CLINICAL STUDY

Percutaneous Image-Guided Cryoablation for the Treatment of Phantom Limb Pain in Amputees: A Pilot Study

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ABSTRACT

Purpose: To prospectively evaluate percutaneous image-guided nerve cryoablation for treatment of refractory phantom limb pain (PLP) in a pilot cohort for purposes of deriving parameters to design a larger, randomized, parallel-armed, controlled trial.

Materials and Methods: From January 2015 to January 2016, 21 patients with refractory PLP underwent image-guided percutaneous cryoneurolysis procedures. Visual analog scale scores were documented at baseline and 7, 45, and 180 days after the procedure. Responses to a modified Roland Morris Disability Questionnaire were documented at baseline and 7 and 45 days after the procedure.

Results: Technical success rate of the procedures was 100%. There were 6 (29%) minor procedure-related complications. Disability scores decreased from a baseline mean of 11.3 to 3.3 at 45-day follow-up (95% confidence interval 5.8, 10.3; $P < .0001$). Pain intensity scores decreased from a baseline mean of 6.2 to 2.0 at long-term follow-up (95% confidence interval 2.8, 5.6; $P < .0001$).

Conclusions: Image-guided percutaneous nerve cryoablation is feasible and safe and may represent a new efficacious therapeutic option for patients with phantom pains related to limb loss.

ABBREVIATIONS

AE = adverse event, PLP = phantom limb pain, RLP = residual limb pain, RMDQ = Roland Morris Disability Questionnaire, SAE = serious adverse event, VAS = visual analog scale

Approximately 185,000 amputations are performed each year in the United States, and studies estimate that nearly 3.6 million people will be living with limb loss worldwide by 2050 (1,2). A common complaint among amputees is phantom limb pain (PLP), a phenomenon in which unpleasant sensations, often painful and severe, are perceived to originate from an absent limb. PLP occurs in 50%–80% of amputees, and there is no consistent evidence to support any specific pain control modality or intervention in this setting (1,3–7). The objectives of this study were to (*a*) evaluate the safety and feasibility of a separated 2-step procedural methodology consisting of computed tomography (CT)–guided perineural diagnostic injection and cryoablation in the setting of refractory PLP; (*b*) confirm the reproducibility of treatment response in relation to the findings of previous studies; and (*c*) derive estimates for key study parameters, such as recruitment rates, potentially

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Appendices A and B, Figures E1–E5, and Tables E1 and E2 are available online at *www.jvir.org*.

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confounding variables, and the treatment effect and its variation to inform the planning and design of a larger, parallel-armed, randomized controlled clinical trial investigating the efficacy of cryoablation for the treatment of PLP.

MATERIALS AND METHODS

This study was approved by the university institutional review board and complied with the Health Insurance Portability and Accountability Act. The trial was registered before patient enrollment on ClinicalTrials.gov (NCT02366832).

Subjects

Subjects were recruited from January 2015 to January 2016 from local vascular surgery, orthopedic surgery, and physical medicine and rehabilitation practices. All patients reported phantom pains and/or unwanted sensations related to a previously amputated upper or lower limb that were refractory to conventional treatment (eg, mirror therapy, physical therapy, anxiolytic medications, antidepressant medications, opioids, external cream application, γ-aminobutyric acid agonists) for at least 6 months. To undergo cryoablation, each patient was required to have documented symptomatic relief from an image-guided perineural injection of bupivacaine and betamethasone. Demographic details for the cohort are listed in **Table 1**, and inclusion and exclusion criteria are listed in **Table 2**.

Table 1. Subject Demographic Data

Factors	Values
Number of patients	21
Age, y, mean (range)	56.9 (34—91)
Female sex	12 (60%)
Time since amputation, y, mean (range)	10.2 (1–50)
Preoperative pain intensity, mean ± SD	6.2 ± 2.2
Residual limb pain	
Yes	8 (38.1%)
No	13 (61.9%)
Neuroma	
Yes	13 (61.9%)
No	8 (38.1%)
Site of amputation	
Upper extremity	4 (19%)
Above elbow	1 (25%)
Below elbow	1 (25%)
Complete forequarter	2 (50%)
Lower extremity	17 (81%)
Above knee	10 (58.8%)
Below knee	7 (41.2%)
Reason for amputation	
Peripheral vascular disease	7 (33.3%)
Neoplasm	1 (4.8%)
Thrombosis	2 (9.5%)
Trauma	9 (42.9%)
Tumor	2 (9.5%)

Note–Values are presented as number (%) unless indicated otherwise.

Interview

During initial consultation, each patient was questioned regarding the distribution and severity of their phantom pains as well as the presence or absence of residual limb pain (RLP). Each symptom complex was classified according to the algorithm presented in **Figure E1** (available online at *www.jvir.org*), and target nerves were identified (**Figs E2, E3** [available online at *www.jvir.org*]).

Block

Serial axial unenhanced CT images of the residual limb were obtained before any intervention. If a neuroma was identified along the expected course of the offending nerve, that location was the default target. The nerves in question also were evaluated with ultrasound (**Fig 1a, b**). The patients were positioned in the prone or decubitus position on the CT table, depending on the nerve to be targeted. After obtaining subcutaneous and tract anesthesia with 1% lidocaine (Hospira, Inc, Lake Forest, Illinois), a 22-gauge spinal needle was advanced under CT or ultrasound guidance to the target nerve or neuroma. Needle position was confirmed with fluoroscopic CT. Injections of 4 mL of 0.25% bupivacaine (Hospira, Inc) and 6 mg of betamethasone (Schering-Plough Corp, Kenilworth, New Jersey) were performed. The patient was monitored for 2 hours after the injection and then discharged. During the subsequent 24 hours, the patients were asked whether or not there was an improvement in symptoms after the injection, and a binary response was recorded as either "yes" or "no."

Ablation

All ablation procedures were performed under conscious sedation induced with intravenous midazolam (Hospira, Inc) and fentanyl (West-Ward Pharmaceuticals Corp, Eatontown, New Jersey). Using technique and targeting analogous to the diagnostic injections, a 17-gauge IceSphere cryoablation needle (Galil Medical, Inc Arden Hills, Minnesota) was advanced under imaging guidance to the previously identified nerve and/or neuroma. When position was confirmed, the probe temperature was decreased to −40°C over 10 minutes using the Galil Visual-ICE system. Images were obtained and reviewed 8 minutes into the freeze. A passive thaw cycle was then undertaken for 5 minutes, followed by a second 10-minute freeze and subsequent final 5-minute passive thaw (**Figs 2** and **3a–d**).