The Hildner Lecture

Interventional Cardiology at a Pivot Point

Anthony DeMaria
Judith and Jack White Chair in Cardiology
University of California, San Diego

Potential Conflict: Editor, Structural Heart: Journal of the Heart Team
Interventional Cardiology has revolutionized the treatment of Acute Coronary Syndromes
Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials

*Ellen C Keeley, Judith A Boura, Cindy L Grines*

Lancet 2003; 361: 13–20
Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non–ST-Segment Elevation Acute Coronary Syndrome
A Meta-Analysis of Individual Patient Data

Keith A. A. Fox, BSc, MB, ChB,* Tim C. Clayton, BSc, MSc,† Peter Damman, MD,‡ Stuart J. Pocock, BSc, MSc, PhD,† Robbert J. de Winter, MD, PhD,‡ Jan G. P. Tijssen, PhD,‡ Bo Lagerqvist, MD, PhD,§ Lars Wallentin, MD, PhD,§ for the FIR Collaboration

Cumulative Risk of CV Death or MI
Recent studies have questioned the role of interventional cardiology in *Stable Coronary Artery Disease*
Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O’Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group®
Critique of COURAGE Trial

• Only bare metal stents
• Enroll only 7% of patients screened
• Cross-over rate of 32%
• Optimal medical therapy difficult for busy practice
• Angina was not an endpoint
Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial

Rasha Al-Lamee, David Thompson, Hakim-Moulay Dehbi, Sayan Sen, Kane Tang, John Davies, Thomas Keohkle, Michael Miekewicz, Rajfi Kaprielian, Isbjoern Melin, Sukhjinder S Nijjar, Ricardo Petracca, Christopher Cook, Yousof Ahmad, James Howard, Christopher Baker, Andrew Sharp, Robert Gerber, Saeed Talwar, Ravi Assamull, Jami Mayet, Roland Wersel, David Coller, Matthew Shun-Shin, Simon A Thom, Justin E Davies, Darrel P Francis, on behalf of the ORBITA investigators*

Summary
Background Symptomatic relief is the primary goal of percutaneous coronary intervention (PCI) in stable angina and is commonly observed clinically. However, there is no evidence from blinded, placebo-controlled randomised trials to show its efficacy.

Methods ORBITA is a blinded, multicentre randomised trial of PCI versus a placebo procedure for angina relief that was done at five study sites in the UK. We enrolled patients with severe (≥70%) single-vessel stenoses. After enrolment, patients received 6 weeks of medication optimisation. Patients then had pre-randomisation assessments with cardiopulmonary exercise testing, symptom questionnaires, and dobutamine stress echocardiography. Patients were randomised 1:1 to undergo PCI or a placebo procedure by use of an automated online randomisation tool. After 6 weeks of follow-up, the assessments done before randomisation were repeated at the final assessment. The primary endpoint was difference in exercise time increment between groups. All analyses were based on the intention-to-treat principle and the study population contained all participants who underwent randomisation. This study is registered with ClinicalTrials.gov, number NCT02862593.

Findings ORBITA enrolled 230 patients with ischaemic symptoms. After the medication optimisation phase and between Jan 6, 2014, and Aug 11, 2017, 200 patients underwent randomisation, with 105 patients assigned PCI and 95 assigned the placebo procedure. Lesions had mean area stenosis of 84-4% (SD 10-2), fractional flow reserve of 0.69 (0-16), and instantaneous wave-free ratio of 0.76 (0.22). There was no significant difference in the primary endpoint of exercise time increment between groups (PCI minus placebo 16.6 sec, 95% CI -8.9 to 42.0, p=0.200). There were no deaths. Serious adverse events included four pressure-wire related complications in the placebo group, which required PCI, and five major bleeding events, including two in the PCI group and three in the placebo group.

