

## Original Article

# Does implantation of verruca plantaris into the abductor hallucis muscle belly in conjunction with CO<sub>2</sub> laser ablation prevent recurrence?



Emily E. Zulauf<sup>a</sup>, Hannah Sahli<sup>a</sup>, Kevin Alexander<sup>a</sup>, Matthew DeMore III<sup>b</sup>, Duane J. Ehredt Jr.<sup>c,\*</sup>, Jill Kawalec<sup>d</sup>

<sup>a</sup> Kent State University College of Podiatric Medicine, Independence, OH, USA

<sup>b</sup> Podiatry Inc., Cleveland, OH, USA

<sup>c</sup> Division of Foot/Ankle Surgery and Biomechanics, Kent State University College of Podiatric Medicine, Independence, OH, USA

<sup>d</sup> Kent State University College of Podiatric Medicine, Independence, OH, USA

## ARTICLE INFO

## Keywords:

Keywords: Immunization

Inoculation

Plantar

Recalcitrant

Wart

## ABSTRACT

Often times, conservative treatment is unsuccessful in long-term resolution of recalcitrant verrucae plantaris lesions. In addition to being aesthetically displeasing, severe cases that are left untreated can be debilitating, often leading to chronic pain, gait abnormalities, and further cutaneous spread. Inoculation through implantation of verrucae plantaris into a muscle was previously postulated to provoke an immune response against the human papilloma virus, resulting in auto-immunization. The purpose of this study was to determine the rate of recurrence following two methods of treatment: A) Surgical removal and subsequent implantation of verruca plantaris into the contralateral abductor hallucis muscle belly and B) Surgical excision of verrucae plantaris. A retrospective chart review of 43 consecutive patients was performed. Group A was comprised of 25 patients who underwent surgical removal of verrucae plantaris followed by implantation of a biopsied specimen into the contralateral abductor hallucis muscle belly. Group B was comprised of 18 patients who underwent only surgical removal of the verrucae. The presence or absence of verrucous lesions was recorded at a post-operative follow-up at an average of 27.5 months. Correlations between recurrence of disease and age, sex, and medical comorbidities were evaluated. Our results suggest that implantation of verruca plantaris into the abductor hallucis muscle belly yields no significant difference in clinical recurrence rates when compared to surgical removal.

## 1. Introduction

Verrucae plantaris (plantar warts) are a well-known dermatologic condition seen by foot and ankle specialists with a multitude of potential treatment options ranging from simple topical solutions to invasive surgical excision. Plantar warts are caused by the human papillomavirus (HPV), specifically strains 1, 2, 4, 27 and 57 [1]. These lesions present most commonly in children and adolescents. It is estimated that 10% of school-aged children are infected with plantar warts before adulthood [2]. Children at increased risk of HPV infection include those who have infected family members and a high percentage of infected classmates [2]. Females are more commonly infected than males with a peak incidence at 13 years old [3].

Although many topical conservative treatments for plantar warts exist, there is a paucity of evidence-based treatment guidelines in the current medical literature. Salicylic acid is a common first-line agent reported to have some therapeutic effect in treatment of plantar warts

[4]. The reported recurrence of warts with salicylic acid use is close to 19% [5], thus it is only a successful treatment in roughly 81% of cases.

To the authors' best knowledge, the cost burden of cutaneous warts has not been investigated in the United States. In the United Kingdom, the equivalent of \$64.5 million USD was spent on all forms of conservative treatment [5]. The same report determined that in-office salicylic acid is a more cost-effective treatment compared to cryotherapy, which yields statistically similar results at a higher cost [5].

Unfortunately, current conservative therapies can be ineffective in cases of verrucous lesions that have failed to respond to standard salicylic acid treatments over a period of several months to years. These recurrent cases leave both the patient and the physician frustrated. Once conservative regimens fail to resolve patients' symptoms, more invasive treatment options for removal, such as surgical excision, may be explored.

In 1980, Panacos et al. first described surgical implantation of verruca plantaris as a treatment option for recalcitrant lesions. They

\* Corresponding author at: KSUCPM, 6000 Rockside Woods Blvd., Independence, OH 44131, USA.

E-mail address: [dehredt@kent.edu](mailto:dehredt@kent.edu) (D.J. Ehredt).

theorized that implantation of lesions containing HPV would provoke an immune response, thereby eliminating recalcitrant lesions [6]. Current literature suggests that adaptive cell-mediated immunity is key in combatting HPV, leading to the belief that an autogenic graft would trigger an immune response, causing regression of HPV viral load [7]. The Panacos technique initially showed promising results; however, to our best knowledge, the technique has not been systematically evaluated in the medical literature.

