Percutaneous Cryoablation for Treatment of Biopsy-proven Fibroadipose Vascular Anomaly

A Single-center Experience

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Abstract

Objective: To evaluate the clinical outcomes of patients with fibroadipose vascular anomaly (FAVA) treated via percutaneous cryoablation.

Design: A 14-month retrospective study identified patients (<21 years old) with biopsy-proven diagnoses of FAVA. Appropriate evaluation in the vascular anomalies clinic preceded imaging, biopsy, and ablation therapy. Studied parameters included postablation MRI findings, pain, motor function, and complications of ablation therapy.

Setting: A single, tertiary care pediatric hospital.

Patients: Nine patients (median 12 years, range 8–16 years; 8 females, 1 male) met inclusion criteria.

Interventions: Percutaneous cryoablation.

Primary Outcome Measurement: Clinical success of cryoablation, defined as improvement of patient symptoms, including pain, functional restriction, and swelling.

Results: Percutaneous biopsy demonstrated histological consistency with FAVA for all lesions. All patients underwent technically successful cryoablation therapy. One patient required repeat ablation. Symptoms resolved in 5 patients and improved in 4 patients. There were 5 minor complications and no major complications.

Conclusions: These findings further validate previously published cohorts and demonstrate that percutaneous cryoablation is a potentially efficacious treatment option for FAVA with a favorable safety profile.

Keywords: Fibroadipose vascular anomaly, Percutaneous cryoablation, Sclerotherapy, Venous malformation

Introduction

Fibroadipose vascular anomaly (FAVA) is a recently described vascular malformation with few case series describing its clinical course in children and adolescents. It is characterized by infiltration of dense fibrous and fatty tissue within skeletal muscle, most commonly involving a single limb. Accompanying pain is multifactorial and can present as persistent, focal, and neurogenic. The replacement of normal muscle tissue with fibroadipose tissue compromises muscular function and may ultimately result in painful flexion contracture in the affected limb. Fibrofatty infiltration around the muscle’s neurovascular supply can cause perineural fibrosis and subsequent ischemic stress in nerve fibers. Because of the overlapping clinical appearance with low-flow vascular malformations, FAVA is commonly misdiagnosed and subsequently treated with ineffective therapies.

Image-guided percutaneous cryoablation demonstrates favorable outcomes in the treatment of multiple malignancies and benign lesions involving major visceras and musculoskeletal soft tissues, and may serve as an efficacious minimally invasive treatment option for patients with FAVA. One prior, single-institution case series showed that cryoablation significantly lowered average pain scores and improved pain interference from preprocedure to 1-month follow-up in patients presenting with FAVA lesions. Only one other single-institution, case series of 5 patients with FAVA suggested that cryoablation may be an efficacious therapy for this entity.
The objective of this retrospective study is to add to the limited existing literature about FAVA by describing the presentation, diagnostic work-up, and treatment outcomes of pediatric and adolescent patients with pathologically proven FAVA treated via percutaneous cryoablation at a single, multidisciplinary, vascular anomalies center.

Materials and methods
A retrospective review, following institutional review board approval, identified 9 patients from August 2018 to December 2019 who were diagnosed with FAVA at a multidisciplinary vascular anomalies center. All research was conducted in accordance with the Declaration of the World Medical Association. Inclusion criteria were patients <21 years old who were diagnosed with FAVA via percutaneous or surgical biopsy and had available clinical, radiologic, and histopathologic data.

Preprocedural assessment
Patients were referred from primary care (most commonly general pediatric practice), orthopedics, and general surgery practices. They most commonly presented with an existing diagnosis of venous or low-flow vascular malformation. All patients had preprocedural, contrast-enhanced MRI of the affected body region. The MRI provided characterization of lesion borders (well-defined versus ill-defined), distribution, signal characteristics, pattern of contrast enhancement (homogenous vs. heterogenous), and adjacent neurovascular structures (Figure 1). All biopsy samples supplied histologic confirmation of FAVA (Figure 2). Biopsy specimens were obtained before cryoablation, either during a prior procedure or during the ablation session before cryoprobe placement. If the histologic diagnosis was not available from a prior procedure, a preliminary histologic diagnosis was obtained from a frozen tissue sample sent for immediate pathology review at the beginning of the ablation procedure.