Interpretation In patients with medically treated angina and severe coronary stenosis, PCI did not increase exercise time by more than the effect of a placebo procedure. The efficacy of invasive procedures can be assessed with a placebo control, as is standard for pharmacotherapy.
ORBITA: Secondary Endpoints

**Secondary endpoint results**

**CCS class improved in both groups**

<table>
<thead>
<tr>
<th>CCS at enrolment</th>
<th>PCI</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS IV</td>
<td>37%</td>
<td>40%</td>
</tr>
<tr>
<td>CCS III</td>
<td>61%</td>
<td>57%</td>
</tr>
<tr>
<td>CCS II</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>CCS I</td>
<td>2%</td>
<td>3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CCS at pre-randomization</th>
<th>PCI</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS IV</td>
<td>24%</td>
<td>33%</td>
</tr>
<tr>
<td>CCS III</td>
<td>53%</td>
<td>43%</td>
</tr>
<tr>
<td>CCS II</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>CCS I</td>
<td>9%</td>
<td>14%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CCS at follow-up</th>
<th>PCI</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS IV</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>CCS III</td>
<td>35%</td>
<td>34%</td>
</tr>
<tr>
<td>CCS II</td>
<td>13%</td>
<td>20%</td>
</tr>
<tr>
<td>CCS I</td>
<td>39%</td>
<td>29%</td>
</tr>
</tbody>
</table>

**Blinded evaluation of ischaemia reduction**

<table>
<thead>
<tr>
<th>Peak stress wall motion index score</th>
<th>PCI</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-randomization</td>
<td>1.11 (0.18)</td>
<td>1.11 (0.18)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>1.03 (0.06)</td>
<td>1.13 (0.19)</td>
</tr>
<tr>
<td>Δ (Pre-randomization to follow-up)</td>
<td>-0.08 (0.17)</td>
<td>0.02 (0.16)</td>
</tr>
</tbody>
</table>

p<0.0001

**Difference in Δ between arms**

-0.09 (-0.15 to -0.04)

p=0.0011
ORBITA Trial: Critique

• Patients had excellent exertional capacity and little angina

• 30% of lesions were not flow limiting by functional testing

• Cross-over from medical therapy to PCI occurred in 4/95 patients

• Follow-up duration was short (6 weeks)

• Medical therapy involved intense provider action (calls 2-3/week)

• Applies only to single vessel disease
Studies have shown that the relationship between myocardial ischemia and obstructive coronary disease is imperfect.

Corollary: Revascularization will be less effective in those in whom ischemia is not due to obstruction.
Discordance between Ischemia and Obstruction

- Coronary obstruction may be absent in stable angina and infarction
- Patients with coronary obstruction may be angina free
- Multiple non-atherosclerotic causes of ischemia exist
- Ischemia increases event rate even in the absence of obstruction
- Treating obstructions may not eliminate events/symptoms
No coronary artery disease (defined as <20\% stenosis in all vessels) was reported in 39.2\% of the patients.

were moderately more likely to have obstructive coronary artery disease than those who did not undergo any testing (41.0\% vs. 35.0\%; P<0.001; adjusted odds ratio, 1.28; 95\% CI, 1.19 to 1.37).

CONCLUSIONS

In this study, slightly more than one third of patients without known disease who underwent elective cardiac catheterization had obstructive coronary artery disease. Better strategies for risk stratification are needed to inform decisions and to increase the diagnostic yield of cardiac catheterization in routine clinical practice.
Obstructive Coronary Atherosclerosis and Ischemic Heart Disease: An Elusive Link!

Mario Marzilli, MD,* C. Noel Bairey Merz, MD,† William E. Boden, MD,‡ Robert O. Bonow, MD,§ Paola G. Capozza, MD,* William M. Chilian, PhD,|| Anthony N. DeMaria, MD,¶ Giacinta Guarini, MD,* Alda Huqi, MD,* Doralisa Morrone, MD,* Manesh R. Patel, MD,# William S. Weintraub, MD**
Invasive Evaluation of Patients With Angina in the Absence of Obstructive Coronary Artery Disease

Bong-Ki Lee, MD, PhD; Hong-Seok Lim, MD, PhD; William F. Fearon, MD; Andy S. Yong, MBBS, PhD; Ryotaro Yamada, MD; Shigemitsu Tanaka, MD; David P. Lee, MD; Alan C. Yeung, MD; Jennifer A. Tremmel, MD, MS

