Atypical Causes of Exertional Leg Pain: Vascular

Kevin Cohoon, D.O., MSc
Assistant Professor of Medicine
DISCLOSURE

Relevant Financial Relationship(s)
None

Off Label Usage
None
Learning Objectives

- Identify and recognize the pathology and types of atypical causes of exertional leg pain.
- Evaluate the vascular territories affected by atypical causes of exertional leg pain.
- Understand how to assess and treat atypical causes of exertional leg pain according to the vascular territory affected.
Exertional Leg Pain

Atypical Causes

- Extrinsic
- Intrinsic
- Intraluminal
Atypical Exertional Leg Pain

Extrinsic Causes

- Popliteal Artery Entrapment
- Popliteal Vein Compression
- May-Thurner Syndrome
- IVC occlusion
- Hematoma
- Cystic adventitial disease
- Retroperitoneal Fibrosis
- Lymphoma
Popliteal Artery Entrapment (Extrinsic Leg Pain)

**Definition**

- Results in *extrinsic arterial compression* (failed embryonic regression)
- Reported in 3.5% of autopsy cases
- Repetitive insult causes arterial damage and can lead to:

  - Aneurysm; Premature atherosclerosis; Arterial thrombosis with distal embolization.
Popliteal Artery Entrapment (Extrinsic Leg Pain)

Etiology and Symptoms

- Mean age 35 years (range 16 - 55yrs)
- Equal gender
- Symptoms at presentation

- Typical claudication 80%
- Severe ischemia 20%
- Venous entrapment 10%

Angiography Provocative Maneuvers

Popliteal Artery Entrapment (Extrinsic Leg Pain)

Anatomic Variants

MRI very helpful to define anatomic variants

Popliteal Artery Entrapment (Extrinsic Leg Pain)

Diagnostic Evaluation

<table>
<thead>
<tr>
<th>Arm B/P</th>
<th>Right</th>
<th>Systolic</th>
<th>Index</th>
<th>Left</th>
<th>Systolic</th>
<th>Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>162 / 50</td>
<td>PT-Dorsiflexion</td>
<td>132</td>
<td>0.81</td>
<td>112</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PT-Plantarflexion</td>
<td>134</td>
<td>0.83</td>
<td>118</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DP-Dorsiflexion</td>
<td>130</td>
<td>0.80</td>
<td>108</td>
<td>0.67</td>
<td></td>
</tr>
</tbody>
</table>

Doppler

Segmental BP

Ankle/Brachial Index 1.00

Rt Pop Art Distal w/Plantar Flexion

Lt Pop Art Distal w/Plantar Flexion

MCR - Vasc Center Rm 3
08/22/16 10:21:13AM CAK
LEA 14

MCR - Vasc Center Rm 3
08/22/16 10:33:49AM CAK
LEA 13

©2016 MFMER | 3537671-9
Popliteal Artery Entrapment (Extrinsic Leg Pain)

Diagnostic Evaluation

Magnetic Resonance
Neutral Position

Magnetic Resonance
Plantar Flexion

Angiography ± Provocative Maneuvers
Popliteal Artery Entrapment (Extrinsic Leg Pain)

Treatment

Surgical

• Opening the narrowed section of the artery

Resection of right medial head of the gastrocnemius
Popliteal Vein Compression (Extrinsic Leg Pain)

Etiology and Symptoms

Reported in: ~27% of healthy individuals

Symptoms at presentation:
• Chronic Venous insufficiency
• Deep venous thrombosis
• Edema and Pain

Venous Compression can be from:

- Aneurysmal popliteal artery
- Popliteal cysts
- Popliteus muscle sling
- Adjacent fibrous band

Br J Radiol. 2013 Oct; 86(1030)
Popliteal Vein Entrapment (Extrinsic Leg Pain)

Diagnostics and Treatment

MR Venogram before /after surgical release: medial head of the gastrocnemius muscle

Treatment

Compression Stockings
Resection of anatomical etiology
Anticoagulation for DVT

? Cause for Increased Compartment Pressures
Chronic Exertional Compartment Syndrome
May-Thurner Syndrome (Extrinsic Leg Pain)

Etiology and Demographic

- Left Iliac vein is compressed by right Iliac artery
- Most often diagnosed in individuals:
  - 20–50 years of age.

