials

A systematic review of the literature was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guidelines.

PubMed Search Terms:

- Foot OR Ankle

AND

- Surgery OR operation OR operative OR surgical

AND

- Neuropathic pain OR neuralgia

Inclusion & Exclusion Criteria

Articles were included if they met the following criteria:

1. The main study population was patients experiencing neuropathic pain following surgical intervention
2. The surgical intervention included at least one of the following:
    a. Ankle surgery
    b. Foot surgery
3. The pain experienced by the subjects was neuropathic pain and not simply incisional nerve pain
4. The studies that were performed used only human subjects
5. The neuropathic pain was clearly defined and diagnosed

Articles were excluded if they met the following criteria:

1. Non-surgical neuropathic pain
2. Animal Studies
3. Patients who were previously experiencing neuropathic pain

Results

Our systematic review of the literature yielded 19 studies. Neuropathic pain was determined via painDETECT scores, McGill Pain Questionnaires, Douleur Neuropathic en 4 Questions Questionnaire, and retrospective chart reviews.

Five studies addressed our first question in regard to the incidence rates of distant neuropathic pain following foot or ankle surgery. Three of these studies included patients who had experienced some sort of neuropathic pain following any type of foot or ankle surgery, while two of these studies focused on the incidence rates of neuropathic pain when a popliteal nerve block was used for foot or ankle surgery.

Six studies addressed our second question regarding the risk factors of developing distant neuropathic pain following foot or ankle surgery. From our systematic review, there were eight notable different factors that had a positive correlation with developing distant neuropathic foot pain and several other different factors that turned out to have no correlation. Most notably, smoking, age, and psychological distress had a positive correlation, while tourniquet placement/tourniquet time notably had no correlation.

Our third question in regard to the various relief interventions for distant neuropathic pain following foot or ankle surgery was addressed by thirteen different studies. Notable relief interventions from our systematic review included ultrasound-guided radiofrequency ablations of the sural nerve, sural nerve neurectomies, and popliteal nerve blocks, as each of these relief interventions showed promising results in multiple studies.

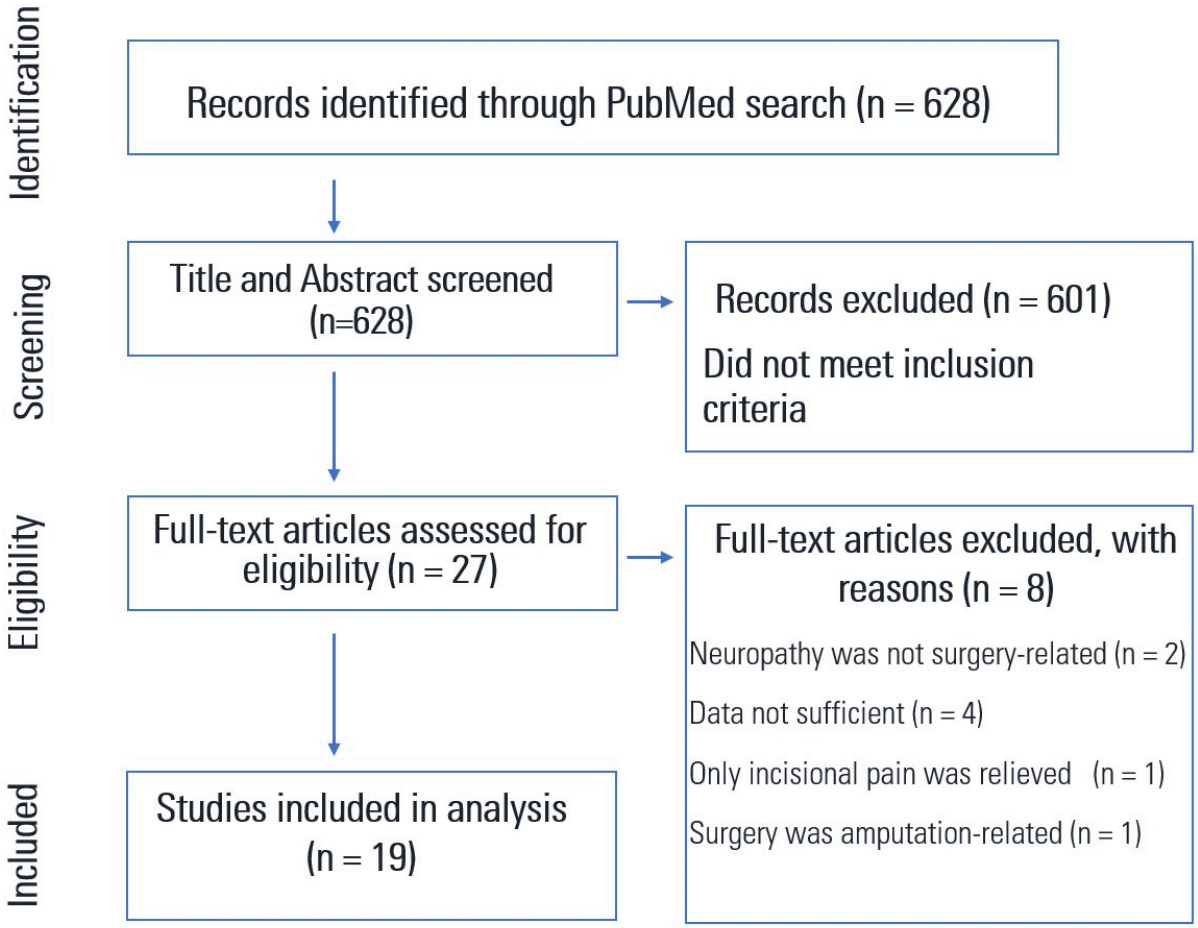

Figure 1: Prisma Flow Diagram

628 articles were identified using the following described search strategy in congruence with PRISMA guidelines. The titles as well as the abstracts were then screened, which eliminated 601 of those articles because they did not meet the described inclusion criteria (pain following surgical intervention, foot/ankle surgery, specifically neuropathic pain, human subjects, diagnosis). The remaining 27 articles were then evaluated and assessed for their eligibility, to which 8 articles were then excluded on the basis of 2 studies where the neuropathy was not surgery related, 4 studies where the data was not sufficient, 1 study where only the incisional nerve pain was followed up on,