Procedural technique
Before cryoablation, our team reviewed all available patient imaging to determine the precise location and extent of the lesion. Written informed consent was obtained on all patients, and all procedures were performed under general anesthesia. When appropriate, the hospital’s pain team administered a nerve block to reduce immediate postprocedural pain. Neurophysiologic monitoring was used in 2 patients to help monitor motor-evoked potentials and somatosensory-evoked potentials of nearby nerves. Ultrasound was used to confirm lesion borders during the procedure and guide cryoprobe placement. An argon gas only–based cryoablation system (Galil/Boston Scientific, Marlborough, Massachusetts) was used to generate the ice ball. Multiple probes (15G and 17G) were often used in various configurations to cover the lesion in its entirety. Two 10-minute freeze cycles and two 5-minute active thaw cycles were employed for all lesions. Passive thaw was not performed. Figure 3 shows typical intraprocedural images obtained during cryoablation. A sterile glove filled with warm saline was placed on the overlying skin to help prevent thermal injury. The freeze cycle was stopped if there were any signs of skin blanching or blunting/loss of motor-evoked potentials of adjacent nerves.

Postintervention
Patients returned to vascular anomalies clinic for follow-up 1 month after cryoablation. Those with persistent pain underwent postprocedural MRIs and additional clinical follow-up when appropriate.

Outcomes
The primary outcome for this study was clinical success of percutaneous cryoablation, defined as resolution or improvement of symptoms. Symptoms included pain with palpation, pain with activity, and functional restriction. The secondary outcome was the technical success of ablation procedure, defined as the ability to localize the probe within the lesion and cover the entire lesion with the ablation zone. Major and minor complications were recorded.11

Results
Patient demographics
Nine patients with pathologically proven FAVA underwent percutaneous cryoablation during the study period. Mean patient age was 11.8 years (range: 8–16 years), and gender distribution was 8 females and 1 male.

Presenting clinical symptoms
The most common referring diagnosis was venous malformation (N = 7). Two patients were identified as having FAVA at presentation. All patients exhibited constant pain with activity (N = 9) and pain with palpation. No patients had paresthesia. The most common location of FAVA was in calf musculature (N = 5) with 3 patients demonstrating

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**Figure 1.** MRI appearance of FAVA: A, Axial T2-weighted MRI of a 12-year-old woman showing a heterogenous, intramuscular mass in the medial head of the gastrocnemius muscle (red dashed arrow). B, Axial T1-weighted MRI without fat saturation showing intralesional fat content (red arrow). C, Axial T1-weighted MRI postcontrast showing avid enhancement of the lesion, typical in FAVAs. FAVA, fibroadipose vascular anomaly; MRI, magnetic resonance imaging.
lesion infiltration in the medial head of the gastrocnemius, 1 patient with infiltration in the lateral soleus and lateral head of the gastrocnemius, and 1 patient with infiltration localized to the distal soleus. Patients also presented with FAVA in the quadriceps (N = 3) and paralumbar/parasacral musculature (N = 1), specifically the iliocostalis lumborum. Four (4/5) patients with calf lesions presented with flexion contractures, toe-walking, moderate to severe muscle atrophy, and inability to dorsiflex actively or passively. Two patients exhibited superficial discoloration, such as that commonly seen with congenital venous malformations. Table 1 lists all presenting clinical symptoms, previous treatments, and imaging findings.

**Previous treatment**

Seven patients underwent sotradecol sclerotherapy before cryoablation. These patients received an average of 2 treatments (range: 2–5 treatments). After sclerotherapy, all patients demonstrated either worsening pain or lack of symptom improvement. Due to either failure of sclerotherapy (N = 7) or high suspicion for FAVA at presentation (N = 2), percutaneous biopsy was performed for all lesions (N = 9).

**Procedure-related outcomes**

Technical success = 100%. The average number of cryoprobes used per procedure = 3 (range: 1–5). The average procedure time = 56.7 minutes (range: 47–75).

**Postablation clinical course**

Patients returned to clinic for follow-up 1 month after cryoablation. Average follow-up was 9 months (range: 1–14 months). Six patients had resolved or improved pain. Three patients exhibited persistent pain that warranted follow-up MRIs (N = 3). One patient required repeat ablation 6 months following initial ablation. Symptoms ultimately resolved in 5 patients and were improved in 4 patients. In the 4 patients with improved pain, the pain was not activity-limiting and was deemed insignificant by the patients. These patients demonstrated marked satisfaction in their reduction in pain and swelling and did not seek further treatment. Of the 4 patients who presented with flexion contractures, 3 patients required surgical repair for persistent toe-walking after ablation with resolution of toe-walking. One of these 3 patients had surgical repair prior to referral for treatment of the FAVA. One patient had resolution of flexion contracture.