CT scan & Venogram Left Iliac Vein with Balloon
May-Thurner Syndrome (Extrinsic Leg Pain)

Symptoms and Treatment

Many asymptomatic

Left Leg Pain is Associated with:

- Unprovoked left iliofemoral DVT (Caution: PFO ~33%)
- Chronic venous insufficiency

Treatment:

Venoplasty ± Stenting
Anticoagulation for DVT
Retroperitoneal Fibrosis (Extrinsic Leg Pain)

Etiology and Demographic

- Rare inflammatory fibrotic process involving both medium and large sized vessels
- Incidence: 1.38 cases per 100,000 people
- Most often diagnosed in:
  - Mean 57 years of age.
  - Male to female ratio: 1.6:1.0

Circumferential encasement of aorta

Retroperitoneal Fibrosis (Extrinsic Leg Pain)

Morbidity

- Ureteric obstruction and renal failure
- Venous hypertension and insufficiency

Circumferential encasement of aorta and vena cava
Right hydronephrosis

Left Leg Wound from Venous HTN and Insufficiency

Retroperitoneal Fibrosis (Extrinsic Leg Pain)

**Treatment**

- **Medical:** Corticosteroid, methotrexate, cyclophosphamide, and azathioprine

- **Surgical/Endovascular:**
  - Prevent rupture or causing organ complications (renal failure)

> MR of lower thoracic and abdominal aorta.

F18-Fluorodeoxyglucose PET (coronal view) uptake in the ascending and abdominal aorta.

Retroperitoneal Fibrosis (Extrinsic Leg Pain)

Treatment

Endovascular: Inferior Vena Cava or Left Iliac Venoplasty ± Stent

Left Leg Wound from Venous HTN
Venogram with narrow IVC and left Iliac vein
Balloon Venoplasty to IVC and left Iliac vein
Healing Leg Wound 2 months later

Atypical Exertional Leg Pain

Intrinsic Causes

- External Iliac Artery Endofibrosis
- Fibromuscular Dysplasia
- Buerger’s Disease
- Takayasu Arteritis
- Iliac Artery Vasospasm
- Coarctation
- Aneurysm
- Early Atherosclerosis
- Early Atherosclerosis
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Clinical Features

- Male predominance
- Average age 25 years
  - 15% professional
  - 48% top amateur
- Ride 8 – 35,000 km/year
- Long-distance runners
- Rugby players and body-builders

Tour de France
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Clinical Features

- External iliac artery (90%)
  - Left leg predominance
  - Bilateral 15%

- Symptoms in legs:
  Claudication (1st sx): 100% F, 90% M

Others: contractures (25%), swelling (20%), palsy (10%), numbness (5%), and fatigue (2%)
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Pathophysiology

Wall stress due to body position
- Repetitive hyperflexion of thigh
- Prominent bending of external iliac artery

Wall stress due to arterial anatomy
- Proximal fixation at aortic bifurcation
- Distal fixation by taut inguinal ligament
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Non-Invasive Arterial Lower Extremity Studies

Doppler

- Femoral: Biphasic
  - Gain %: 25

- Sup Femoral: Biphasic
  - Gain %: 24

- Popliteal: Biphasic
  - Gain %: 36

- Post Tibial: Biphasic
  - Gain %: 65

- Dors. Pedis: Biphasic
  - Gain %: 74

- Post Ex Femoral Monophasic
  - Gain %: 18

- Ankle/Brachial Index: 0.90

- Segments:
  - Brachial: 148
  - Femoral: 144
  - 121 (PT) 123 (DsP)

R) Femoral: Biphasic

Gain %: 25

R) Post Ex Femoral Monophasic

Gain %: 18
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Pathological Features

Histopathologic features %

- Wall thickening * 100
- Intimal hyperplasia 80
- Adventitial hyperplasia 80
- Medial hypertrophy 60
- Luminal thrombus 40

* Symmetric (60%), asymmetric (40%)

Intimal Hyperplasia

Microscopy (VVG, Low-Power)

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Pathological Features

Adventitial Hyperplasia 80%

Gross Specimen (Cross-Sections)

Microscopy (VVG, Low-Power)

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Pathological Features

Eccentric Wall Thickening

Gross Specimen (Cross-Sections)

- Intima
- Media
- Adventitia

Microscopy (VVG, Low-Power)

- Lumen

Concentric Wall Thickening

Gross Specimen (Cross-Sections)

- Intima
- Media
- Adventitia

Microscopy (VVG, Low-Power)

- Lumen

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Pathological Features

Luminal Thrombosis

Gross Specimen (Cross-Sections)

Microscopy (H&E, Low-Power)