and 1 study where the neuropathic pain was related to an amputation. This left 19 total studies to be deemed eligible for the systematic literature review.

Study Type	Research Question Addressed	Authors	Year	Sample Size (n)	Age (y)	Follow-up Time	Outcomes
Case Report	Relief Interventions (3)	Abd-Elsayed et al	2018	1	65	2 months	Relief Intervention: - Pulsed radiofrequency ablation - 80% improvement in pain
Retrospective Cohort Study	Risk Factors (2)	Anantavorsakul et al	2020	32	59.7	8.4 years	Risk Factors: - Depression is a risk factor for increased pain and decrease in motor function subsequent to surgery - Smoking is correlated with higher pain scores
Retrospective Case Series	Incidence Rates (1) Relief Risk Factors (2)	Anderson et al	2015	1014	49.8	1 year	Incidence Rate: 13.3% [135/1014] - 5% had complications related to the popliteal nerve block - 8 patients had motor dysfunction, 118 had sensory dysfunction, 9 had both Risk Factors: - Age - Tourniquet Pressure
Retrospective Cohort Study	Relief Interventions (3)	Besmens et al	2022	30	43.5	27.5 months	Relief Intervention: - Sural nerve neurectomy - 22/30 patients had persistent pain - Neurectomy is a valuable option but only ¼ of patients will be pain-free afterwards
Retrospective Cohort Study	Relief Interventions (3)	Bhatia et al	2021	60	43.87	1-3 months	Relief Intervention: - Perineural local anesthetic + conventional medical management vs conventional medical management alone (LA-S vs CMM) - No analgesic benefit is added through the addition of a perineural local anesthetic
Case Report	Relief Interventions (3)	Chae et al	2016	1	51	2 weeks, 4 months	Relief Intervention: - Superficial peroneal nerve block + pulsed radiofrequency ablation - Pain relief was maintained through the 4 months follow-up
Retrospective Observational Study	Relief Interventions (3)	Cozzarelli et al	2010	82	42	5, 10, 12 years	Relief Intervention: - Radiofrequency nerve ablation - Treated neurogenic heel pain - 73 were pain-free after ablation after 12 years - 6 were pain free after ablation + further treatment after 12 years - 3 had no relief after ablation + further treatment after 12 years
Retrospective Case Series	Relief Interventions (3)	Cychosz et al	2023	21	47	33.7 months	Relief Intervention: - Sural nerve neurectomy with proximal implantation - Treats sural neuromas and sural neuritis - Median FAAM improved: 40.6 to 66.1 (P = 0.032) - FAAM sports improved: 14.1 to 41.1 (P = 0.002)

							- Median VAS improved: 9.0 to 3.0 (P < 0.001) - Median SF-36 improved: 31.4 to 43.4 (P = 0.004)
Case Report	Relief Interventions (3)	Gallo Pellitero et al	2023	1	54	-	Relief Intervention: - Ultrasound-guided radiofrequency ablation - Complete cessation of pain - No side effects
Prospective Cohort Study	Incidence Rates (1) Risk Factors (2)	Gartke et al	2012	147	55	2, 6, 14, 34 weeks	Incidence Rate: 24% [23/147] - Incidence rates are much higher than in previous literature - The rate dropped from 41% to 24% over the course of 8 months - Patients experienced both late-onset neuropathy and acute neuropathy Risk Factors: - Smoking is correlated with neuropathy - Tourniquet placement, tourniquet time, use of prophylactic antibiotics, type of anesthesia, level of anesthesia training, chronic pain, and patient age were NOT associated with neuropathy
Case Report	Relief Interventions (3)	Girtler et al	2013	1	34	3 months	Relief Intervention: - Topical 8% capsaicin patch - Resulted in the reappearance of a burning sensation - It took the patient 3 months to recover from her pain levels pre-treatment
Case Report	Relief Interventions (3)	Messina et al	2011	1	50	1 month, 2 months, 2 years	Relief Intervention: - Spinal cord stimulation - Patient had recurrent neuromas of the foot, developing neuropathic pain - Spinal cord stimulation through implantation resulted in complete pain disappearance
Prospective Randomized Control Pilot Study	Relief Interventions (3)	Noori et al	2021	49	56.7	1 year	Relief Intervention: - Popliteal fossa and saphenous nerve blocks vs Popliteal fossa and saphenous nerve blocks + dexamethasone - No differences in the incidence of neuropathic pain were observed, but the nerve block itself still proved effective for relieving neuropathic pain
Retrospective Observational Study	Relief Interventions (3)	Provenzano et al	2002	834	48	3 months	Relief Intervention: - Popliteal fossa nerve block - All patients who receive a PFNB reported no neuropathic complications 3 months following intervention
Retrospective Observational Study	Incidence Rates (1) Risk Factors (2)	Rbia et al	2017	271	50	5.8 years	Incidence Rate: 23% [61/271] - DN4 & MPQ utilized - 84% (51/61) of neuropathic pain patients reported an impaired quality of life - Pain was frequently characterized as sharp, burning, hypo-esthetic, tingling Risk Factors: - Age Range 40-60
Prospective Observational Longitudinal	Incidence Rates (1) Risk Factors (2)	Remérand et al	2014	260	58	1 year	Incidence Rate: 3% [9/260] - Extremely rate, but only the first 2 questions were utilized on the DN4 questionnaire

