Uncommon Vascular Diseases Are More Frequent Than You Think!

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Director of Gonda Vascular Center
University of California, Los Angeles
Low Frequency Vascular Diseases

No conflicts or disclosures
VQI studies common vascular procedures entered prospectively
  - Evaluates “real world” practice

Patient safety organization (PSO) allows sharing of data
  - Outcomes “benchmarked” against other institutions and surgeons
  - Feedback used to improve outcomes and modify practice

Short- and long-term data available in large volumes

Does not evaluate rare or uncommon vascular diseases
Addresses uncommon vascular diseases

Vascular Low Frequency Diseases defined as those that are not entered into VQI
  - A single institution cannot accumulate enough patients to report significant outcomes data
  - Case reports, small series, and large series collected over many years are often the only publications available
  - Prospective randomized trials are impossible

Represent significant proportion of cases in many vascular surgery programs
  - We estimate ~20% of new patients at UCLA have an uncommon “low frequency” disease or problem
System for Investigation of VLFD’s

- Identify low-frequency diseases through patient needs
- Conduct thorough literature review.
- Ideal candidates:
  - Small case series
  - Contradictions between studies on management
  - Evolution of management over years (e.g. imaging, endovascular options, etc)
- Develop a database and analyze single institution’s (UCLA) data
- Present and publish single-center experience

**Diagram:**

1. Perform Literature Review
2. Develop Single-Center Database and Collect Data
3. Analyze and Publish Single-Center Experience
4. Modify Existing Database, Develop Multi-Institution Database and Collect Data
5. Analyze and Publish Multi-Institution Results
6. Write Evidence Summary/Review

**Prospective study**
Expansion to Multi-Institutional Study

- Determine if there are still unanswered questions
  - Modify the database
- Invite regional/national/international societies, and VLFDC institutions
- Provide all documents to facilitate expedited review
  - IRB Information
    - Literature review
    - Current results/UCLA (or single-center) experience
  - Standardized data collection form
    - De-identified data
      - Provide tips/hints at collecting and documenting to ensure standardization (ICD-9/10, CPT, etc)
    - Streamlined process dramatically reduces time required for data entry
- Publish multi-institutional study

Flowchart:

1. Perform Literature Review
2. Develop Single-Center Database and Collect Data
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4. Modify Existing Database, Develop Multi-Institution Database and Collect Data
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6. Write Evidence Summary/review
7. Contribute to Practice Guidelines
Disseminate Knowledge Through Review Articles, Practice Guidelines and Develop Prospective Trials

- Publish review articles/evidence summaries
  - Useful for modifying practice and educating many specialties

- Remaining initiatives
  - Participate in practice guidelines
  - Evidence-based publication, usually by multiple institutions or societies
  - Use information gained from retrospective studies to design and implement prospective trial

- Perform Literature Review
- Develop Single-Center Database and Collect Data
- Analyze and Publish Single-Center Experience
- Modify Existing Database, Develop Multi-Institution Database and Collect Data
- Analyze and Publish Multi-Institution Results
- Write Evidence Summary/review
- Prospective study
- Contribute to Practice Guidelines
Reasons for Physicians and Institutions To Collaborate

- “Real world” data - both community based and academic physicians and surgeons participate
  - Only participate when topic is of interest
  - Have input into database development
  - IRB submission packet and standardized data collection save time
  - Opportunity to analyze and critique data
  - Largest contributor presents results at national and international meetings
  - Co-authorship on all publications

- New research ideas can be generated at any institution with VLFDC assistance
Uncommon Aneurysms

Isolated Femoral Artery Aneurysms
Rare, 5/100,000 individuals

Textbook indications for repair:
- Symptoms/ischemia
- Size ≥ 2.5-cm, growth, thrombus

Most reports pre-date modern imaging era (before 1990s)

Limitations are small number of patients, mixed etiology, and short follow-up period
## Isolated Femoral Aneurysm: Literature Review