Circulation. 2015;131

Figure 1. Demonstrative cases of (A) epicardial endothelial dysfunction, (B) low fractional flow reserve (FFR) with occult diffuse-epicardial disease, (C) microvascular dysfunction, and (D) myocardial bridging. A. Paradoxical vasoconstriction after intracoronary acetylcholine injection. B. This angiographically nonobstructive left anterior descending artery (LAD) showed diffuse atherosclerosis on intravascular ultrasound (IVUS) and low FFR. C. There was no significant angiographic stenosis in the LAD, but the index of microcirculatory resistance was high. D. An IVUS image of myocardial bridging during diastole and systole. An echolucent area surrounding the coronary artery is seen during the entire cardiac cycle.
International standardization of diagnostic criteria for microvascular angina

Peter Ong, Paolo G. Camici, John F. Beltrame, Filippo Crea, Hiroaki Shimokawa, Udo Sechtem, Juan Carlos Kaski, C. Noel Bairey Merz

On behalf of the Coronary Vasomotion Disorders International Study Group (COVADIS)

1. Symptoms of myocardial ischemia
   a. Effort and/or rest angina
   b. Angina equivalents (i.e. shortness of breath)

2. Absence of obstructive CAD (<50% diameter reduction or FFR > 0.80) by
   a. Coronary CTA
   b. Invasive coronary angiography

3. Objective evidence of myocardial ischemia
   a. Ischemic ECG changes during an episode of chest pain
   b. Stress-induced chest pain and/or ischemic ECG changes in the presence or absence of transient/reversible abnormal myocardial perfusion and/or wall motion abnormality

4. Evidence of impaired coronary microvascular function
   a. Impaired coronary flow reserve (cut-off values depending on methodology use between ≤2.0 and ≤2.5)
   b. Coronary microvascular spasm, defined as reproduction of symptoms, ischemic ECG shifts but no epicardial spasm during acetylcholine testing.
   c. Abnormal coronary microvascular resistance indices (e.g. IMR > 25)
   d. Coronary slow flow phenomenon, defined as TIMI frame count >25.

*Definitive MVA is only diagnosed if all four criteria are present for a diagnosis of microvascular angina.

Suspected MVA is diagnosed if symptoms of ischemia are present (criteria-1) with no obstructive coronary artery disease (criteria-2) but only (a) objective evidence of myocardial ischemia (criteria-3), or (b) evidence of impaired coronary microvascular function (criteria-4) alone.
Techniques to Assess Coronary Physiology

• FFR or iFR

• Reduced Coronary Flow Reserve
  • Non-invasive
    • Vasodilator PET or CMR or Transthoracic Doppler
  • Invasive
    • Coronary Velocity Reserve (Doppler wire)
    • Coronary Blood Flow Reserve (pressure/thermodilution wire)
    • Hyperemic Microvascular Resistance (Doppler)
    • Index of Microvascular Resistance (thermodilution)
    • Coronary Microvascular Spasm (acetylcholine)
    • TIMI Frame Count
Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

Pim A.L. Tonino, M.D., Bernard De Bruyne, M.D., Ph.D., Nico H.J. Pijls, M.D., Ph.D., Uwe Siebert, M.D., M.P.H., Sc.D., Fumiaki Ikeno, M.D., Marcel van `t Veer, M.Sc., Volker Klauss, M.D., Ph.D., Ganesh Manoharan, M.D., Thomas Engstrøm, M.D., Ph.D., Keith G. Oldroyd, M.D., Peter N. Ver Lee, M.D., Philip A. MacCarthy, M.D., Ph.D., et al., for the FAME Study Investigators
MACE

Death or MI
Coronary revascularization will be effective when ischemia is caused by epicardial obstruction

Corollary: Interventional cardiologists must define and apply techniques to identify when ischemia is caused by epicardial vs microvascular obstruction

Interventionalists should focus on physiology
Definition of **STRUCTURAL**

1: of or relating to the physical makeup of a plant or animal body *<structural defects of the heart>*

2: of, relating to, or affecting **structure** *<structural stability>*
Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study

Joanna L. d’Arcy†, Sean Coffey‡, Margaret A. Loudon¹, Andrew Kennedy¹, Jonathan Pearson-Stuttard¹, Jacqueline Birks¹,³, Eleni Frangou¹,³, Andrew J. Farmer², David Mant², Jo Wilson¹, Saul G. Myerson¹, and Bernard D. Prendergast¹*