Cohort Study							- Moderate to severe chronic postoperative pain was significantly associated with neuralgia Risk Factors: - Acute postoperative pain - Prior surgery/trauma
Case Report	Relief Interventions (3)	Shim et al	2014	1	27	2 months	Relief Intervention: - Neuroma formed following ankle arthroscopy - Neuroma excision and nerve graft significantly improved the patient's pain
Prospective Cohort Survey Study	Incidence Rates (1) Risk Factors (2)	Sidon et al	2019	533	49.7	-	Incidence Rate: 12.4% [66/533] - painDETECT questionnaire utilized Risk Factors: - Smoking - Prior surgery - Ankle-level pathology vs forefoot pathology - Obesity - Diabetes had no effect on neuropathic pain
Case Report	Relief Interventions (3)	Sørensen et al	2023	1	9	20 months	Relief Intervention: - Virtual Reality - Similar to mirror therapy, VR helped alleviate almost all neuropathic pain over the course of ~1.5 years

Incidence Rates:

There were 5 research articles that answered our first research questions about the incidence of neuropathic pain following foot or ankle surgery. In Anderson et al, neuropathic pain was assessed when a popliteal nerve block was used for foot or ankle surgery. Of the 1014 patients that were assessed retrospectively, the complication rate for the patients that developed neuropathic symptoms was 13.3% (135/1014). Of these 135 patients, 8 patients had motor deficits, 118 had sensory deficits, and 9 had both sensory and motor deficits. The average time for the neuropathic symptoms to subside was 53.2 days, but there were 13 patients whose neuropathic pain symptoms never resolved after an entire year. However, only 52 (5%) experienced neuropathic symptoms specifically related to the popliteal nerve block. This research article also included risk factors for neuropathic pain, but these will be discussed later.

In Gartke et al, the researchers hypothesized that the incidence rates of neuropathic symptoms are much higher than previously thought. They performed a prospective cohort study of 147 surgical patients who had previously undergone foot or ankle surgery for at least more than 30 minutes. Each patient completed a questionnaire at each follow-up appointment at 2 weeks, 6 weeks, 14 weeks, and 34 weeks, and

neuropathic pain was diagnosed by the Douleur Neuropathic en 4 Questions (DN4) neuropathic pain questionnaire. The DN4 questionnaire is a screening tool consisting of 10 questions designed to dissociate between somatic pain and neuropathic pain. It asks 3 questions about the type of pain, 4 about the associated symptoms, 2 questions about any numbness, and 1 question about the amplification of pain by rubbing the area. If the respondent scores anything above a 4, they are diagnosed with neuropathic pain. For the results, the researchers found that at the end of 2 weeks, 41% of patients (60/147) experienced neuropathic symptoms. At the end of 6 weeks, 31% (45/147) experienced neuropathic symptoms. At the end of 14 weeks, 26% (34/147) experienced neuropathic symptoms. At the conclusion of the study at 34 weeks, this number dropped to 24% (23/147). Interestingly, there were 20 patients that had late onset neuropathy 6 weeks or later, and 18 patients reported that their neuropathic pain symptoms appeared and subsided at least twice. Comparatively from week 2 to week 34, they found that there is a 69% chance that a patient's neuropathic pain will subside somewhere along this time frame. The researchers concluded that the incidence of neuropathic pain following foot or ankle surgery was much higher than what they had previously thought (0%-14%).

In another research article that investigated both the incidence and risk factors of neuropathic pain following ankle surgery, Rbia et al concluded that 23% (61/271) experienced neuropathic pain following ankle surgery. The researchers conducted an observational retrospective study in which an initial 527 questionnaires were sent out, and then a return of 271 questionnaires were completed and able to be analyzed. Of these 271 respondents, their pain symptoms were assessed via the McGill Pain Questionnaire (MPQ) and the Douleur Neuropathic en 4 Questions (DN4). The latter was the same questionnaire that the previous study utilized, but the MPQ analyzes subjective pain statistically by inquiring the respondent about the type of pain that is experienced 12 weeks postoperatively. It asks if the pain is burning, stabbing, numb, has excessive sensitivity or sensation, pain, etc, as well as if the symptoms are present to determine temporary vs permanent symptoms. If permanent, duration/intensity is asked as well. Of the 271 included respondents, 48% (129/271) experienced postoperative pain, but 23% (61/271) experienced persistent neuropathic pain symptoms. 51 of these neuropathic pain patients reported an impaired quality of life.

Additionally, the DN4 questionnaire was able to detail that 97% of the symptoms were characterized by a sharp sensation, 96% had a burning sensation, and 92% described having total or complete loss of feeling in the area.