Only 4 studies on diagnosis and management of isolated femoral artery aneurysms (FAA)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Title</th>
<th>Patients</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baird RJ et al.</td>
<td>Arteriosclerotic Femoral Artery Aneurysms</td>
<td>30</td>
<td>1977</td>
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<tr>
<td>Graham LM et al.</td>
<td>22 Year interval, isolated FAA; dated imaging modalities</td>
<td>172</td>
<td>1980</td>
</tr>
<tr>
<td>Sapienza P et al.</td>
<td>Femoral Artery Aneurysms: Long term Follow-up and Results of Surgical Treatment</td>
<td>22 (13 isolated)</td>
<td>1996</td>
</tr>
<tr>
<td>Piffaretti G et al.</td>
<td>Single institution, small patient numbers, mixed aneurysm series</td>
<td>27</td>
<td>2011</td>
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</table>
Isolated Femoral Aneurysm Management

Clinical Significance of Arteriosclerotic Femoral Artery Aneurysms

Linda M. Graham, MD; Gerald B. Zelenock, MD; Walter W. Whitehouse, Jr, MD; Errol E. Erlandson, MD; Thomas L. Dent, MD; S. Martin Lindermauer, MD; James C. Stanley, MD

63 “true” femoral aneurysms- 30 % thrombosed, 3/3 profunda aneurysms required an amputation, and SFA aneurysms had a poor patency. “Because of the high morbidity associated with femoral aneurysms, an aggressive approach is warranted”. This has led to the common textbook recommendation to treat femoral aneurysms like popliteal aneurysms.

Graham recommended asymptomatic FAA repair only when it reaches 2.5 cm, while Cutler recommends repair of all FAA. Most papers mix “true” degenerative femoral aneurysms with infected, anastomotic, and pseudoaneurysms.
Isolated FAA: Single-Center Study (10 Year UCLA Experience)

### Results

- FAA patients = 19 (17 M, 2 F)
- Mean diameter = $3.3 \pm 1.1$ cm

- **No acute complications in conservatively managed group**
- Early (<30 days) postoperative complications
  - Leg ischemia ($n=1$)
  - Hematoma ($n=1$)
  - No cardiac complications, limb loss, or wound infection
- Long-Term Outcomes (mean time = 1.5 yrs)
  - No limb loss
  - All ambulatory
  - Mortality ($n=2$)

### Prior Aneurysms Treated

<table>
<thead>
<tr>
<th>Aneurysms Treated</th>
<th>Synchronous Aneurysms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracoabdominal</td>
<td>0</td>
</tr>
<tr>
<td>AAA</td>
<td>5</td>
</tr>
<tr>
<td>Hypogastric</td>
<td>2</td>
</tr>
<tr>
<td>Iliac</td>
<td>3</td>
</tr>
<tr>
<td>Femoral</td>
<td>4</td>
</tr>
<tr>
<td>Popliteal</td>
<td>6</td>
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</table>

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</tr>
<tr>
<td>Femoral</td>
<td>4</td>
</tr>
<tr>
<td>Popliteal</td>
<td>14</td>
</tr>
</tbody>
</table>
Isolated FAAs are relatively benign

FAA’s behave differently than popliteal aneurysms

Raised questions about current recommendations for FAA management and treatment

- There were not enough cases to draw meaningful conclusions

Need for multi-institutional study to change practice guidelines
Current Management of Femoral Artery Aneurysms Is Too Aggressive for Its Natural History

On behalf of the Vascular Low Frequency Disease Consortium:

Gustavo S. Oderich, MD; Peter F. Lawrence, MD, Michael P. Harlander-Locke, MPH, Misty D. Humphries, MD, Gregory J. Landry, MD, Jeffrey L. Ballard, MD, Christopher J. Abularrage, MD, Bernardo Mendes, MD, Michelle Mueller, MD, Preston Flanigan, MD, William C. Pevec, MD, and Nasim Hedayati, MD, and Sam S. Ahn, MD
Participants
Synchronous Aneurysms
(236 FAA in 182 patients)