The purpose of this study was to expand on Panacos' work and evaluate the rate of clinical recurrence after implantation of verrucae plantaris lesions into the patients' contralateral abductor hallucis muscle belly. It was hypothesized that implantation would provoke an immune response to combat HPV, thereby eliminating recurrence of verrucous lesions. Our primary aim was to assess the recurrence rate of verrucae plantaris clinically, and our secondary aim was to determine if patient co-morbidities affected the results of the procedure. In the current study, the charts of 43 consecutive patients were reviewed and evaluated the effect of surgical implantation of recalcitrant verruca plantaris into the contralateral abductor hallucis muscle belly.

## 2. Materials and methods

### 2.1. Study population

A retrospective evaluation was performed on 43 consecutive patients with recalcitrant plantar verrucae. The primary aim of this investigation was to evaluate the effect of surgical implantation of recalcitrant verruca plantaris into the contralateral abductor hallucis muscle belly. Each patient underwent one of two procedures and was monitored for a minimum of 12 months for recurrence of lesions. Patients in Group A underwent surgical excision and implantation of the verrucous lesion into the contralateral abductor hallucis muscle belly. Patients in Group B underwent surgical excision only. All pre-operative and post-operative evaluations, as well as procedures were performed by a single surgeon in Cleveland, Ohio between May 2012 and October 2015. Inclusion criterion for our study was a history of recalcitrant verrucae plantaris confirmed by histopathologic examination. All patients for this manuscript had histopathologically confirmed verrucous lesions from their intra-operative specimens. The presence or absence of verrucous lesions was recorded at a follow-up period that ranged from 12 months to 48 months.

Prior to initial investigation, formal Institutional Review Board approval was granted at Kent State University. The de-identified medical records for all 43 consecutive patients were retrieved and evaluated by the authors. Clinical patient variables including age, gender, history of type 1 diabetes mellitus, history of type 2 diabetes mellitus, history of cancer, and history of allergies were recorded.

### 2.2. Surgical technique

#### 2.2.1. Group A: surgical excision and implantation

All procedures were performed in a formal operating room with the patient in the supine position. A local block of 10 cc 0.5% bupivacaine plain was administered in two locations: the lesion site and the implantation site on the contralateral foot for a total of 20 cc. Both feet were prepped and draped in the usual sterile fashion using povidone-iodine scrub and povidone-iodine paint. All patients received prophylactic antibiotics pre-operatively, based on the hospital's previously set guidelines (cefazolin 1 g if under 80 kg or 2 g if over 80 kg, and clindamycin 900 mg if penicillin allergy). No patients received continued antibiotics post-operatively. Hyperkeratotic tissue was debrided using a #15 surgical blade [Fig. 1]. A 1.5 mm punch biopsy of a lesion's core was removed and placed into a sterile container of 4% chlorhexidine gluconate solution for at least three minutes in preparation for implantation [Fig. 2]. The base of the lesion was then cauterized using a carbon dioxide laser [Fig. 3]. All excised tissue, less the core lesion used



Fig. 1. Pre-operative biopsy site; prepped by debridement of hyperkeratotic tissue.

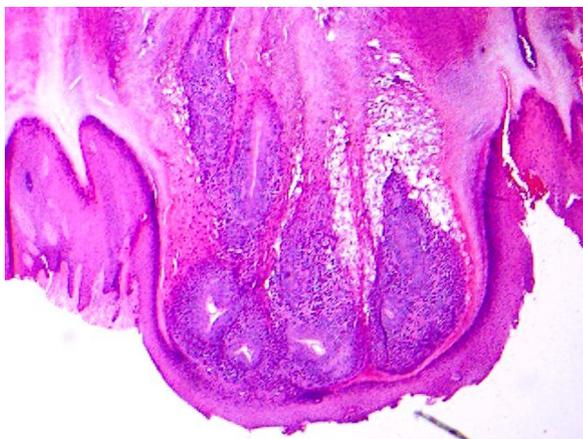


Fig. 2. A 1.5 mm punch biopsy of the central part of the lesion is placed into antiseptic cleanser.