In Remérand et al, a prospective longitudinal cohort study was performed to determine incidence rates and associated risk factors of chronic pain and neuropathic pain following orthopedic foot surgery. The researchers included foot surgical patients and asked them to participate in a phone interview call a year following their surgery. Of the 436 patients who were reached out to, a total of 260 were able to meet all of the inclusion criteria. In the phone call a year following the surgery, the DN2 questionnaire was used, which self-evaluated the pain intensity of the respondents. Following the study, it was determined that only 9 of the 260 patients (3%) experienced chronic neuropathic pain. This statistic falls far below the previous literature's incidence rates, but this may be attributed to the lack of follow-up times after the surgery, as well as the fact that the neuropathic pain assessment was based on only the first 2 questions in the DN4 questionnaire. This study was limited to only a telephone call, so the incidence rate may have been undermined due to the lack of physical examination on each patient. Although Remérand et al may have not produced the most reliable incidence rate results, he also sheds light on our second research question regarding the risk factors of neuropathic surgery, which will be discussed later.

Our final research article concerning incidence rates of neuropathic surgery was conducted by Sidon, et al. He conducted a cross-sectional study to determine both incidence rates and risk factors for patients to develop NP symptoms after foot or ankle surgery. Unlike the previous researchers, he utilized a painDETECT questionnaire, which scores NP from 0-38 by asking 9 questions. If a patient scores anywhere between 0-12, a neuropathic component to their pain is unlikely, 13-18 is ambiguous, and 19-38 indicates that the pain the patient is experiencing is more than 90% likely. Due to the large sample size of 533 respondents in Sidon's cross-sectional study, he can boast that he has a 99% power to detect the prevalence of NP as low as 11%. Of the 533 patients, 12.4% fell above the painDETECT score of 18, indicating that there is a very high likelihood that their pain can be classified as neuropathic pain.

Risk Factors:

There were 6 research articles in our systematic literature review that detailed the various risk factors that lead to an increased likelihood of developing neuropathic pain following foot or ankle surgery. Anantavorasakul et al touched on the risk factors of traumatic neuromas that develop post-operatively, which result in neuropathic pain. A total of 32 subjects were included in this retrospective cohort study, and each subject's medical chart was reviewed to determine patient, neuroma, and treatment factors. Of these 32 subjects, 27 of them presented their complications due to surgery, not trauma. To determine risk factors, the four types of patient-reported outcome measures were used. The PROMIS (Patient-Reported Outcomes Measurement Information System) mobility v.2.0 computer adaptive testing, the PROMIS depression v.10 CAT (Computer Adaptive Testing), the PROMIS pain interference v1.1 CAT, and the NRS (Numerical Rating Scale) for pain. The PROMIS motility determines the function of the lower extremities, the PROMIS pain interference assesses the subject's ability to cope with pain, the PROMIS depression determines whether pre-existing depression construed any results, and the NRS determines pain severity, where a score greater than 8 indicated severe pain, moderate pain is scored 6-7, mild pain was scored 1-5, and no pain is a 0. From these various patient-reported outcome measurements, the researchers concluded that depression scores were associated with lower PROMIS mobility (β=−0.38, 95% CI: [−0.6, −0.16], p=0.001), PROMIS pain interference (β=0.68, 95% CI: [0.38, 0.97], p<0.001), and higher NRS pain scores (β=0.1, 95% CI: [0.04−0.16], p=0.001), all independently. Not only that, but smoking was also a risk factor that was associated with higher NRS pain scores (β=1.59, 95% CI: [0.01, 3.2], p=0.049;).

In Anderson et al (as discussed previously), neuropathic pain was assessed when a popliteal nerve block was used for foot or ankle surgery. Of the 1014 patients that were assessed retrospectively, there were a couple risk factors that were identified as being correlated with postoperative neuropathic pain. Patient characteristics/demographics, block methods, and tourniquet usage were all considered. Of the patient characteristics,

age was the only risk factor that was shown to have statistical significance (P = 0.039), as the average age for those who developed postoperative neuropathic pain symptoms was 47.3 ± 15 years, while the average age for those patients who did not develop postoperative neuropathic pain symptoms was 50.2 ± 17.2 years. When analyzing tourniquet use, only tourniquet pressure showed statistical significance (P = 0.013), but the tourniquet pressure in those patients who developed these symptoms only had a higher tourniquet pressure of 7 mmHg. Interestingly enough, smoking, diabetes, tourniquet time/location, and block procedure techniques did not reveal any statistical significance for developing neuropathic pain symptoms.

Referring back to the prospective cohort study done by Gartke et al, the risk factor that was found to be associated with neuropathic pain was smoking; however, she determined that tourniquet placement, tourniquet time, and use of prophylactic antibiotics, type of anesthesia, level of anesthesia training, chronic pain, and age were not significantly associated with neuropathic pain {Gartke, 2012 #18}. Of the 147 surgical patients, 68% who developed neuropathic pain symptoms were smokers, while 53% were non-smokers, which was statistically significant. The prevalence of neuropathic pain for tourniquet placement was not significant as the thigh versus ankle placement of the tourniquet allowed for 54.6% vs 50.0% of the patients to develop neuropathic pain, respectively. Spinal (54.6%) versus general anesthesia (55.3%) was not statistically significant for patients to develop neuropathic pain, and whether patients received prophylactic antibiotics (58.3%) or not (54.7%) was not statistically significant either. Those patients who had a history of chronic pain prior to surgery had slightly higher incidence rates of neuropathy (57.9%) vs those who did not have chronic pain (54.2%), but this was not statistically significant either.