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**Figure 2.** Histopathologic appearance of FAVA. The core needle biopsy, all shown at 100X magnification, demonstrated extensive dense fibrous tissue (black arrows, A), fat (black arrows, B) and abnormal vessels (green arrows, B) infiltrating bundles of skeletal muscle (black arrows, C). The skeletal muscle showed atrophy. There were vascular clusters consisting of thin-walled back-to-back blood-filled sacs (stars, C), these clusters were surrounded by lymphocytic aggregates (green arrows, C). The abnormal vessels were composed of large and irregular malformed vessels with muscularized walls, thin-walled vessels lacked smooth muscle, mimicking pulmonary alveoli and lymphatic channels highlighted by D2-40 immunohistochemistry stain (black arrows, D).

**Figure 3.** Sonographic appearance of cryoablation: A, Grayscale ultrasound showing an intramuscular heterogeneously echoic, intramuscular mass (red arrows). B, Growing ice-ball (red arrows) with characteristic posterior acoustic shadowing. C, Full-expansion of the ice ball (red arrows) following two 10-minute ablation cycles showing complete coverage of the lesion.
### Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Clinical History</th>
<th>Location of Lesion</th>
<th>Physical Examination Findings</th>
<th>Previous Sclerotherapy Treatment</th>
<th>Initial Diagnosis</th>
<th>Preablative MRI Findings</th>
<th>Postablative MRI Findings</th>
<th>Post-Ablation Symptoms</th>
<th>Other Therapies</th>
<th>Complications</th>
<th>Length of Follow Up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>Right back pain with pain radiating down right leg, worse with standing or increased activity</td>
<td>Right iliocostalis lumborum (5, 5, 5, 5)</td>
<td>Tender to palpation, no discoloration, very deep mass</td>
<td>No</td>
<td>FAVA</td>
<td>Intramuscular, approximately 20% adipose tissue, overlying edema present</td>
<td>None</td>
<td>Pain improved, no significant pain on standing or increased activity, no reported tenderness, patient resumed normal activity with full functional mobility</td>
<td>None</td>
<td>None</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>Pain for 5 mo in RLE, pain became worse after sclerotherapy</td>
<td>Right lateral soleus and lateral head of gastrocnemius</td>
<td>Tender to palpation, palpable mass, no discoloration, toe-walking</td>
<td>Yes (2 STS sclerotherapies)</td>
<td>WM</td>
<td>Intramuscular, approximately 20% adipose tissue, mild surrounding edema, predominantly vessels and fibrous tissue (3.9 x 3.8 x 3 cm)</td>
<td>3 mo MRI—decreased involvement/enhancement, 6 mo MRI—continued decreased involvement, persistent area of enhancement along medial border requiring additional cryoablation (6.4 x 1.1 x 1.1 cm; 92% reduction in volume)</td>
<td>Pain improved, then recurred, toe-walking and pain while walking improved after tendonotomy and PT, patient regained full functional mobility</td>
<td>PT and right heel triple cut tenotomy</td>
<td>None</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>Pain for 6 mo in RLE, treated with ibuprofen; pain became worse after sclerotherapy</td>
<td>Right medial head of gastrocnemius</td>
<td>Tender to palpation, palpable mass, no discoloration, toe-walking</td>
<td>Yes (3 STS sclerotherapies)</td>
<td>WM</td>
<td>Intramuscular, approximately 25% adipose tissue, mild surrounding edema, predominantly vascular, (11.2 x 5.6 x 2.6 cm)</td>
<td>Pain improved, no significant pain while walking or increased activity, numbness at skin injury, persistent toe-walking corrected by tenotomy</td>
<td>Right heel triple cut tenotomy</td>
<td>Skin ulceration, blanching during the second freeze cycle, given course of antibiotics, healed without complication; transient numbness</td>
<td>None</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>Right ankle pain and swelling after dancing, pain improved but recurred after first two sclerotherapy treatments and became worse after third treatment</td>
