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American Heart Association Scientific Sessions 2014, Chicago, IL

Emerging Researchers from 3CPR Council:
How to Build a Road Map for Your Career in Cardiopulmonary, Critical Care, Perioperative and Resuscitation Research

Quality & Outcomes Research in Pulmonary Arterial Hypertension

#AHA2014
@American_Heart
@drjohnjryan
November 15th 2014
Outcomes Research

“the study of the end results of health services that takes patients’ experiences, preferences, and values into account — is intended to provide scientific evidence relating to decisions made by all who participate in health care.”

Clancy & Eisenberg. Science. 1998
Randomized Controlled Trials in PAH

- Instrumental in identifying the vast majority of FDA-approved therapies.

- Heterogeneous range of PAH substrates accounts for inconsistent rates of clinical benefit.

- RCTs have been successful at providing outcome data despite the (relatively) low prevalence of PAH.
### PAH Registries: 1981-present

<table>
<thead>
<tr>
<th>PH Registry</th>
<th>Date of Enrollment</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH registry (3)</td>
<td>1981–1988</td>
<td>194</td>
</tr>
<tr>
<td>PH connection (6)</td>
<td>1982–2006</td>
<td>578</td>
</tr>
<tr>
<td>French registry (7)</td>
<td>2002–2003</td>
<td>674</td>
</tr>
</tbody>
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<thead>
<tr>
<th>Registry</th>
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<th>Sample Size</th>
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</thead>
<tbody>
<tr>
<td>REVEAL Registry (5)</td>
<td>2006–2007</td>
<td>2525</td>
</tr>
<tr>
<td>PAH registry in China (8)</td>
<td>1999–2004</td>
<td>72</td>
</tr>
<tr>
<td>PAH registry in UK and Ireland (1)</td>
<td>2001–2009</td>
<td>482</td>
</tr>
</tbody>
</table>

*Thenappan, Ryan, Archer. AJRCCM 2012*
Pulmonary Hypertension Registry of the UK & Ireland

• Aim: To create a registry of incident PAH.

• 482 patients:
  – 93% idiopathic, 5% heritable, & 2% anorexigen.

• REVEAL risk score, and PH Connection survival equation accurately predicted survival:
  – 1-year survival: 93%.
  – 5-year survival: 61%.

Yi Ling:
Then - Pulmonary vascular research fellow at SPVU.
Now – recently completed MD.

Ling et al. AJRCCM 2012
A study of PH misdiagnosis

- Aim: Determine the accuracy of PH diagnoses in patients referred to PH centers.

- 140 patients:
  - mean age of 56 years.
  - 86 (61%) were WHO FC III or IV.

- 33% had received a misdiagnosis.

- 57% of the prescriptions contrary to published guidelines.

Deano et al. JAMA Int Med 2013
The heterogeneity of clinical practice patterns PAH experts

- Aim: to characterize the clinical management strategies used by PAH experts in PAH diagnosis, drug therapy, and clinical assessment.

- Marked disagreement in the role of RHC in PAH management beyond diagnosis.

- Considerable agreement in favor of echocardiography for the routine monitoring of right ventricular function.

Brad Maron: Then - BWH. Now – BWH.
### Role of Left Heart catheterization in PAH

<table>
<thead>
<tr>
<th>LHC survey question</th>
<th>Response, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHC is not a part of the cardiopulmonary hemodynamic assessment in my practice</td>
<td>58 (55.2)</td>
</tr>
<tr>
<td>LHC is always performed unless contraindicated</td>
<td>30 (28.5)</td>
</tr>
<tr>
<td>LHC is performed only if the transpulmonary gradient is $\geq 10$ mmHg</td>
<td>6 (5.7)</td>
</tr>
<tr>
<td>LHC is performed only if the pulmonary capillary wedge pressure is $&lt; 15$ mmHg</td>
<td>5 (4.7)</td>
</tr>
</tbody>
</table>
Preferred Inotrope in RVF from PAH

- Dobutamine: 50.4% (N=53)
- Milrinone: 21.9% (N=23)
- Dopamine: 10.5% (N=10)
- Norepinephrine: 5.7% (N=6)
- Phenylephrine: 0.9% (N=1)
- Other: 0.4% (N=12)

Ryan, Butrous, Maron. Pulm Circ 2014
Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR)

- A questionnaire comprising three sections evaluating symptoms, activity levels, and QoL.
- Uncertain correlation with clinical deterioration.

McKenna et al. Quality of Life Research 2006

McCabe et al. CHEST 2013

Colm McCabe: Then – Research Fellow, PVDU. Now – Consultant Respiratory Physician, Hammersmith.
Reappraisal of the NIH risk stratification equation


• The observed 1-, 3- and 5-yr survival were significantly higher than the predicted survival.

• A new survival prediction equation was developed:
  
  \[ P(t) = e^{-A(x,y,z)t}. \]
  
  – where \( P(t) \) is probability of survival.
  – \( t \) the time interval in years.

Thenappan, et al. ERJ 2010
Summary

• The field of PAH has heavily depended on registries & RCTs which has given insight into this rare disease.

• Registries & Surveys offer insight to clinical practice.

• Young investigators and early career researchers have led this field of research in PAH.

3CPR Early Career Networking Lunch,
Tuesday, November 18th 12:00pm - 1:30 pm:
Hyatt Regency McCormick Place, Grant Park AB.
Email: john.ryan@hsc.utah.edu
@drjohnjryan

Queen’s University
Stephen Archer, MD

University of Utah
Nathan Hatton, MD
Jess Harris, MD

University of Minnesota
Thenappan Thenappan, MD

University of Kent
Ghazwan Butrous, MD

Yale University
Harlan Krumholz, MD
Emily Bucholz, MS

Harvard Medical School
Bradley Maron, MD

St Luke’s Roosevelt
Saurav Chatterjee, MD

Northwestern University
Jonathan Rich, MD

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