Referring back to the retrospective case series performed by Rbia et al, the researchers examined possible predictors of neuropathic pain symptoms. When using a univariate analysis, it was determined that age, hypertension, thyroid disorder, and lower back pain were significantly associated with neuropathic pain. The researchers also found that neuropathic pain was associated, but not statistically significantly correlated, with

alcohol consumption, lower educational level, or unemployment. However, it is important to consider that there is a relationship between advanced age and other such comorbidities, such as hypertension, dislocation, or late complications. Therefore, the researchers conducted a multivariate analysis, which concluded that there was a singular predictor of developing neuropathic pain following ankle surgery, which was an age range between 40 and 60 years old (adjusted OR = 3.42, 95% CI = 1.12-10.43, *P* = .031). On the other hand, they were able to identify three other risk factors for persistent pain (somatic/nociceptive pain), but no neuropathic pain characteristics. These risk factors included hypertension (adjusted OR = 0.14, 95% CI = 0.29-0.64, *P* = .012), ankle dislocation (adjusted OR = 0.29, 95% CI = 0.11-0.78, *P* = .014), and late complications (adjusted OR = 0.09, 95% CI = 0.02-0.43, *P* = .003). The authors noted that while these risk factors cannot be influenced, they provide valuable knowledge to the surgeon to identify patients who have an increased risk of developing postoperative neuropathic pain.

In the prospective longitudinal cohort study performed by Remérand et al, the associated risk factors of chronic pain and neuropathic pain following orthopedic foot surgery were determined. Upon univariate analysis, 12 factors were initially associated with moderate-to-severe chronic postoperative neuropathic pain, but upon multivariate analysis that included eight perioperative variables, only two variables remained that were shown to be significantly associated with moderate-to-severe chronic post operative pain (CPOP) during walking. The first variable associated with CPOP was the patient experiencing acute postoperative pain (<48 hours postoperatively). The second variable that was associated with CPOP was if the patient experienced a prior surgery or trauma of the foot. This may indicate that the patient already has an increased sensitivity to pain, but a more realistic assumption is that a prior surgery marks a greater severity of the bone. Another interesting finding by Remérand et al was that an administration of ketamine is not associated with a decreased frequency of CPOP. It is also important to note that the site of surgery, whether it be performed on the hindfoot, ankle, or hallux/lesser toes, does not influence the rate of developing chronic postoperative pain.

The last study in our systematic literature review that covers the risk factors associated with neuropathic pain is a prospective cohort study done by Sidon et al, which was previously discussed when covering its findings on incidence rates of neuropathic pain. From the patient-reported pain questionnaires (painDETECT), several risk factors were determined that showed a high correlation with the development of neuropathic pain following foot or ankle surgery. Patients who currently smoked were statistically more prone to develop neuropathic pain than those who did not smoke (23.2% vs 11.1%), while those patients who were former smokers had about the same risk of developing neuropathic pain as those patients who never smoked (12.0% vs 10.8%, P = 0.016). Another risk factor that was statistically significant was if the patient had a prior foot or ankle surgery, which nearly doubled the risk of developing neuropathic pain symptoms versus those patients who had never had surgery on that foot or ankle (19.4% vs 10.8%, P = 0.027). Another risk factor for developing neuropathic pain was those who had an ankle-level pathology versus a forefoot pathology (13.2% vs 10.5%, P = 0.062), as well as obesity, which is classified as those patients who had a BMI over 30. For those patients, they had an increased risk of developing neuropathic pain symptoms than their non-obese counterparts (15.6% vs 10%, P = 0.06). An interesting finding from this study was that diabetes mellitus proved to have no effect on the risk of developing neuropathic pain following surgery (16% vs 12.0%).

Relief Interventions:

There were 13 research articles in our systematic review that detailed the various relief interventions for neuropathic pain following foot or ankle surgery. In the first article that we will discuss, pulsed radiofrequency ablation was utilized to treat sural neuralgia. In the case report by Abd-Elsayed et al, sural neuralgia is defined as persistent pain in the sural nerve that provides the fifth toe, lateral foot, and lateral posterior leg sensation. In the first case report, a 65-year-old female presented tingling in her right foot subsequent to right foot surgery, describing a sharp 8/10 pain. After failing physical therapy, NSAIDs, and gabapentin, a right sural nerve block was used using a local anesthetic, which was then proceeded by a PRF ablation, resulting in an 80% improvement in her pain after 2 months.

In Besmens et al, a thorough medical chart review from 2010 to 2020 was conducted to examine the results of sural neurectomies, which is a procedure performed on an injected sural nerve to treat neuropathic pain. Sural nerve neuromas can arise subsequent to an injury from a prior surgery. A retrospective cohort study was performed on 30 different patients, 12 male and 18 female, with a median of 43.5 years. In 26 of these cases, the neuropathic pain could be attributed to prior surgery. Before proceeding with a sural neurectomy, other treatments had failed, such as physical therapy, opiate pain medication, neuropathic pain medication (pregabalin), or topical anesthetics. After these conservative treatments had failed, the patients prepared to undergo a sural nerve neurectomy. First, a diagnostic injection prior to surgery was performed in 25 of the patients, in which 22 stated they had significant relief, 1 had partial relief, and 2 had no relief. Then proceeding with the neurectomy, only 8 patients reported their pain being relieved, leaving 22 patients to have persisting pain. Therefore, it was concluded that a sural nerve neurectomy remains a valuable surgical treatment as the surgical morbidity is minor, but only about a quarter of the patients will be satisfied and without any pain subsequent to surgery.

