Imaging of Chronic Thromboembolic Pulmonary Arterial Hypertension (CTEPH)

Carole Dennie MD FRCPC
Professor of Radiology and Medicine
Head, Thoracic and Cardiac Imaging Sections
The Ottawa Hospital
Co-director Cardiac Radiology and MRI
University of Ottawa Heart Institute
• No disclosures
Objectives

• Describe utility of CT, MR and V/Q imaging to evaluate patients with suspected CTEPH

• List typical and subtle CT imaging features of CTEPH

• Discuss advances in treatment of CTEPH and importance of imaging to guide therapy
Introduction

• Precapillary PH with segmental defect on V/Q and typical findings on CT after at least 3 months of anticoagulation
• 0.6-3.8% following acute PE
• 19% referred for PH
• Incomplete resorption of emboli with organization into fibrous tissue incorporated into intima
• Development of distal arteriopathy in obstructed and nonobstructed vascular bed

Chronic Thromboembolic PH

• Risk factors
  – Previous PE (OR=19.0)
  – Younger age (OR=1.79 per decade)
  – Larger perfusion defect (OR=2.22 per decile \( \downarrow \) perfusion)
  – Inadequate anticoagulation
  – Non-O blood group
  – Ventriculoatrial shunt or infected pacemaker (OR=76)
  – Chronic inflammation (osteomyelitis, IBD)
  – Thrombophilic disorder (30%) – lupus anticoagulant and anticardiolipin antibody, \( \uparrow \) factor VIII
  – Splenectomy (OR=18)

Role of Imaging

- Confirm diagnosis
- Characterize extent and distribution of disease – “roadmap”
Diagnostic Algorithm

Echo

- No PH
- PH
  - V/Q
    - Unlikely CTEPH
    - Likely CTEPH
      - CTPA
        - Proximal CTEPH - roadmap
        - !Distal CTEPH
          - CMR +/- MRPA
        - Right heart cath
          - PA sarcoma, vasculitis, fibrosing mediastinitis
CTEPH - Treatment

• Lifelong anticoagulation +
• Surgical pulmonary thrombendarterectomy (PEA)
  – Median sternotomy, cardiopulmonary bypass and 2 periods of hypothermic circulatory arrest
• > 80% patients surgical candidates
• Mortality = < 5% in experienced centers
• Survival post PEA – 82% 5 year, 75% 10 year

Machuca T et al. Can J Cardiol 2015;31:509-14
Predictors of Good Surgical Outcome

• Clinical
  – Pulmonary vascular resistance (PVR) < 15 Wood units (1200 dyn•s•cm$^{-5}$)
  – Surgery in an experienced center

• Imaging
  – Disease in main, lobar and/or proximal segmental arteries

Ventilation/Perfusion Scanning

• Pivotal role – highly sensitive especially if SPECT
• Normal V/Q essentially excludes CTEPH
• Understates degree of vascular obstruction at angiography and surgery

Soler X et al. Respirology 2011;16:131-137
At least one, or more commonly several segmental or larger perfusion defects
CT Angiographic Findings

- Cardiac
- Arterial
- Pulmonary parenchymal
# CTEPH – CTA Vascular Findings

<table>
<thead>
<tr>
<th>Mural filling defect</th>
<th>Complete occlusion</th>
<th>Bands</th>
<th>Webs</th>
<th>Collateral systemic supply</th>
</tr>
</thead>
</table>

Bergin et al. Radiology 1997;204:695-702  
Kauczor et al. JCAT 1994;18(6):855-861  
CTPA - Meta-analysis of Diagnostic Accuracy

• Dong et al. PLoS ONE 2015
  – Main and lobar arteries
    • Pooled sensitivity = 95% (95%CI:92-97%)
    • Pooled specificity = 96% (95%CI:94-97%)
  – Segmental arteries
    • Pooled sensitivity = 88% (95%CI:87-90%)
    • Pooled specificity = 89% (95%CI:87-91%)
CTEPH - CT Parenchymal Findings

| Mosaic attenuation | Scars from prior infarction |

Worthy et al. Radiol 1997;205:465-470
Sherrick et al. AJR 1997;169:79-82
Rémy-Jardin et al. Radiol 1997;203:355-360
Arakawa et al. JCAT 2003; 27:735-742
Magnetic Resonance Angiography

- Similar to CTA findings
- Almost as effective as CTA in depicting proximal extent of disease

Mural Filling Defect
Segmental Narrowing
CMR Imaging

• Cine imaging - right and left ventricular function

• Cine phase-contrast imaging
  – Flow velocities
  – Pulmonary artery distensibility
  – Right and left pulmonary artery/ascending aorta
    • Shunting through systemic artery collaterals