<table>
<thead>
<tr>
<th>LOCATION</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral FAAs</td>
<td>45</td>
<td>25</td>
</tr>
<tr>
<td>Other Aneurysm</td>
<td>161</td>
<td>88</td>
</tr>
<tr>
<td>Aortic</td>
<td>113</td>
<td>62</td>
</tr>
<tr>
<td>Iliac</td>
<td>109</td>
<td>60</td>
</tr>
<tr>
<td>Popliteal</td>
<td>86</td>
<td>47</td>
</tr>
</tbody>
</table>

113 71 94 88 64
108 46 36 83 14
14 6 20 5
## Treatment of FAA

<table>
<thead>
<tr>
<th>Operative Repair</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open repair</td>
<td>138 patients (76%) had 177 FAAs</td>
</tr>
<tr>
<td>Interposition graft</td>
<td>142 FAAs (80% of repairs)</td>
</tr>
<tr>
<td>Bypass graft</td>
<td>35 FAAs (20% of repairs)</td>
</tr>
<tr>
<td>Endovascular repair</td>
<td>3 patients (2%) had 3 SFA aneurysms</td>
</tr>
</tbody>
</table>

236 FAAs in 182 patients
Factors Associated with Development of Acute FAA-related Complications

12 patients (5%) developed acute complications

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter ≥ 4-cm</td>
<td>5.192</td>
<td>1.535-17.564</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intraluminal thrombus</td>
<td>4.386</td>
<td>1.221-15.756</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age &lt;60 years</td>
<td>3.882</td>
<td>1.382-13.224</td>
<td>.004</td>
</tr>
<tr>
<td>Ipsilateral FAA</td>
<td>3.083</td>
<td>.874-10.878</td>
<td>.08</td>
</tr>
<tr>
<td>Contralateral FAA</td>
<td>1.384</td>
<td>.146-18.640</td>
<td>.741</td>
</tr>
<tr>
<td>Popliteal Aneurysm</td>
<td>.603</td>
<td>.186-1.961</td>
<td>.755</td>
</tr>
<tr>
<td>Rapid Expansion</td>
<td>3.882</td>
<td>1.382-13.224</td>
<td>.793</td>
</tr>
</tbody>
</table>
Conclusions
Isolated Femoral Artery Aneurysms

- Acute complications rarely develop in asymptomatic FAA ≤3.5 cm and this should be adopted as the new threshold for elective repair.
- Chronic intra-luminal thrombus may reduce the size threshold for elective repair.
- Current recommendation to repair all symptomatic FAA should remain unchanged.

From the Society for Vascular Surgery

The current management of isolated degenerative femoral artery aneurysms is too aggressive for their natural history.

Peter F. Lawrence, MD, Michael P. Harlander-Locke, BS, Gustavo S. Oderich, MD, Misty D. Humphries, MD, Gregory J. Landry, MD, Jeffrey L. Ballard, MD, and Christopher J. Abularrage, MD, for The Vascular Low-Frequency Disease Consortium, Los Angeles, Calif; Rochester, Minn; Salt Lake City, Utah; Portland, Ore; Orange, Calif; and Baltimore, Md

The Contemporary Guidelines for Asymptomatic Renal Artery Aneurysms Are Too Aggressive: A North American Experience

On behalf of the Vascular Low-Frequency Disease Consortium:

Dawn M. Coleman, MD; Peter F. Lawrence, MD; Jill Q. Klausner, BS; Michael P. Harlander-Locke, MPH; James C. Stanley, MD; Audra Duncan, MD; Gustavo S. Oderich, MD; Adnan Z. Rizvi, MD; Tazo S. Inui, MD; Robert J. Hye, MD; Matthew W. Mell, MD; Naoki Fujimura, MD/PhD; Nathan K. Itoga, MD; Misty Humphries, MD; Jacob Loeffler, BS; Paul G. Bove, MD; Christopher J. Abularrage, MD; Robert J. Feezor, MD; Amir F. Azarbal, MD; Matthew R. Smeds, MD; Joseph S. Ladowski, MD; York N. Hsiang, MD; Vivian M. Leung; Josefina A. Dominguez, MD; Fred A. Weaver, MD; Mark D. Morasch, MD
Participants
The Use of Cryopreserved Aortoiliac Allograft for Aortic Reconstruction in the United States