Table 2  New diagnosis of valvular heart disease

<table>
<thead>
<tr>
<th></th>
<th>None/trivial</th>
<th>Mild</th>
<th>Significant (moderate/severe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any VHD</td>
<td>1231 (49.2%)</td>
<td>1110 (44.4%)</td>
<td>159 (6.4%)</td>
</tr>
<tr>
<td>Left-sided VHD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>1948 (77.9%)</td>
<td>494 (19.8%)</td>
<td>58 (2.3%)</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>2491 (99.6%)</td>
<td>7 (0.3%)</td>
<td>2 (0.1%)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>2118 (84.7%)</td>
<td>341 (13.6%)</td>
<td>41 (1.6%)</td>
</tr>
<tr>
<td>Calcific aortic valve disease—AoScl and stenosis</td>
<td>1617 (64.7%)</td>
<td>866 (34.6%)a</td>
<td>17 (0.7%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>None/Trivial/Mild</th>
<th>Significant (moderate/severe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right-sided VHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>2433 (97.3%)</td>
<td>67 (2.7%)</td>
</tr>
<tr>
<td>Pulmonary regurgitation</td>
<td>2493 (99.7%)</td>
<td>7 (0.3%)</td>
</tr>
</tbody>
</table>
Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery?

Bernard Lung1*, Agnès Cachier1, Gabriel Baron2, David Messika-Zeitoun1, François Delahaye3, Pilar Tornos4, Christa Gohlke-Bärwolf5, Eric Boersma6, Philippe Ravaud2, and Alec Vahanian1
# Failure of Guideline Adherence for Intervention in Patients With Severe Mitral Regurgitation

David S. Bach, MD, Mazen Awais, MD, Hitinder S. Gurm, MD, Sarah Kohnstamm, MD
Ann Arbor, Michigan

(J Am Coll Cardiol

## Table 4
Prevalence of Indications for Surgical Intervention for Chronic Severe Mitral Regurgitation in Patients With Organic Mitral Regurgitation Based on the 1998 ACC/AHA Guidelines*

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Operated</th>
<th>Unoperated</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>112</td>
<td>59</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>53 (47%)</td>
<td>29 (49%)</td>
<td>24 (45%)</td>
<td>0.68</td>
</tr>
<tr>
<td>LVIDS $\geq$45 mm</td>
<td>11 (10%)</td>
<td>5 (8%)</td>
<td>6 (11%)</td>
<td>0.61</td>
</tr>
<tr>
<td>LVEF $\leq$60%</td>
<td>50 (45%)</td>
<td>26 (44%)</td>
<td>24 (45%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>26 (23%)</td>
<td>14 (24%)</td>
<td>12 (23%)</td>
<td>0.89</td>
</tr>
<tr>
<td>RVSP $&gt;50$ mm Hg</td>
<td>25 (22%)</td>
<td>9 (15%)</td>
<td>16 (30%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Any indication</td>
<td>96 (86%)</td>
<td>57 (97%)</td>
<td>39 (74%)</td>
<td>$&lt;0.0001$</td>
</tr>
</tbody>
</table>
Interventions in Congenital Heart Disease

- Closure Devices
  - Atrial septal defect / Patent foramen ovale
  - Ventricular septal defect
  - Patent ductus arteriosus

- Balloon dilation
  - Pulmonic stenosis (aortic stenosis)
  - Pulmonary artery stenosis

- Dilation and Stenting
  - Coarctation of the aorta

- Transcatheter valves
ASD and PFO Occluder Devices

Figure 2  Various patent foramen ovale (PFO) Closure Devices: (A) Amplatzer PFO Occluder (AGA Medical, MN, USA). (B) NMT Septal Occluder (NMT Medical, MA, USA). (C) Helex Septal Occluder (WL Gore and Associates, AZ, USA). (D) Premere (St. Jude Inc., MN, USA). (E) Occlutech PFO Occluder (Occlutech, Jena, Germany). (F) Solsysafe (Swissimplant Inc., Solothum, Switzerland) (G). SeptRx (Secant Medical, PA, USA) (H). PFx (Cierra, CA, USA).
Patent foramen ovale closure versus medical therapy in cases with cryptogenic stroke, meta-analysis of randomized controlled trials