<td>Right distal soleus</td>
<td>No pain to palpation, bluish palpable lump</td>
<td>Yes (5 STS sclerotherapies)</td>
<td>WM</td>
<td>Superficial, approximately 33% adipose tissue, soft tissue fibrosis located in superficial subcutaneous soft tissues Intramuscular serpiginous, enhancing venous structures with surrounding fat (approximately 10% adipose tissue)</td>
<td>None</td>
<td>Pain resolved, transient numbness in lateral ankle</td>
<td>None</td>
<td>Transient numbness</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>Pain progressed over 2 y and continued after first sclerotherapy treatment, pain is worse with walking and standing, atrophy of calf and contracture of Achilles tendon tenotomy procedure performed before discovery of the vascular malformation</td>
<td>Right medial head of gastrocnemius</td>
<td>Nontender to palpation, blue/purple discoloration, atrophy of right gastrocnemius, flexion contracture</td>
<td>Yes (1 STS sclerotherapy)</td>
<td>WM</td>
<td>Intramuscular, approximately 5% adipose tissue, predominantly vascular, surrounding edema</td>
<td>None</td>
<td>Pain resolved</td>
<td>PT</td>
<td>None</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>Left thigh mass biopsied by ortho, referred to VAC</td>
<td>Left thigh, rectus femoris</td>
<td>Tender, firm, no discoloration, palpable lump</td>
<td>No</td>
<td>Venous Malformation</td>
<td>Intramuscular, approximately 25% adipose tissue, predominantly vascular, moderate surrounding edema</td>
<td>None</td>
<td>Pain improved but still tender to palpation with mild swelling, patient is able to walk and run, residual symptoms resolved at 6 mo follow-up</td>
<td>Achilles tendon lengthening procedure</td>
<td>Transient numbness</td>
<td>10</td>
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<tr>
<td>7</td>
<td>12</td>
<td>1 y history of worsening left leg pain, worse with activity, toe walking; no pain improvement after sclerotherapy treatment</td>
<td>Left gastrocnemius medial head</td>
<td>Decreased strength, unable to dorsiflex foot past 25°; soft, tender to palpation, no discoloration, palpable lump, toe walking</td>
<td>Yes (2 STS sclerotherapies)</td>
<td>WM</td>
<td>Intramuscular, approximately 5% adipose tissue, predominantly vascular, surrounding edema</td>
<td>None</td>
<td>Pain resolved, transient numbness over anterolateral ankle, no motor deficits, persistent toe walking</td>
<td>None</td>
<td>None</td>
<td>9</td>
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<td>8</td>
<td>12</td>
<td>RLE pain for 2.5 y, suffered trauma to area since that time, swelling and pain with use, pain relieved with rest</td>
<td>Right thigh rectus femoris</td>
<td>Nontender, palpable lump, soft</td>
<td>Yes (1 STS sclerotherapy)</td>
<td>WM</td>
<td>Intramuscular and subcutaneous, approximately 10% adipose tissue, extensive surrounding edema</td>
<td>8 mo MRI—smaller size, less enhancement (8.4 x 3.2 x 1.4 cm; 18% reduction in volume)</td>
<td>Pain improved, patient reported mild pain with tenderness to palpation, no limitations to walking or activities of daily living, moderate persistent swelling (improved with PT)</td>
<td>PT</td>
<td>Small blistering in the mid portion of the lesion, healed with no permanent skin injury</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>1 y history of pain, worse with increased activity, pain worsened after sclerotherapy</td>
<td>Left thigh vastus lateralis</td>
<td>Palpable mass, tender to palpation</td>
<td>Yes (2 STS sclerotherapies)</td>
<td>WM</td>
<td>Intramuscular and subcutaneous, approximately 10% adipose tissue, predominantly fibrous tissue, (8.6 x 3.7 x 1.4 cm)</td>
<td>Pain resolved with activity, only minimal residual pain w/ palpation along the inferior most component</td>
<td>None</td>
<td>None</td>
<td>9</td>
<td></td>
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</tbody>
</table>