Fig. 3. Remaining lesion is cauterized with a carbon dioxide laser.

for implantation, was sent to the pathology lab for formal histological examination [Fig. 4]. On the contralateral foot, a one-centimeter incision was made approximately 3–5 cm distal to the origin of the abductor hallucis muscle. Blunt instrumentation was used to dissect the implantation site. The verrucous tissue was removed from the 4% chlorhexidine gluconate solution and was lavaged with approximately 30cc of normal sterile saline. A hemostat was used to implant the verrucous tissue deep into the abductor hallucis muscle belly. The incision site was flushed with copious amounts of normal sterile saline and closed with 4-0 nylon suture [Fig. 5]. The plantar surface treated with laser excision was dressed with 1% silver sulfadiazine and the incision site for implantation on the contralateral foot with was dressed



**Fig. 4.** Hematoxylin and eosin stained histopathology of plantar verruca curettage specimen. Massive hyperkeratosis with papillomatosis, parakeratosis, acanthosis and diagnostic viral inclusion bodies. (100×).



**Fig. 5.** The biopsied core is implanted into abductor hallucis on the contralateral foot and is closed with 4-0 nylon.

with povidone-iodine. Dry sterile dressings were applied to both feet followed by ace bandages for edema management. Post-operatively, patients were placed in surgical shoes and allowed immediate full weight bearing as tolerated. Sutures were removed approximately two-weeks post-operatively and the excision sites were allowed to granulate and heal secondarily with standard local wound management.

### 2.2.2. Group B: surgical excision only

Patients underwent the standard surgical excision of verrucous lesions coupled with a carbon dioxide laser treatment to cauterize the base of the lesions. The surgical site was dressed with 1% silver sulfadiazine followed by a dry sterile dressing and ace bandage to the

operative foot. Post-operatively, patients were placed in surgical shoes and allowed immediate full weight bearing as tolerated. Sutures were removed approximately two-weeks post-operatively and the excision sites were allowed to granulate and heal secondarily with standard local wound management.

### 2.3. Statistical analysis

Descriptive and inferential statistics were performed using IBM SPSS Statistics 22<sup>®</sup> (IBM Corporation, Armonk, NY) software. Associations between recurrence of verrucae plantaris and type of procedure, gender, history of diabetes type 1, history of diabetes type 2, history of cancer, and history of allergies were statistically analyzed using a Fischer's exact test with statistical significance defined as  $p \leq 0.05$ . Associations between recurrence of verrucae plantaris and age and BMI were statistically analyzed using a Wald logistic regression with statistical significance defined as  $p \leq 0.05$ .

### 3. Results

A total of 43 consecutive procedures were reviewed. Of these, 25 (58.14%) procedures (Group A) surgically removed the verrucous lesions and implanted a biopsied specimen into the contralateral abductor hallucis muscle belly (11 (44.0%) males and 14 (56.0%) females; Table 1). The remaining 18 (41.86%) procedures (Group B) underwent surgical removal of verrucous lesions only (5 (27.8%) males and 13 (72.2%) females; Table 1). The mean age of the study population was 26.3 (range 6–64) years. The mean age of patients for Group A at the time of surgery was 23.8 (range 6–48) years. The mean age of patients for Group B at the time of surgery was 29.9 (range 6–64) years. The mean follow-up duration was 27.5 (range 8–48) months.

Associations between recurrence of verruca plantaris and type of procedure, gender, history of diabetes type 1, history of diabetes type 2, history of cancer and history of allergies were statistically analyzed using a Fisher's exact test with significance defined as  $p \leq 0.05$ ; Table 2. Associations between recurrence of plantar warts and age and BMI were statistically analyzed using a logistic regression with significance defined as  $p \leq 0.05$ ; Table 3.

When considering all patients, there were no statistically significant associations between recurrence of plantar warts and type of procedure, gender, histories of diabetes type 1, diabetes type 2, cancer and allergies, age and BMI. When considering patients who underwent surgical removal of verruca followed by implantation into the abductor hallucis muscle belly in the contralateral foot, there were no statistically significant associations between recurrence of warts and gender, histories of diabetes type 1, diabetes type 2, cancer and allergies, age and BMI. When considering patients who underwent surgical removal of the plantar wart only, there were no statistically significant associations between recurrence of warts and gender, histories of diabetes type 1, diabetes type 2, cancer and allergies, age and BMI.

Of the 43 total patients in the study, 8 (18.6%) experienced a

**Table 1**

A statistical description of the treatment groups.