Elsayed Abo-salem1 · Bernard Chaitman1 · Tarek Helmy1 · Eric Adjei Boakye2 · Hassan Alkhawam1 · Michael Lim1

(A) Stroke
RESPECT
REDUCE
CLOSE
CLOSURE I
PC trial
Total (fixed effects) RR: 0.48
95% CI: (0.22-0.75), p=0.001

(B) Transient ischemic attacks
RESPECT
CLOSE
CLOSURE I
PC trial
Total (fixed effects) RR: 0.60
95% CI: (0.50-0.74), p=0.001

(C) Atrial Fibrillation
RESPECT
REDUCE
CLOSE
CLOSURE I
PC trial
Total (fixed effects) RR: 0.54
95% CI: (0.39-0.85), p=0.001

(D) All-causes Death
RESPECT
REDUCE
CLOSE
CLOSURE I
PC trial
Total (fixed effects) RR: 0.81
95% CI: (0.65-1.00), p=0.05

Journal of Neurology
https://doi.org/10.1007/s00415-018-8750-x
Interventions in Valve Disease

• Aortic Valve
  • TAVR

• Mitral and Tricuspid Valves
  • Leaflets: *MitraClip*
  • Annuloplasty
  • Ventricular reshaping
  • Chordal Implantation
  • Mitral prostheses

• Prosthetic Valves
  • Paravalvular leaks
  • Valve in valve procedures
Fastest procedure ever to go from “Gee Whiz” to “Ho Hum”
TAVI Prostheses

Sapien-Edwards

Corevalve-Medtronics
Imaging for TAVR

CTA Aortic Annulus Sizing for TAVR

Echo for Post-TAVR PVL
## RCTs for TAVR vs Surgery for Aortic Stenosis

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study Design</th>
<th>Population</th>
<th>Valve for TAVR</th>
<th>Follow up</th>
<th>Main Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTNER II</td>
<td>Prospective, multicenter,</td>
<td>Intermediate surgical risk patients who had severe degenerative aortic valve</td>
<td>Edwards SAPIEN XT</td>
<td>2 years</td>
<td>SAVR and TAVR procedures were similar in the rate of mortality and disabling stroke. However, TAVR was associated with lower rates of bleeding, AKI, and new-onset AF, while SAVR was associated with lower rates of VAC and paravalvular AR.</td>
</tr>
<tr>
<td>Trial [8]</td>
<td>randomized trials</td>
<td>stenosis with Echo-derived criteria: mean gradient &gt;40 mmHg or jet velocity greater than 4.0 m/s and an initial aortic valve area of &lt;0.8 cm².</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STACCATTO</td>
<td>Prospective, randomized trial</td>
<td>Operable patients, older than 75 years old with severe aortic stenosis (valve area &lt; 1 cm²)</td>
<td>Edwards SAPIEN</td>
<td>3 months</td>
<td>Despite the premature termination, the authors concluded that transapical TAVR has more complications and lower success rates than SAVR in low risk patients.</td>
</tr>
<tr>
<td>Trial [11]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOTION</td>
<td>Multicenter, randomized,</td>
<td>Patients &gt; 70 years old with severe aortic valve stenosis and no significant coronary artery disease</td>
<td>CoreValve</td>
<td>2 years</td>
<td>After 2 years of follow up, the rates of mortality, stroke, and myocardial infarction were similar in both SAVR and TAVR groups.</td>
</tr>
<tr>
<td>Trial [9]</td>
<td>superiority trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US PIVOTAL</td>
<td>Multicenter, randomized,</td>
<td>Intermediate surgical risk patients with severe aortic stenosis and an aortic valve Area ≤ 0.8 cm² or an AVA index ≤0.5 cm²/m²</td>
<td>CoreValve</td>
<td>2 years</td>
<td>The rates of 2-year death or stroke were lower in the TAVR group, compared to the SAVR group.</td>
</tr>
<tr>
<td>Trial [10]</td>
<td>non-inferiority trial</td>
<td></td>
<td></td>
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</tbody>
</table>

Table 1 shows a summary of the design and main findings of included studies.
Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis

1-Year Results From the All-Comers NOTION Randomized Clinical Trial

Hans Gustav Harsted Thyregod, MD,* Daniel Andreas Steinbrüchel, MD, DMSc,* Nikolaj Ihlemann, MD, PhD,† Henrik Nissen, MD, PhD,‡ Bo Juel Kjeldsen, MD, PhD,‡ Petur Petursson, MD,‡ Yanping Chang, MS,¶ Olaf Walter Franzen, MD,¶ Thomas Engstrem, MD, DMSc,¶ Peter Clemmensen, MD, DMSc,¶ Peter Bo Hansen, MD,¶ Lars Willy Andersen, MD, DMSc,¶ Peter Skov Olsen, MD, DMSc,* Lars Søndergaard, MD, DMSc

BACKGROUND Transcatheter aortic valve replacement (TAVR) is an option in certain high-risk surgical patients with severe aortic valve stenosis. It is unknown whether TAVR can be safely introduced to lower-risk patients.

OBJECTIVES The NOTION (Nordic Aortic Valve Intervention Trial) randomized clinical trial compared TAVR with surgical aortic valve replacement (SAVR) in an all-comers patient cohort.

METHODS Patients with severe aortic valve disease were randomized 1:1 to TAVR or SAVR to determine the composite rate of death from any cause, stroke, or MI after 1 year.

RESULTS A total of 280 patients were randomized at 3 Nordic centers. Mean age was 79.1 years, and 81.8% were considered low-risk patients. In the intention-to-treat population, no significant difference in the primary endpoint was found (13.1% vs. 16.3%: p = 0.43 for superiority). The result did not change in the as-treated population. No difference in the rate of cardiovascular death or prosthesis reintervention was found. Compared with SAVR-treated patients, TAVR-treated patients had more conduction abnormalities requiring pacemaker implantation, larger improvement in effective orifice area, more total aortic valve regurgitation, and higher New York Heart Association functional class at 1 year. SAVR-treated patients had more major or life-threatening bleeding, cardiogenic shock, acute kidney injury (stage II or III), and new-onset or worsening atrial fibrillation at 30 days than did TAVR-treated patients.

CONCLUSIONS In the NOTION trial, no significant difference between TAVR and SAVR was found for the composite rate of death from any cause, stroke, or MI after 1 year. (Nordic Aortic Valve Intervention Trial [NOTION]; NCT01057173) (J Am Coll Cardiol. 2015;65:2184–94) © 2015 by the American College of Cardiology Foundation.
The Future of TAVR

• Resolve the durability question

• Extend to low risk AS patients

• Extend to asymptomatic aortic stenosis
MitraClip

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald D. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators*
Transcatheter Mitral-Valve Repair in Patients with Heart Failure

Minimally Invasive Approaches to Treat *Mitral Regurgitation*

**Challenges**
- No direct access
- Larger annulus with saddle shape
- Proximity of circumflex
- Role of functional MR
Impact of Tricuspid Regurgitation on Long-Term Survival

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Palo Alto and San Francisco, California

Figure 1. Kaplan-Meier survival curves for all patients with tricuspid regurgitation (TR). Survival is significantly worse in patients with moderate and severe TR.
Transcatheter Therapies for Tricuspid Regurgitation

Coaptation Device

Heterotopic Cavoval Valve Implantation

Annuloplasty Devices

Challenges of Transcatheter Therapies for Tricuspid Regurgitation

- Large tricuspid annulus dimensions
- Nonplanar and elliptical annulus shape
- Absence of calcium
- Right ventricular morphology
- Proximity of other structures (coronary sinus, AV node and His bundle, vena cava, right coronary artery)

Interventions in Heart Rhythm Disorders

• Left Atrial Appendage Closure

• Ablation of Arrhythmias
  • Atrial Fibrillation
  • Ventricular arrhythmias
Left Atrial Appendage Occlusion
Measurements for LAA Occlusion
5-Year Outcomes After Left Atrial Appendage Closure
From the PREVAIL and PROTECT AF Trials