**Abbreviations:** FAVA, fibroadipose vascular anomaly; PT, physical therapy; RLE, right lower extremity; STS, sodium tetradecyl sulfate; US, ultrasound; VAC, vascular anomalies clinic; VM, vascular malformation.
with cryoablation, alone. All patients regained full functional mobility and successfully returned to hobbies and activities without limiting pain. Four patients had minor complications from cryoablation, all of which resolved (skin blistering = 1, skin ulceration + transient numbness = 1, transient numbness = 3). There were no major complications.

Discussion

FAVA is a recently described complex vascular anomaly that significantly affects the quality of life of children and adolescents. Although improved recognition of its presenting symptoms, it is often misdiagnosed as a tumor, rheumatological disorder, or a low-flow vascular anomaly, resulting in delayed diagnosis and ineffective. When appropriately diagnosed, a number of therapeutic options for FAVA have been published including surgical resection, oral medication, and sclerotherapy; although no option has been shown to be superior to another.

Multiple therapeutic options have been published for the treatment of FAVA. Alomari et al. postulated that sclerotherapy and surgical excision serve as efficacious treatment options to manage the complex symptomatology of FAVA. However, the solid, fibrofatty component of FAVA often limits the effectiveness of sclerotherapy treatments as sclerotherapy targets just the vascular portion of the lesion. Consequently, patients often experience recurrent pain and continual motor dysfunction following sclerotherapy. Surgical excision, in addition to requiring a longer recovery and its association with higher risks, can be difficult due to the depth of involvement of the lesion and its diffuse and infiltrative, intramuscular growth pattern. Incomplete lesion resection and lesion recurrence are common outcomes that further complicate the treatment of FAVA. Noninvasive treatment options for treatment of FAVA include oral sirolimus, as this lesion has been shown to result from a somatic activating mutation in PIK3CA. However, oral sirolimus requires regular serologic monitoring, and duration of treatment is unclear.

This retrospective study corroborates previously published cohorts on the typical presentation of FAVA and further supports existing literature suggesting that percutaneous cryoablation is an efficacious, minimally invasive treatment option. In this cohort, 8 of 9 patients were young females who presented with constant pain aggravated by palpation. Muscular involvement was most commonly localized to the gastrocnemius muscle, resulting in flexion contracture and a firm, exquisitely tender mass. This is in contrast to the clinical presentation of spongiform venous malformations (VMs). VMs most often present as asymptomatic or with episodic pain triggered by microthrombosis, engorgement, and exertional exercise. VMs show less severe functional impairment, demonstrate no sex predilection, and favor the quadriceps and intrinsic muscles of the foot when localized to the lower extremity. By identifying these discrepancies in clinical presentation, physicians may be able to more adeptly diagnose and treat patients with FAVA.

Importantly, 7 patients in our study had lesions initially diagnosed as venous malformations, leading to treatment with sclerotherapy. Subsequently, patients who received sclerotherapy exhibited either worsening pain or a lack of symptom improvement. This is most likely due to the significant fibrofatty involvement that makes FAVA less responsive to sclerotherapy. This supports multiple previously published studies that have demonstrated sclerotherapy alone is ineffective in relieving symptoms of FAVA.

Percutaneous cryoablation has been suggested to be a relatively safe and minimally invasive treatment option for symptomatic FAVA lesions in pediatric patients. Cryoablation has the ability to treat both pain derived from inflamed-fibrofatty tissue and neuropathic pain. Additionally, cryoablation permits the visualization of the ice ball with real-time imaging, thereby confirming coverage of the entire lesion and potentially preventing injury to adjacent structures. While previous studies have evaluated the efficacy of cryoablation therapy as a treatment option for vascular anomalies, this retrospective study supports prior literature that demonstrates percutaneous cryoablation as an efficacious therapy as an alternative treatment option for FAVA. Shaikh et al. treated a young patient cohort (mean age 15.8 years) with cryoablation and demonstrated an improvement in all aspects of pain, including pain now, pain in the last 24 hours, and pain interference on everyday social life. Although pain was less rigorously assessed, our study similar found cryoablation therapy was able to resolve pain symptoms in 5 of our patients and improve symptoms in the other 4 patients. Because patients who presented with flexion contractures required surgical repair and subsequent physical therapy, treatment of FAVA should remain a multidisciplinary approach to achieve optimal results for patients.

There are several limitations to this study. Because of the relatively low incidence of FAVA, our retrospective study consisted of a small number of patients, thereby limiting the ability to truly assess the significance of the improved clinical parameters as a result of cryoablation. Many patients underwent prior sclerotherapy, which may have affected the overall success of subsequent cryoablation treatment. Additionally, some patients underwent additional therapy, such as Achilles tendon lengthening and physical therapy, which limit the ability to attribute clinical improvement solely to cryoablation. Additionally, as with other vascular anomalies, the rate of recurrence of FAVA is largely unknown. Thus, the clinical follow-up time in this study likely underestimates rates of recurrence of this vascular anomaly. Last, as the suspected diagnosis changed in a number of patients throughout their clinical course, no formal pain measurement index was used to assess preprocedure and postprocedure pain. Moving forward, as the vascular anomaly community continues to improve the recognition and diagnosis of FAVA, formal pain measurement indices may be helpful in comparing the efficacy of different therapies.

Conclusion

Percutaneous cryoablation appears to be a safe and efficacious treatment option for FAVA lesions in pediatric and adolescent patients. Additional studies with larger cohorts that aim to further evaluate the diagnostic work-up of FAVA and efficacy and safety of percutaneous cryoablation are warranted.

Acknowledgments

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References