In Bhatia et al, the researchers investigated the analgesic benefits of adding a perineural local anesthetic and steroids (LA-S) to conventional medical management (CMM) and compared this to CMM alone in patients that had moderate-to-severe (M/S) neuropathic pain following trauma to the ankle or foot. It is noted that this study does not specifically give the number of patients whose trauma is related to surgery, but it is mentioned that the patient's foot traumas are due to crush injury, fractures, ligament tears/sprains, or surgery. This retrospective double cohort study included patients who were experiencing M/S neuropathic pain following trauma/surgery, who had persistent pain despite surgery and who had failed at least 6 weeks of anti-inflammatory medication and physical therapy. Pain intensity was measured at 1-3 months post-intervention, which was measured by the NRS. Before the intervention, the median pain score for both groups was 7 on the NRS scale. After comparing the LA-S with the CMM cohort to the CMM alone cohort, it was initially determined via univariate analysis that the perineural LA-S cohort reported lower pain 1-3 months status post-intervention

compared to the CMM alone cohort (5.50 vs 7.00, $P < 0.01$). However, the researchers had to take into account the possibility of the patient anticipating worse outcomes prior to the intervention. When multivariate analysis was utilized, it was determined that there was no statistically significant beneficial analgesic effect with the addition of the perineural LA-S with CMM when compared to the CMM group alone. This 'pre-intervention catastrophizing' may be associated with the reduction in analgesic benefit. Therefore, it can be concluded that a local anesthetic and steroids provide no better outcome to neuropathic pain patients following foot or ankle surgery.

In Chae et al, the researchers explore a case report in which an ultrasound-guided pulsed radiofrequency ablation was used on the superficial peroneal nerve. A case report on a 51-year-old patient who presented mechanical allodynia and thermal allodynia, which first presented a year prior from an ankle fracture, resulting in ankle surgery. Medication and physical therapy did not relieve her pain, so she then resorted to a lumbar sympathetic block and neurolysis, which diminished her Visual Analog Scale (VAS) pain score from 7-8/10 to 2-3/10. However, her pain persisted, so a superficial peroneal nerve block was attempted, which reduced her allodynia, but only for a few days. She then resorted to a peroneal radiofrequency ablation on the superficial peroneal nerve. This ablation lasted 120 seconds at 45V, which was repeated 3 times. The pain relief reduced her allodynia from a 7-8/10 to 2-3/10, which not only persisted for the 2-week follow-up but persisted through the 4-month follow-up. At the 4-month follow-up, the pain had increased to a 5-6 but was still improved from before the ablation. In another case report by Gallo Pellitero, et al, ultrasound-guided radiofrequency ablation of the sural nerve was conducted. This case report follows a 54-year-old patient with a long medical history of several ankle surgeries, resulting in severe neuropathic pain. Conservative treatment failed him, therefore the ultrasound-guided radiofrequency ablation was performed, revealing a complete recovery, no residual pain, and no side effects.

In Cozzarelli et al, a retrospective analysis was conducted on radiofrequency nerve ablation's effectiveness in treating neurogenic heel pain. He argues that this procedure is extremely efficient and effective in treating this type of chronic neuropathic pain, and

may help eliminate the need for open nerve surgery. Medical records from November 1994 to December 1995 were reviewed to search for patients who underwent radiofrequency nerve ablation subsequent to foot or ankle surgery. These patients presented chronic heel pain for over a year, failed conservative treatment, and had a postoperative period longer than 4 years. Of these patients, radiofrequency nerve ablation was performed on the patient's foot. Long-term relief was determined through a telephone interview in which the patients rated their pain on a scale of 0-10. The first interview was conducted 5 years postoperatively, the second interview was conducted 10 years postoperatively, and the third interview was conducted 12 years postoperatively. After 5 years, 79 patients were completely pain-free, 7 patients were pain-free after further treatment, and 3 patients had no relief even after further treatment. After 10 years, 75 patients were completely pain-free, 6 patients were pain-free after further treatment, and 3 patients had no relief even after further treatment. After 12 years, 73 patients were completely pain-free, 6 patients were pain-free after further treatment, and 3 patients had no relief even after further treatment (note: some patients dropped out of the long-term study, explaining the loss of participants). Over this time frame, the radiofrequency nerve ablation proved to have an 89% success rate.

In Cychosz et al, the sural nerve is once again the focus as he investigates the outcomes of sural nerve neurectomy with proximal implantation for sural neuromas and chronic sural neuritis. Sural neuritis and neuromas usually result from prior surgery to the lateral hindfoot or from other traumas to the ankle/foot. It is noted that this study does not specifically give the number of patients whose trauma is related to surgery, but it is mentioned that the patients developed neuromas or sural neuritis subsequent to surgery or other traumas. For the study, the researchers gathered 21 patients who underwent neurectomy with proximal implantation of the sural nerve. After surgery, the patients experience vast improvements from the preoperative to their postoperative FAAM (Foot and Ankle Ability Measure) and VAS (Visual Analog Scale) scores. Median FAAM scores improved from 40.6 to 66.1 ($P = 0.032$). FAAM sports scores improved from 14.1 to 41.1 ($P = 0.002$). Median VAS scores improved from 9.0 to 3.0 ($P < 0.001$). Lastly, median SF-36 physical component summary scores improved from 31.4 to 43.4 ($P = 0.004$). Therefore, the researchers were able to conclude that sural neuroma excision and

proximal implantation provide significant pain improvement for patients who present painful sural neurons and sural neuritis.