Kreitner et al. Radiol 2004;232:535-543
Ley et al. AJR 2002;179:1209-1215
Pre and Post-op RV Function

**Pre-op**

- Right heart cath
- Mean PAP 53 mm Hg

<table>
<thead>
<tr>
<th>Cardiac Function</th>
<th>Normal Range (M) (MRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction</td>
<td>EF 35.3</td>
</tr>
<tr>
<td>End Diastolic Volume</td>
<td>EDV 190.5</td>
</tr>
<tr>
<td>End Systolic Volume</td>
<td>ESV 123.2</td>
</tr>
<tr>
<td>Stroke Volume</td>
<td>SV 67.3</td>
</tr>
<tr>
<td>Cardiac Output</td>
<td>CO 4.17</td>
</tr>
</tbody>
</table>

**Post-op**

- Mean PAP 24 hours post-op = 37 mm Hg

<table>
<thead>
<tr>
<th>Cardiac Function</th>
<th>Normal Range (M) (MRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction</td>
<td>EF 56.9</td>
</tr>
<tr>
<td>End Diastolic Volume</td>
<td>EDV 155.5</td>
</tr>
<tr>
<td>End Systolic Volume</td>
<td>ESV 87.0</td>
</tr>
<tr>
<td>Stroke Volume</td>
<td>SV 88.5</td>
</tr>
<tr>
<td>Cardiac Output</td>
<td>CO 8.32</td>
</tr>
</tbody>
</table>
## Pre and Post-op MPA Flow

<table>
<thead>
<tr>
<th></th>
<th>PRE-OP</th>
<th>POST-OP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Velocity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Velocity:</td>
<td>66.43 cm/sec</td>
<td>98.51 cm/sec</td>
</tr>
<tr>
<td>Average Velocity:</td>
<td>13.69 cm/sec</td>
<td>24.68 cm/sec</td>
</tr>
<tr>
<td><strong>Flow</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Flow Over Range:</td>
<td>81.37 ml/sec</td>
<td>125.82 ml/sec</td>
</tr>
<tr>
<td>Average Flow Per Minute:</td>
<td>3.86 l/min</td>
<td>6.09 l/min</td>
</tr>
<tr>
<td>Forward Volume:</td>
<td>48.82 ml</td>
<td>66.93 ml</td>
</tr>
<tr>
<td>Reverse Volume:</td>
<td>0.000 ml</td>
<td>2.13 ml</td>
</tr>
<tr>
<td>Net Forward Volume:</td>
<td>48.82 ml</td>
<td>64.80 ml</td>
</tr>
</tbody>
</table>
Pre and Post-op Flow Right Pulmonary Artery

Preop

Net forward volume 6.4 ml/heartbeat

Post-op

Net forward volume 24.6 ml/heartbeat
Advanced Imaging Technologies
Research Tools

• Dual energy CTPA
• 3D dynamic contrast-enhanced lung perfusion MRI
• MR ventilation/perfusion scanning

Rajaram S et al. Thorax 2013;68(7):677-678
Hoey ETD et al. AJR 2011;196:524-532
Challenging Cases
Case # 1

- 54 year-old female with no prior DVT or PE presenting with 6-month history of increasing SOBOE
  - 5 months prior to Dx
    - Normal exercise stress test
    - Normal PFT’s
    - Negative leg vein Doppler
    - Positive D-dimer
3 Months Prior to Diagnosis
3 Month F/U for Nodule
In Retrospect...
Lung Reconstruction

Follow-up 3 months earlier
Case # 1

• Referred to Pulmonary Hypertension Clinic with class III NYHA dyspnea

• Echocardiogram
  – Severe RV dilatation and dysfunction
  – RVSP = 93 mm Hg

• Underwent PEA
Teaching Points

• 57% of patients with CTEPH present with acute PE
• History – long-standing dyspnea prior to “acute” PE
• Look for subtle signs of underlying chronic PE at time of acute PE
• Recommend echo – sPAP>40 mmHg unlikely due to acute PE alone

Suggest follow-up imaging to ensure resolution

Guérin L et al. Thromb Haemost 2014;112:598-605
Case # 2

- 59 year non-smoker steel inspector
  - 4 years prior to diagnosis
    - Increasing SOBOE
    - No prior history of DVT or PE
    - Negative exercise stress test and stress myoview
    - Mildly reduced FEV$_1$ on PFT’s ➔ Dx “COPD”
  - 1 year prior to diagnosis
    - Unenhanced CT thorax ➔ mosaic attenuation
Case # 2

• 6 months prior to diagnosis
  – CTPA shows pulmonary hypertension and “no PE”
  – Patient referred to PH Clinic at tertiary care center with NYHA Class III dyspnea
  – Dx - probable Group 1 PH
Case # 2