Stenosis

Thrombosis

Thrombus

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Pathological Features

Post Angioplasty Restonsis

Microscopy (VVG, Low & Medium Power)

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Iliac Artery Endofibrosis (Intrinsic Leg Pain)

Treatment

**Medical**
- Modify aggravating activities/intensity, avoiding repetitive hip flexion.
- Calcium channel blockers (rarely effective)

**Resection**
- Segmental resection of stenotic artery
- Release of inguinal ligament from artery

**Bypass**
- End-to-end tube graft
- ↓ restenosis and pseudoaneurysm
- 77% symptom-free and perform at desired activity.

Gross Specimen

Iliac Artery Vasospasm (Intrinsic Leg Pain)

Clinical and Diagnostics

- Similar to Iliac Artery endofibrosis.
  - Femoral bruit not present at rest

- External iliac artery involvement

- Symptoms
  - Exercise induced thigh or calf claudication

Right Iliac Vasospasm

Angiography Iliac Artery
Iliac Artery Vasospasm (Intrinsic Leg Pain)

Diagnostics

Pre-Exercise

Post-Exercise

Angiography Iliac Artery

Right Iliac Vasospasm
Iliac Artery Vasospasm (Intrinsic Leg Pain)

Treatment & Surgical Procedures

Medical
• Modify aggravating activities, avoiding repetitive hip flexion, decreasing exercise intensity.
• Calcium channel blockers (rarely effective)

Resection
• external iliac artery patch angioplasty (endarterectomy and saphenous vein patch)
Coarctation (Intrinsic Leg Pain)

**Etiology and Symptoms**

- Narrowing descending aorta, typically located at insertion of ductus arteriosus distal to left subclavian.
- Accounts: 4-6% of all congenital heart defects.
- Prevalence: 4 per 10,000
- Symptoms: “radial-femoral delay”; HTN; Claudication

**Gross Specimen (Cross-Sections)**

Courtesy of Dr. Maleszewski/Dr. Edwards, Mayo Clinic
Coarctation (Intrinsic Leg Pain)

**Associated Conditions:**
- Bicuspid aortic valve, VSD, intracranial aneurysm, Patent ductus arteriosus, Turner's syndrome

**Left untreated,** severe coarctation may lead to heart failure and premature death.

**Treatment:** Surgical or percutaneous treatment (gradient >20mmHg)
Coarctation: Abdominal (Intrinsic Leg Pain)

Conditions and Treatment
Coarctation: Abdominal (Intrinsic Leg Pain)

Treatment

CT Angiography Reconstruction

Right Axillary Artery to Right Femoral and Right to Left femoral-femoral Crossover Bypass

Descending Thoracic Aorta to Infrarenal Aorta Bypass Graft. Graft from Infrarenal to SMA.

ABI: 0.63  0.60
ABI: 0.95  0.90
ABI: 1.06  1.07
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Definition

- Non-atherosclerotic, non-inflammatory arterial disease
- Affects medium-sized arteries.
- Most often diagnosed in individuals aged: 15–70 years of age. Reported from infancy to 89 years of age.

Angiography Iliac Artery

Circulation 2012; 125: 3182-3190
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Definition

Associated with stenosis, aneurysms, dissections, and/or occlusion of arteries.
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Etiology

- The cause of FMD is unknown.
- Female predominance

Female to male ratio is ~4.5-9 to 1
Epidemiology

Diagnosed more often in whites and less frequently in Hispanic and Asian populations.

95% Whites
2% Blacks
1% Hispanic or Asians
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Vascular Territories Affected

Any Median-Sized Artery Can Be Affected
Median Vascular Territories Affected = 1.8±1 (max: 7)

- Renal: 75%
- Extracranial Carotid: 73%
- Lower extremity: 60%
- Vertebral: 33%
- Mesenteric: 22%
- Intracranial: 17%
- Upper extremity: 16%

Circulation. 2012; 125: 3182-3190
J Am Coll Cardiol. 2013; 61 (10_S)
Three main types of dysplasia and histologically are classified according to the arterial wall layer affected by collagen deposition:

- **Medial dysplasia** (accounts ~80%)
- **Intimal dysplasia** (accounts ~10%)
- **Adventitial dysplasia** (very uncommon)
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Histology Classifications: Pathology and Types

- Medial dysplasia (accounts ~80%)
  - Medial fibroplasia (~75%)
    - Media: thin (aneurysmal) & thick (excess collagen) areas
  - Perimedial fibroplasia (~5-10%)
    - Excess collagen deposition in outer half (causes stenosis).
- Medial hyperplasia (rare)
  - Smooth muscle cell hyperplasia without fibrosis.