	Surgical removal and implantation	Surgical removal only	p-Value
Number of subjects	25 (F = 14, M = 11)	18 (F = 13, M = 5)	
% Male/% Female	44.0%/56.0%	27.8%/72.2%	$p = 0.278$
Mean subject age, in years	23.8 ± 13.7 (6–48)	29.9 ± 17.7 (8–64)	$p = 0.229$
Mean BMI	23.2 ± 8.3 (11.1–53.8)	23.3 ± 6.5 (8.4–33.6)	$p = 0.983$
Mean months post-op at follow-up	20.4 ± 9.5 (8.1–33.9)	26.6 ± 9.6 (11.9–49.5)	$p = 0.043$
Recurrence of verruca	16.0%	22.2%	$p = 0.605$
Reported history of DM1	20.0%	11.1%	$p = 0.436$
Reported history of DM2	28.0%	44.4%	$p = 0.264$
Reported history of cancer	44.0%	44.4%	$p = 0.977$
Reported history of allergies	12.0%	16.7%	$p = 0.663$

**Table 2**

Fisher's exact test: associations between recurrence of verruca and predictor variables (N = 25 (implantation), N = 18 (no implantation)).

	All patients	Surgical removal and implantation	Surgical removal only
Recurrence and gender	p = 0.125	p = 0.288	p = 0.533
Recurrence and history of DM1	p = 0.597	p = 1.000	p = 0.405
Recurrence and history of DM2	p = 0.419	p = 0.548	p = 1.000
Recurrence and history of cancer	p = 1.000	p = 1.000	p = 1.000
Recurrence and history of allergies	p = 0.308	p = 0.422	p = 1.000

recurrence of verruca at the time of follow-up. In Group A, four out of 25 (16%) patients experienced recurrence of verruca at the time of follow-up. In Group B, four out of 18 patients (22.2%) experienced recurrence of verruca at the time of follow-up. In contrasting percent recurrence of verrucous lesions in each procedure, it was observed that the rate of recurrence was 6% higher in clinical cases with only surgical removal. However, statistical results indicated no significant association between recurrence and type of procedure ( $p = 0.701$ ). None of the patients from either group suffered a post-operative infection or wound healing problem.

#### 4. Discussion

Implantation of verruca plantaris to provoke an immune reaction is not well described in current medical literature. In 1980, Panacos et al. described use of graft implantation for auto-immunization against verruca plantaris [6]. Immunology studies have discovered lymphocytes and mononuclear phagocytes adjacent to keratinocytes infected with HPV, suggesting cell-mediated immunity plays a role in combating the virus [7]. It was believed that an autogenic graft could trigger an immune response, causing regression of HPV and eliminating clinical recurrence.

Panacos' approach was later modified with implantation of the verrucous tissue into the subcutaneous fascia of a predetermined recipient site on the contralateral foot. The implanted specimen was secured to the fascia in a non-weight bearing location via a 3–4 cm incision, typically posteromedial to the head of the first metatarsal. A 98.4% resolution rate was recorded; however, full documentation was only available for 23 of 62 patients. Of those 23 clinical cases reported, 22 patients achieved full resolution [8].

Nischal et al. published a more modern approach in 2012 with the aim of evaluating safety and efficacy of autoimplantation therapy. Their modified technique involved insertion of pared verruca tissue into the subcuticular layer of either the non-dominant forearm or upper anteromedial thigh. A micropore plaster was applied to the margins of the implantation site. At three months post-operative, 20 out of 35 patients showed complete resolution. Their method was believed to offer a less-traumatic therapy for resolution of verrucous lesions by eliminating a wound at the donor site [9].

Topical acids, cryotherapy, immunotherapy, and excision are historically well documented treatment strategies for pedal warts [10]. Although, a multitude of treatment strategies exist, concise recommendations based on outcomes data are relatively sparse. Of those available treatments, those most documented center around electro-surgical (pulsed dye laser therapy (PDL)) [11,12] and needling procedures [13]. PDL has been used successfully for approximately two

decades and has a reported success rate of 50–100% [11,12]. The mechanism of action centers around thermal necrosis of the warty tissue and subsequent debridement and destruction of that tissue. Needling, however, is a technique that employs controlled trauma to the wart tissue. It is believed that this evokes an inflammatory response that results in migration of immune cells to the local area and eventual cell mediated immune response to the virus. In 2017, Cunningham et al. demonstrated the effectiveness of this technique as compared to standard cryotherapy. Their results showed that needling was effective in reducing wart tissue by 64.7%.

Immunologic studies continue to emphasize the role of the immune system in resolution of verrucae. Normal, well-functioning immune systems demonstrate greater success with conventional verruca treatment, while solutions for patients with immune abnormalities continue to be sought [14]. Our study aimed to more thoroughly evaluate one of those solutions — a modified version of Panacos' original technique.