- Echocardiogram confirms severe PH
- Leg vein Doppler – no DVT
- Repeat CTPA reports PH without CTEPH
- Right heart cath
  - mPAP = 56 mm Hg, PVR = 17.4 Wood units
- Cardiac MRI
  - RVEF = 16%, Indexed RVEDV = 188 cc
- What next?
Ventilation Perfusion Scan

Anterior  RAO  LAO
Digital Subtraction Angiogram
CTPA Revisited
Thick MIP’s
Final Diagnosis
Distal CTEPH

Treatment?
Survival in Patients with PH

![Cumulative survival curves according to the initial $P_{PA}$. Dotted line represents predicted survival among men 40-50 years old.](image)

Figure 2. Cumulative survival curves according to the initial $P_{PA}$. Dotted line represents predicted survival among men 40-50 years old.
Advances in Treatment of Distal CTEPH

• Distal thromboendarterectomy
• Medical therapy - Riociguat
• Percutaneous pulmonary angioplasty
Pulmonary endarterectomy for distal chronic thromboembolic pulmonary hypertension

Andrea M. D'Armini, Marco Morsolini, Gabriella Mattiucci, Valentina Grazioli, Maurizio Pin, Adele Valentini, Giuseppe Silvaggio, Catherine Klersy, Roberto Dore

September 2014, 148(3) p.1005-1012.e2
Survival after PEA

Advances in Medical Therapy

- Stimulates soluble cyclic guanilase activity
- Promotes vasodilation and inhibits smooth muscle proliferation
- Recommended for inoperable CTEPH or residual/recurrent PH after PEA (recommendation level I-B)
Survival with Riociguat at 1 Year (CHEST-2)

93% 1 yr (95% CI[88-96])

Time from start of extension study treatment days:

Patients alive: 237 223 166 105 74
Deaths: 0 3 6 8 10
Percutaneous Pulmonary Angioplasty

- First described in 2001
- Data published in 127 patients as of 2013
- Requires multiple procedures
- Reported hemodynamic results impressive and equal to PEA in experienced centers

Percutaneous Pulmonary Angioplasty

Pre

Post

Percutaneous pulmonary angioplasty

- Complications in 10-52% of patients
  - Vessel rupture
  - Reperfusion lung injury
- No randomized controlled trials
- No long-term outcome studies
- 2013 CTEPH guidelines
  - Should not replace PEA

Case # 2 – Treatment and F/U

• Medical therapy - Riociguat

• One year f/u
  – Right heart cath at one year
    • Mean PAP = 45 mm Hg (56)
    • PVR = 7.8 Wood units (17.6)
  – Cardiac MR
    • RVEF = 21% (16%)
    • Indexed RVEDV = 148 cc (188 cc)
  – Symptomatic improvement and slight improvement in 6 minute walking distance
Case # 2 – Teaching Points

• Ventilation/perfusion scan crucial to diagnosis

• Distal CTEPH findings very subtle on CTPA
  – Thin (0.5-1 mm) axial, coronal and sagittal reconstructions help to detect webs
  – MIP’s to detect stenosis, beading, rapid tapering
Ventilation/Perfusion Scanning

• 98.5% negative predictive value compared to CT (80%)
• Not performed in 43% of patients with PH

Machuca T & de Perrot M. Can J Cardiol 2015:31:510-514
McLaughlin VV et al. Chest 2013;143:324-32
Diagnostic and Management Algorithm

1. Symptoms/signs/history suggestive of PH
   - ECG, chest radiography, PFTs, blood gases, TTE, HRCT

2. PH of unknown origin
   - Perform V/Q lung scan
   - Unmatched perfusion defects
   - Reduced perfusion in ≥1/2 segment

   - Normal
     - CTEPH excluded
     - Refer to a specialist centre

   - Consider other causes
     - No
       - Right heart catheterisation
         - Mean PAP ≥25 mmHg, PCWP ≤15 mmHg
         - PVR >2 Wood units
         - Pulmonary angiography

       - Yes
         - Pulmonary endarterectomy

       - No
         - Additional information by CT- and MRI-angiography

   - Yes
     - Vasoreactivity indicating elevated mean PAP at baseline or abnormally fast elevation during exercise
     - Consider medical therapy#

   - No
     - Patient operable?
Diagnostic Algorithm

V/Q

Unlikely CTEPH

Likely CTEPH

CTPA

Proximal CTEPH - roadmap

Right heart cath

?Distal CTEPH

PA sarcoma, vasculitis, fibrosing mediastinitis

Pulm angio

Multidisciplinary team + second opinion
Conclusion

• CTPA excellent for preoperative mapping of disease in operable patients
• Be aware of acute on chronic PE
• Distal CTEPH can be subtle on CTPA
• V/Q remains modality of choice to exclude CTEPH