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Current Opinions in Rheumatology 2000, 12:41-47
Multifocal type of FMD ("string of beads") is most common medial type (68%–91%).

- Alternating thinned medial wall layer with thickened fibromuscular ridges containing collagen.
Symptoms of claudication, emboli, femoral or abdominal bruit, ~60% with external iliac arteries affected.

Lesions below the inguinal ligament are uncommon.

Leg Pain
- Aneurysm
- Dissections
Fibromuscular Dysplasia (Intrinsic Leg Pain)

What about Dissections and Aneurysms?

Dissections

Aneurysms

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Patients with dissection:
18.5% had >1 vessel (max: 3)

Patients with aneurysm:
17.3% had >1 vessel (max: 4)
Fibromuscular Dysplasia (Intrinsic Leg Pain)

Diagnostic Modalities

- Duplex Ultrasound
- Computed Tomography Angiography
- Conventional Angiography
- Magnetic Resonance Angiography
Fibromuscular Dysplasia (Intrinsic Leg Pain)

When to Consider FMD

Onset of HTN at 35 years of age

- Severe and recurrent headaches, migraine type
- Dissection of a peripheral artery
- Pulsatile tinnitus (swooshing or whooshing)
- Cervical bruit in a patient <60 years without CV risk factors.

Resistant HTN

Epigastric bruit and high blood pressure

Circulation. 2012; 125: 3182-3190
James Fuller "Jim" Fixx

• Authored the 1977 best-selling book *The Complete Book of Running*.

• Died at age 52 of a *fulminant heart attack*.
Atherosclerosis (Intrinsic Leg Pain)

Early Atherosclerosis

CT Angiography: Atherosclerosis of Left Renal, Aorta, Left Iliac Artery

Aortic Atherosclerosis with Atheroemboli to Kidneys

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Vasculitis (Intrinsic Leg Pain)

Takayasu Arteritis

Elevated Inflammatory Markers

Onset

18 months rx

ABI: 0.74  0.67

ABI: 1.1  1.19


Kermani TA, Warrington KJ. Vasc Med. 2010;15:135

Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Atypical Exertional Leg Pain

Intraluminal Causes

- Deep Vein Thrombosis
- Venous insufficiency
- Embolic Disease
- Performance Enhancing Drugs
- Ateriovenous malformations
- Blood Doping
- Anemia
Deep Vein Thrombosis (Intraluminal Leg Pain)

**Etiology**

- Rare; **potentially devastating** if not recognized/treated
- 500,000 VTE events per year
- Study of 243 high school/college football deaths, PE was cause in 2.1%
- **Virchow’s triad:** venous stasis, endothelial damage, hypercoagulability


Courtesy of Dr. Maleszewski/ Dr. Edwards, Mayo Clinic
Deep Vein Thrombosis (Intraluminal Leg Pain)

Etiology and Treatment

Risk Factors:
- Training in high altitude, blood doping, dehydration
- Repetitive microtrauma during endurance sports or collisions.
- Factor V Leiden, prothrombin 20210A mutation (50-60% of cases), antithrombin III, protein C/S deficiency, Lupus anticoagulant
- Oral contraceptives (5x increased risk)

Treatment: Underlying cause and Anticoagulation

Courtesy of Dr. Maleszewski/Dr. Edwards, Mayo Clinic
BMJ. 2009;339:b2921
Performance Enhancing Drugs (Intrinsic Leg Pain)

Types and Affects to Lower Extremities

- Reported use in 5-31% of athletes
- Erythropoietin (EPO): Thromboembolic events
- Growth Hormones: Edema, Arthralgia, Myalgia
- Stimulants (amphetamine and combinations): Raynaud phenomenon, MI, tremor, etc.
- Anabolic Steroids: Early Atherosclerosis with increased LDL and suppress HDL
Atypical Exertional Leg Pain

Summary Points

Important to recognize that there are several other etiologies (vascular) to exertional leg pain in the athlete.

Consider a one time evaluation with a vascular specialist and development of a multidisciplinary approach.

When evaluating athlete for leg pain, think of vascular territories affected by extrinsic, intrinsic, and intraluminal causes.

Clinical spectrum of vascular leg pain is broad
• Edema to Death (PE)
Questions & Discussion
cohoon.kevin@mayo.edu

Vascular Sports Medicine Clinic
Phone: (507) 266-6717