Vivek Y. Reddy, MD, a,b Shephal K. Doshi, MD, c Saibal Kar, MD, d Douglas N. Gibson, MD, e Matthew J. Price, MD, e Kenneth Huber, MD, f Rodney P. Horton, MD, g Maurice Buchbinder, MD, h Petr Neuzil, MD, PhD, b Nicole T. Gordon, BSEE, i David R. Holmes, Jr, MD, j on behalf of the PREVAIL and PROTECT AF Investigators

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke or SE</td>
<td>0.82</td>
<td>0.3</td>
</tr>
<tr>
<td>Ischemic stroke or SE</td>
<td>0.96</td>
<td>0.9</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>1.7</td>
<td>0.08</td>
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<tr>
<td>Ischemic stroke or SE &gt; 7 days</td>
<td>0.2</td>
<td>0.0022</td>
</tr>
<tr>
<td>Disabling/Fatal Stroke (MRS change of ≥2)</td>
<td>1.4</td>
<td>0.3</td>
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<tr>
<td>Non-Disabling Stroke</td>
<td>0.45</td>
<td>0.03</td>
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<tr>
<td>CV/unexplained death</td>
<td>1.37</td>
<td>0.35</td>
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<tr>
<td>All-cause death</td>
<td>0.59</td>
<td>0.03</td>
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<tr>
<td>Major bleed, all</td>
<td>0.73</td>
<td>0.04</td>
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<tr>
<td>Major bleeding, non procedure-related</td>
<td>0.91</td>
<td>0.6</td>
</tr>
<tr>
<td>Major bleeding, non procedure-related</td>
<td>0.48</td>
<td>0.0003</td>
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</tbody>
</table>

Hazard Ratio (95% CI)

Favors WATCHMAN ←→ Favors Warfarin

![Graph showing 5-year outcomes after left atrial appendage closure with hazard ratios and event rates for various outcomes.](image)
Interventions in Heart Failure

- Left atrial decompression devices
- Ventricular partition devices
  - PARACHUTE, REVIVENT
- Alcohol septal ablation (HCM)
- Impella
- CardioMEMS
- Valve and Shunt procedures
Interatrial Shunts for Heart Failure
One-Year Outcomes After Transcatheter Insertion of an Interatrial Shunt Device for the Management of Heart Failure With Preserved Ejection Fraction

David M. Kaye, MD, PhD; Gerd Hasenfuß, MD; Petr Neuzil, MD; Martijn C. Post, MD; Robert Doughty, MD; Jean-Noël Trochu, MD, PhD; Adam Kolodziej, MD; Ralf Westenfeld, MD; Martin Penicka, MD; Mark Rosenberg, MD, PhD; Antony Walton, MD; David Muller, MD; Darren Walters, MD; Jorg Hausleiter, MD; Philip Raake, MD; Mark C. Petrie, MD; Martin Bergmann, MD, PhD; Guillaume Jondeau, MD; Ted Feldman, MD; Dirk J. van Veldhuisen, MD; Piotr Ponikowski, MD, PhD; Frank E. Silvestry, MD; Dan Burkhoff, MD, PhD; Christopher Hayward, MD
A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial

Gerd Hasenfuss, Chris Hayward, Dan Burkhoff, Frank E Silvestry, Scott McKenzie, Finn Gustafsson, Filip Malek, Jan Van der Heyden, Irene Lang, Mark C Petrie, John G F Cleland, Martin Leon, David M Kaye, on behalf of the REDUCE LAP-HF study investigators

[Graphs and charts showing data on cardiac output, NYHA functional class, MLWHF score, 6MWT, and exercise time at baseline and 6-month follow-up.]
Revised Balloon Pulmonary Angioplasty for Inoperable Patients with Chronic Thromboembolic Pulmonary Hypertension

Hiroki Mizoguchi, MD; Aiko Ogawa, MD, PhD; Mitsuru Munemasa, MD, PhD; Hiroshi Mikouchi, MD, PhD; Hiroshi Ito, MD, PhD; Hiromi Matsubara, MD, PhD

Pulmonary Balloon Dilation for CTEPH

Mizoguchi et al; Circ Cardiovasc Interv. 2012
FDA Gives Green Light to New Renal Denervation Pivotal Trial

A Study of the ReCor Medical Paradise System in Clinical Hypertension (RADIANCE-HTN)
Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial


Lancet 2017; 390: 2160–70

<table>
<thead>
<tr>
<th>Change in blood pressure from baseline to 3 months (mm Hg)</th>
<th>Renal denervation</th>
<th>Sham control</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>-5.0 (-9.9 to -0.2)</td>
<td>n=35</td>
<td>-0.5 (-3.9 to 2.9)</td>
<td>0.0414</td>
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<tr>
<td>-4.4 (-7.2 to -1.6)</td>
<td>n=36</td>
<td>-0.4 (-2.3 to 1.4)</td>
<td>0.0015</td>
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<td>-7.7 (-14.0 to -1.5)</td>
<td>n=37</td>
<td>-2.3 (-6.1 to 1.6)</td>
<td>0.0002</td>
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<td>-4.9 (-8.5 to -1.4)</td>
<td>n=41</td>
<td>-0.3 (-2.9 to 2.2)</td>
<td>0.0001</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Change in blood pressure</th>
<th>24-h SBP</th>
<th>24-h DBP</th>
<th>Office SBP</th>
<th>Office DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline blood pressure (mm Hg)</td>
<td>153.4</td>
<td>151.6</td>
<td>99.1</td>
<td>98.7</td>
</tr>
<tr>
<td>24-h SBP</td>
<td>162.0</td>
<td>161.4</td>
<td>99.9</td>
<td>101.5</td>
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A multinational clinical approach to assessing the effectiveness of catheter-based ultrasound renal denervation: The RADIANCE-HTN and REQUIRE clinical study designs

Laura Mauri, MD, MSc, Kazuomi Kario, MD, Jan Basile, MD, Joost Daemen, MD, Justin Davies, MBBS, MRCP, PhD, Ajay J. Kirtane, MD, Felix Mahfoud, MD, Roland E. Schmieder, MD, Michael Weber, MD, Shinsuke Nanto, MD, and Michel Azizi, MD, PhD Boston, MA; Tochigi, Hyogo, Japan; Charleston, SC; NL, the Netherlands; London, UK; New York, NY; Homburg/Saar, Erlangen, Germany; Cambridge, MA; and Paris, France

**RADIANCE SOLO Cohort (Essential HTN)**
- Discontinue HTN meds
- Wash-out 4 weeks
- Home BP Monitoring
- Elevated Daytime ABP ≥135/85 mmHg
- Elevated Daytime ABP <170/105 mmHg
- CTA/MRA Duplex
- RDN (n=73)
- Sham (n=73)

**RADIANCE TRIO Cohort (Resistant HTN)**
- Replace HTN meds with fixed dose, triple HTN combo
- Stabilize 4 weeks
- Home BP Monitoring
- Elevated Daytime ABP ≥135/85 mmHg
- CTA/MRA Duplex
- RDN (n=73)
- Sham (n=73)

**REQUIRE (Resistant HTN)**
- Stabilize on 3+ hypertensive medications 4 weeks
- Elevated 24 hour ABP ≥140 mmHg
- CTA/MRA Duplex
- RDN (n=70)
- Sham (n=70)

**Primary Endpoint**
- 2 Month Primary Endpoint: Ambulatory Blood Pressure Monitoring
- 2-6 Month: Pre-defined medication escalation if BP control not achieved
- 6 Month: Ambulatory Blood Pressure Monitoring & Medication Burden
- 12 Month: Ambulatory Blood Pressure Monitoring
- 24 & 36 Month: Clinical Visit and Office Blood Pressure Monitoring

- 3 Month Primary Endpoint: Ambulatory Blood Pressure Monitoring
- 3-6 Month: No change to medications
- 6 Month: Ambulatory Blood Pressure Monitoring
- 12 Month: Ambulatory Blood Pressure Monitoring
The Imager is the Conductor of the Intervention Orchestra
Interventional Cardiology Pivots

• Intervention will always have a role in ischemic heart disease
  • Routine in Acute Coronary Syndromes
  • Selective in Chronic Stable Angina based upon physiology

• Intervention has established a role in structural heart disease

• The role of intervention in structural disease will increase dramatically
  • Intervention will pivot in that direction

• Interventional Cardiology has a very bright future
Refined Balloon Pulmonary Angioplasty for Inoperable Patients with Chronic Thromboembolic Pulmonary Hypertension

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