On behalf of the Vascular Low-Frequency Disease Consortium:

Michael P. Harlander-Locke, MPH, Liv K. Harmon, MD, Peter F. Lawrence, MD, Gustavo S. Oderich, MD, Robert A. McCready, MD, Mark D. Morasch, MD, Robert J. Feezor, MD, Wei Zhou, MD, Jean Bismuth, MD, William C. Pevec, MD, Mateus P. Correa, MD, Jeffrey Jim, MD, Joseph S. Ladowski, MD, Panagiotis Kougias, MD, Paul G. Bove, MD; Catherine M. Wittgen, MD, and John V. White, MD
Participants
Treatment and Outcomes of Aortic Endograft Infection

On behalf of the Vascular Low-Frequency Disease Consortium:

Audra A. Duncan, MD, Matthew R. Smeds, MD, Michael P. Harlander-Locke, MPH, Peter F. Lawrence, MD, Sean P. Lyden, MD, Javairiah Fatima, MD, Kristofer M. Charlton-Ouw, MD, Mark Morasch, MD, Raghu L. Motaganahalli, MD, Peter Nelson, MD, Sherene Shalhub, MD, Paul G. Bove, MD, J. Gregory Modrall, MD, Victor J. Davila, MD, Nasim Hedayati, MD, Ahmed Abou-Zamzam, MD, Christopher J. Abularrage, MD, Catherine M. Wittgen, MD
Participants
Distance to the Base of Skull: A New Predictor of Complications in Carotid Tumor Resection
Participants
Multi-Institutional Experience in the Management of Adventitial Cystic Disease

On behalf of the Vascular Low-Frequency Disease Consortium:
Raghu Motaganahalli, Matthew Smeds, Michael Harlander-Locke, Peter Lawrence, Naoki Fujimura, Hideaki Obara, Randall DeMartino, Giovanni De Caridi, Alberto Munoz, Sherene Shalhub, Susanna Shin, Kwame Amankwah, Hugh Gelabert, David Rigberg, Jeffrey Siracuse, Alik Farber, Sebastian Debus, Christian Behrendt, Jin Joh, Catherine Wittgen
Participants
VLFDC: U.S. Participation to Date
VLFDC Expansion
VLFDC Project Summary

- **Projects**
  - 8 Completed
    - 8 presented at national meetings
    - 8 published (JVS and JVSVL)
  - 9 In Progress

- **2829 patients**

- **141 Investigators**

- **76 Institutions**
  - 55 U.S.
  - 21 International
Contributions of VLFDC to Our Understanding of Low Frequency Vascular Diseases

- **Cryograft for Aortic Graft Infection**
  - Cryopreserved aortoiliac allograft allows for aortic reconstruction with low morbidity and mortality and low rates of complications

- **Femoral Artery Aneurysm**
  - 88% of FAA patients have another aneurysm
  - Acute complications do not develop in asymptomatic isolated FAA ≤3.5 cm.