In another study detailing a neuroma excision, Shim et al detail a case report involving a 27-year-old male who developed superficial peroneal neuropathy following arthroscopic ankle surgery. This man failed 3 months of conservative therapy following a left ankle sprain, to which he then underwent arthroscopic surgery. He developed pain on the medial dorsum of his left foot, experienced ankle allodynia, and was eventually diagnosed with sensory neuropathy. To assess for the compressive source of neuropathy, ultrasonography was used which found a soft tissue lesion that measured 0.82×0.29×0.56-cm. This 2cm neuroma-in-continuity was found on the left medial dorsal cutaneous nerve, which was excised. This excision was then proceeded by a cable nerve graft procedure, which used the medial antebrachial cutaneous nerve that was harvested from the patient's left forearm. After this procedure, the neuropathic pain was managed with analgesics for 7 months, and the patient reported that the pain had substantially improved 2 months following surgery.

One German study investigated a case report involving a 34-year-old female who developed clear neuropathic pain following surgery on her right forefoot. She presented intense swelling and scored a 19 on the pain-DETECT questionnaire, revealing a clear neuropathic component to her pain. To initially treat her pain, she underwent a month-long steroid treatment in congruence with physical therapy, then eventually underwent a right lumbar trunk blockade and neurolysis. This reduced her pain to a 5 on the VAS scale, which was previously a 9. However, burning neuropathic pain persisted, so she began treatment with an approved capsaicin patch. This 8% capsaicin patch is applied to the heel, foot sole, surgical scar, medial dorsum, and inner ankle, and is an agonist of TRPV1 receptors. These nociceptors lie in the epidermis and dermis and lead to inflammatory responses and pain. This patch is painless and was applied for 30 minutes. However, she presented a flare reaction in the area of the capsaicin patch application (except for the surgical scar), which resulted in a VAS score of 8. A local anesthetic was then administered via the epidural catheter. Once the epidural anesthesia wore off, the burning pain ensued. To further treat her neuropathic pain, she

began taking strong opioids, mirror therapy, group therapy, and psychotherapeutic treatment. It took another 3 months for her pain levels to reach pre-capsaicin patch levels. This case report illustrates that although capsaicin patches may serve as a potential remedy for neuropathic pain, the patches may induce nociceptive responses. Therefore, their usage is currently controversial as a sole treatment as it resulted in the reappearance of the patient's central nervous symptoms.

Messina et al detail another case report involving a patient who developed chronic neuropathic pain within the third metatarsal region of the left foot following the appearance of multiple neuromas, subsequent to a Morton's disease surgery. A 50-year-old woman underwent surgical removal of Morton's neuroma, which proved unsuccessful as the plantar pain relapsed and several new neuromas appeared. Then, within a span of 7 years, 3 surgeries were performed to remove these neuromas and their recurrences, which all proved unsuccessful as there was a recurrence subsequent to each surgery. A neurolysis procedure also proved ineffective, along with conservative treatments. Finally, the patient underwent spinal cord stimulation. Under general anesthesia, a spinal electrode was inserted into the T10 epidural space, and an internal pulse general was placed in the left subcostal space. This surgery involved a laminectomy and flavectomy of the T9-T10 intervertebral space as well. The patient experienced a significant reduction in neuropathic pain postoperatively at the 1-month and 2-month follow-up, in which the pain eventually completely disappeared. Her VAS score was 0 and her SF-36 score reached 100, proving that spinal cord stimulation may be a great treatment for neuropathic pain following foot or ankle surgery.

In Provenzano et al, he investigates the seemingly 'underutilized' anesthetic technique of a popliteal nerve block for foot or ankle surgery and its postoperative neuropathic complications. In this retrospective study, 834 patients's charts were included that all received some sort of anesthetic technique. For the patients that were included in the study, 467 patients received the popliteal fossa nerve block (PFNB), but 28 were excluded for other various reasons, yielding 439 patients who were included who received the PFNB. 255 patients received general anesthesia, 91 patients received spinal anesthesia, 10 patient received an epidural anesthesia, and 11 patients received a local

anesthetic via IV sedation. Of the patients that received a PFNB, 347 patient's nerve blocks proved to be successful (79%), while 92 patient's nerve blocks were unsuccessful (21%). These patients whose PFNB did not work, were either converted to general anesthesia (77/92), or were augmented with a local anesthetic (15/92). Each patient was then followed up with 3 months later to get assessed for postoperative neuropathic complications, in which every single PFNB patient did not have any neuropathic complications (excluding 5 patients who had pre existing neuropathy). This study helped to shed light on the practicality and usefulness of a PFNB for foot and ankle surgery. It decreases postoperative complications, preserves contralateral leg strength, and even works as an excellent form of postoperative analgesia.

To touch further on the usage of nerve blocks, in Noori et al, the researchers conducted a prospective, double-blinded randomized control pilot study to determine the postoperative neuropathic complications if dexamethasone was used as an adjunct drug to nerve blocks. Some common anesthetic techniques to reduce neuropathic complications for foot and ankle surgery rely on popliteal fossa and saphenous nerve blocks, but by adding dexamethasone, the nerve block can be prolonged and the patients typically take less narcotics in their postoperative period. The researchers included 49 patients who had foot or ankle surgery, in which the control group (N = 25) received postoperative popliteal and saphenous nerve blocks with bupivacaine and epinephrine solution (40 cc 0.5% bupivacaine with 1:200 000 epinephrine), and the experimental group (N = 24) received postoperative popliteal and saphenous nerve blocks with addition of dexamethasone (40 cc 0.5% bupivacaine with 1:200 000 epinephrine + 2 cc dexamethasone (8 mg). Upon assessment of analgesia duration, incidence of nerve pain, pain satisfaction, and block satisfaction, there was no statistical significance in any group. In terms of neuropathic pain, the control group had 2 out of the 25 patients experience neuropathic pain, while only 3 out of the 24 patients in the experimental group experienced neuropathic pain. 3 of these 5 patient's neuropathic pain was then resolved shortly thereafter with medication, sympathetic blocks, or topical lidocaine. One patient's neuropathic pain disappeared without any treatment, and the other patient's neuropathic pain was never resolved. Unfortunately, this study's sample size was fairly small, the tourniquet time and surgical durations varied, and the nerve block

techniques may have been inconsistent, which may have affected the statistical significance. However, this study does provide some insight on the effectiveness of nerve blocks, and may suggest that the further addition of adjunct drugs may not relieve neuropathic pain more than the nerve blocks itself already do.