Based on the results of our investigation, the hypothesis was rejected. Implantation of a biopsied verrucous lesion into the abductor hallucis muscle belly in the contralateral foot has no effect on clinical recurrence rates when compared to only surgical removal. The authors observed a lower recurrence rate in the experimental group with implantation of the verrucous lesion; however, this decrease in recurrence was not statistically significant. Limitations to our investigation include inaccessibility to virology samples to confirm HPV, including strain verification, small patient population, and the inherent limitations to retrospective cohort studies. Improvements to our study's methodology include an increased patient population size, conducting a randomized prospective study, pathological analysis of lesions to confirm HPV virology and strain, detailed patient charting including Th1 and Th2 dominant conditions, family/patient history of verrucae, detailed comorbidities, treatments and medications, blood serial testing to identify lymphocyte count pre- and post-implantation, and HPV serologic testing to detect antibodies pre- and post-implantation.

Reasons for failure of this technique to evoke an immune response are not completely understood. In our patient population we evaluated those groups with possible immunological abnormalities (diabetes, cancers, and allergies) and found no association to treatment failure and medical comorbidities. Further research is necessary to determine implantation effectiveness in evoking an immune response and decreasing occurrence of verrucous lesions. The results of our investigation can be used as a model for the development of future randomized controlled trials focusing on implantation as a method of treatment for recalcitrant cases of verrucae plantaris.

**Table 3**

Wald statistic: associations between recurrence, age and BMI (N = 25 (implantation), N = 18 (no implantation)).

	All Patients	Surgical removal and implantation	Surgical removal only
Recurrence and age	p = 0.875	p = 0.573	p = 0.704
Recurrence and BMI	p = 0.888	p = 0.738	p = 0.501

The Wald test as it relates to logistic regression determines whether or not an independent variable (exposure, risk factor) statistically significantly predicts the outcome.

**Conflict of interest**

None reported.

**Financial disclosure**

None reported.

**References**

- [1] Bacelieri R, Marchese SE. Cutaneous warts: an evidence based approach to therapy. *Am Fam Phys* 2005;72:647–52.
- [2] VanHaalen FM, Bruggink SC, Gussekloo J. Warts in primary schoolchildren: prevalence and relation with environmental factors. *Br J Dermatol* 2009;161(1):148–52.
- [3] Plasencia JM. Cutaneous warts: diagnosis and treatment. *Prim Care* 2000;27(2):423–34.
- [4] Kwok CS, Gibbs S, Bennett C, Holland R, Abbot R. Topical treatments for cutaneous warts. *Cochrane Database Syst Rev* 2012;9. CD001781.
- [5] Stamuli E, Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, et al. Cost-effectiveness of cryotherapy versus salicylic acid for the treatment of plantar warts: economic evaluation alongside a randomized controlled trial. *J Foot Ankle Res* 2012;5:4.
- [6] Panacos N, Velarde H, Seinwill M. Surgical autoimmunization against verruca plantaris via autogenic graft of papilloma in situ. *Curr Podiatr* 1980:23–5.
- [7] Frazer I. Interaction of human papillomaviruses with the host immune system: a well evolved relationship. *Virology* 2009;384:410–4.
- [8] Romano M, Rex Jr. I, Belanger S. The Panacos graft: a surgical approach to verruca warts. *Podiatr Today* 1997;22:40–4.
- [9] Nischal KC, Sowmya CS, Swaroop MR, Dhruv PA, Basavaraj HB, Sathyanarayana BD. A novel modification of the autoimplantation therapy for the treatment of multiple, recurrent and palmoplantar warts. *J Cutaneous Aesthet Surg* 2012;5(1):26–9.
- [10] Powell J. Papillomavirus research and plantar warts. *Foot* 1998;8:26–32.
- [11] Bristow IR, Walker NPJ. Pulse dye laser treatment for plantar warts. *Foot* 1997;7:229–30.
- [12] Veitch D, Kravvas G, Al-Niaimi F. Pulsed dye laser therapy in the treatment of warts: a review of the literature. *Dermatol Surg* 2017;43(4):485–93.
- [13] Cunningham DJ, Brimage JT, Naraghi RN, Bower VM. Needling versus liquid nitrogen cryotherapy for the treatment of pedal warts: a randomized controlled pilot study. *JAPMA* 2014;104(4):394–401.
- [14] Goihman YM, Goldblum O. Immunotherapy and warts: a point of view. *Clin Dermatol* 2008;26:223–5.