- **Renal artery aneurysm**
  - Asymptomatic aneurysms rarely rupture
  - Growth rate of <1.0 mm per year
  - No adverse outcomes occurred in asymptomatic aneurysms <3cm; guidelines should be increased

- **EVAR/TEVAR/FEVAR (Endograft) Infection**
  - NAIS or cryopreserved allograft, then antibiotic soaked prosthetic grafts, should be considered for reconstruction after complete explantation

- **Cryopreserved Allograft for Hemodialysis Access**
  - Cryopreserved allograft for hemodialysis access is a durable alternative to prosthetic grafts in patients with no autogenous vein
  - Results excellent when used for infected graft
  - Eliminates the need for a two-staged excision and re-implantation

- **Carotid body Tumors**
  - Shamblin class continues to be useful
  - Addition of DTBOS and Volume improve prediction of bleeding and v nerve injury

- **Spontaneous Mesenteric Dissection**
  - Rarely causes AMI (ischemia)
  - Occasionally requires bypass/stent

- **Adventitial Cystic Disease**
  - Resection and bypass are superior to drainage or excision

- **Cryopreserved Allograft for Hemodialysis Access**
  - Cryopreserved allograft for hemodialysis access is a durable alternative to prosthetic grafts in patients with no autogenous vein
  - Results excellent when used for infected graft
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## Current VLFDC Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Current Status</th>
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</thead>
<tbody>
<tr>
<td>Contemporary Diagnosis and Management of Aortic Graft Infections</td>
<td>Case Western/Metro Health Hospital: Multi-Institutional Study Initiation Phase</td>
</tr>
<tr>
<td>Vascular Ehlers-Danlos syndrome</td>
<td>Univ. of Washington: Multi-Institutional Study Data Analysis</td>
</tr>
<tr>
<td>Popliteal Artery Entrapment Syndrome With Occlusion</td>
<td>UCLA: Multi-Institutional Study Data Collection</td>
</tr>
<tr>
<td>Persistent Sciatic Artery</td>
<td>UCLA: Multi-Institutional Study Initiation Phase</td>
</tr>
<tr>
<td>Carotid Artery Aneurysms</td>
<td>UCLA: Multi-Institutional Study Initiation Phase</td>
</tr>
<tr>
<td>Venous Aneurysms</td>
<td>UCLA: Single Institutional Study Initiation Phase</td>
</tr>
<tr>
<td>Management of Venous Ulcers</td>
<td>UCLA Multi-institutional Study Data Analysis</td>
</tr>
<tr>
<td><strong>Prospective Study: Pediatric Abdominal Aortic Coarctation</strong></td>
<td>University of Michigan: Multi-institutional Study Initiation Phase</td>
</tr>
</tbody>
</table>
VLFDC: On the Web

http://surgery.ucla.edu/vlfdc

The VLFDC is a collaborative effort among investigators from institutions across the US and the world to study management and outcomes of uncommon vascular conditions. The collaborative effort allows for a large enough sample size to provide sufficient power for drawing meaningful conclusions that would otherwise be difficult to make with the small numbers of patients treated at any individual institution.

To date, the VLFDC has involved over 75 institutions and 135 investigators in the United States and overseas, and each completed project has resulted in presentations at national conferences and publications in high impact, peer-reviewed journals.
VLFDC: On the Web

- Steps to start a VLFDC project
- Sample templates to get started
- List of domestic and international collaborators
- List of projects in progress
- Links to published projects
- Contact information
Sample Templates

- One page summary sheet
- Invitational letter
- Protocol (to assist with expedited IRB review)
- Data collection sheet
- Data entry manual
Next Steps to Improve VLFDC

- Form an advisory board to oversee consortium activities and select project proposals
- Develop a data auditing system to ensure integrity of data being shared
- Seek sponsorship from a professional society (e.g. Affiliated SVS societies)
- Secure funding for annual advisory board/collaborator meeting and full-time Program Coordinator and consultants (Lit Review, Stats, Graphics)
- Begin conducting prospective trials of uncommon vascular diseases
Get Involved

Contact Us on webpage or by email: vlfdc@mednet.ucla.edu
NSQIP/ VQI are great for common surgical diseases—to benchmark yourself and your institution, but:

Low frequency diseases are encountered in all surgical practices
- Literature is currently not available on the management
- A systematic approach using a standardized multi-institutional database can shed light on these diseases
- Better information on appropriate care will improve outcomes for patients

The process fosters a collaborative relationship among researchers, institutions, and professional societies