In a rather unique case report, Sørensen et al details a case report regarding a 9-year-old boy who presented persistent neuropathic pain and allodynia following a bilateral foot calcaneus extension. He then developed medial foot pain and soreness as well as an inability to invert his feet. Immobilization of an RO-Walker failed, physiotherapy failed, and ibuprofen all failed. With a reported pain of an 8 on the NRS scale, his diagnosis was confirmed of severe chronic neuropathic pain. Several other treatments ensued, all of which had no effect. These included transcutaneous electrical nerve stimulation therapy, a local lidocaine analgesic, and a sural nerve blockade. When mirror therapy was utilized, the adolescent boy said that the experience was similar to a virtual reality game. This is when the Virtual Reality intervention ensued, which helped the boy move his body, including his neuropathic foot. These games also prompted him to see a full-body simulated version of himself, as well as a virtual forum where he could walk around and see himself. The patient used Virtual Reality for 1-2 hours a day, which gradually significantly alleviated his pain. Two months later his allodynia disappeared, he began a physiotherapy training program, and eventually returned to school. At the final follow-up 20 months later since the initial VR intervention, he was essentially without pain with an NRS score of 1-2.

Discussion

Significant Findings

The severity and importance of research surrounding distant neuropathic pain following foot or ankle surgery is largely answered by our first research question: the incidence rates of distant neuropathic pain after foot or ankle surgery. Of the 5 research articles that met our criteria, there was an average of more than 15% of patients developing this

chronic condition. When compared to the general incidence rates following foot or ankle surgery (3%-17%), the incidence rates that we found clearly ended up on the higher end of this spectrum, especially as 2 of the found research articles far surpassed this statistic (23% and 24%). This further proves that anytime a patient may be undergoing a surgery of the ankle or foot, the incidence of neuropathic pain developing cannot be understated.

With regards to our second research question concerning the associated risk factors of distant neuropathic pain after foot or ankle surgery, it appears that most of the literature review was in agreement with common sources, but there was some disagreement. We found that risk factors that had a positive correlation with developing neuropathic pain included smoking, age (40-60 years old), psychological distress/negative mood, obesity, tourniquet pressure, prior surgery, and acute postoperative pain, while there appeared to be no correlation between neuropathic pain and tourniquet placement, time the tourniquet was on, prophylactic antibiotics, type of anesthesia, level of anesthesiology training, diabetes, hypertension, or dislocation. The finding that caused the most dissonance between previous knowledge was that diabetes and hypertension appeared to have no correlation with developing neuropathic pain according to 2 of our included studies. Risk factors alongside incidence rates should be nonnegotiable when it comes to educating patients before undergoing any sort of foot or ankle surgery. Thus, physicians should clearly be made aware of these risk factors in order to ensure that a precautionary approach is taken if they have patients that fall under any of the above risk factor categories.

In our final research question regarding if there were any successful interventions following surgery that provided relief or showed promising results, we were able to distinguish several post operative treatments. These included ultrasound-guided radiofrequency ablation, sural nerve neurectomy, popliteal nerve blocks, peroneal nerve blocks, neurolysis, peripheral nerve stimulation, spinal cord stimulation, and VR (virtual reality). When looking at common neuropathic pain treatments as a whole, previous general literature suggests prescriptions of painkillers, antidepressants, or sometimes surgery. However, this literature review did not focus on medications as

much as it did interventional treatments. These interventional treatments offered varying levels of success, with the ultrasound-guided radiofrequency ablation proving to have the most promising results, as 30.7% (4/13) of the included research articles investigated this specific approach. More studies will need to be conducted on the other surgical interventions, but they all show promising results nonetheless.

Limitations

1. The relief interventions may lack external validity due to the inability to exercise repetition in the studies. Once the neuropathic pain symptoms subside, treatments are typically discontinued.
2. 7 of the 19 studies were limited in terms of sample size (less than 20 patients). This in turn may also affect external validity.
3. There were no restrictions for the exclusion criteria that involved follow-up time for patients. The literature review included follow-up times that ranged from as little as 2 months to as long as 12 years.
4. There were no limitations in regards to the review processes used.

Implications

The findings in our literature review align itself with general conceptions about neuropathic pain for the most part, which should give physicians a sense of confidence when approaching this nervous system phenomenon. It is reasonable to assume that there is about a 1 in 5 chance of patients developing neuropathic pain following foot or ankle surgery, with certain patients being at a higher risk for this happening. Most notably smoking, age, and psychological distress put patients at a higher risk. We can also assume that if surgery is implicated in managing post operative pain, then pulsed radiofrequency ablation should be at the forefront of the physician's consideration. All three research questions (incidence rates, risk factors, and relief interventions) require further studies to establish definitive answers for the most effective ways to approach and manage neuropathic pain.

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