Use of late enhancement for risk stratification in adult congenital heart disease

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Declaration of Interest

No conflicts of interest

British Heart Foundation grant for risk stratification in ACHD research.
Use of late enhancement for risk stratification in adult congenital heart disease

• Why we need better risk stratification tools
• LGE CMR fibrosis imaging can be applied to the RV
• Fibrosis relates to markers of clinical risk
• LGE CMR in ACHD and future potential for risk stratification in future and arrhythmia treatment
Risk stratification - An AICD for all?
Morbidity associated with ICDs in CHD – inappropriate therapies and lead fracture

Inappropriate shock:
- 10% SCD-HEFT
- 21% Paed ICD Registry
- 25% rTOF Leeds
- 30-40% rTOF Euroheart survey

‘14% lead failure’
Berul CI et al. JACC 2008

‘9.1% lead fracture in rTOF’
Low ACHD event rates

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event Rate (% per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD</td>
<td>10</td>
</tr>
<tr>
<td>DCM</td>
<td>9</td>
</tr>
<tr>
<td>HCM</td>
<td>1-4</td>
</tr>
<tr>
<td>ACHD – rTOF</td>
<td>1.2-1.8</td>
</tr>
</tbody>
</table>

The ACHD event rate LOW compared with all trials showing benefit of AICD in primary or secondary prophylaxis.
Conventional risk factors

- Systemic ventricular dysfunction (Systemic RV/Fallot/Fontan)
- Atrial arrhythmia (Systemic RV/Fallot/Fontan)
- Increased QRSd (>180ms TOF, >140ms systemic RV)
- Increased QTd (Systemic RV)
- Decreased \( VO_2 \) and Increased VE/VECO\(_2\) slope
- Decreased RVEF (Fallot)
- Increased RA and increased RVOT size (Fallot; ESC 2012 abstract P5539, Bonello et al.)
- Inducible VT (Fallot)
- Other (Fallot): PR, >10 years post ventriculotomy, late repair, impaired LVEDP/long axis function/LV diastolic function, signal averaged ECG, T wave alternans, heart rate variability
Late gadolinium enhancement CMR

• Could LGE CMR help risk assessment for arrhythmia and sudden cardiac death in ACHD?
LGE CMR – suggests fibrosis

Healthy myocardium, where there is little remaining gadolinium, is nulled and appears dark.

Scarred myocardium. Gadolinium lingers in extracellular spaces and appears bright and implies that myocardial fibrosis is present.
LGE CMR is a determinant of prognosis

• IHD - outcomes, response to revascularisation, drugs and pacing

• DCM
  Wu KC et al., Circ 2003, Assomul RG et al., JACC 2006, Lehrke S et al., Heart 2010

• HCM
  Bruder et al., JACC 2010, O’Hanlon R et al., JACC 2010

– ACHD?
– RV?
– Fontan, Systemic RV, TOF
RV LGE CMR practice and pitfalls

Imaging the RV can be challenging

– Sternal wires
– Epicardial fat
– Thin myocardium
Pathological correlation of RV LGE in systemic RV

Babu-Narayan, Ho, Sheppard, unpublished data
RV LGE and RWMA after Mustard operation for TGA
LGE CMR in the systemic RV after atrial redirection surgery

N=36, mean age 27 ± 7 years

RV LGE patients (22/36) were older (30 vs 22 years, p<0.001) and had:

• ↑ RVESVi (43 vs 35 ml/m², p=0.03)
• ↓ RVEF (57 vs 62 %, p=0.02)
• ↑ QRS duration (108 vs 97 ms, p=0.01)
• ↑ JTs (100 vs 76 ms, p= 0.01)
• ↑ QT dispersion (93 vs 72 ms, p=0.002)

• ↑ documented arrhythmia / syncope (9/22 with vs 1/14 without LGE, p=0.03)

Babu-Narayan et al., Circulation 2005
# TGA — atrial redirection and CCTGA

## Table 2
Clinical, magnetic resonance imaging, and exercise test results in patients with and without late gadolinium enhancement

<table>
<thead>
<tr>
<th>Variable</th>
<th>LGE (n = 14)</th>
<th>LGE Absent (n = 20)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of CTGA</td>
<td>6 (43%)</td>
<td>5 (25%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Age at test (yrs)</td>
<td>27 ± 4</td>
<td>23 ± 6</td>
<td>0.037</td>
</tr>
<tr>
<td>Age at repair (mo)**</td>
<td>10 ± 5</td>
<td>8 ± 4</td>
<td>0.22</td>
</tr>
<tr>
<td>History of arrhythmia</td>
<td>9 (64%)</td>
<td>3 (15%)</td>
<td>0.005</td>
</tr>
<tr>
<td>QRS (ms)</td>
<td>105 ± 12</td>
<td>97 ± 9</td>
<td>0.033</td>
</tr>
<tr>
<td>QTc (ms)</td>
<td>438 ± 41</td>
<td>416 ± 36</td>
<td>0.11</td>
</tr>
<tr>
<td>MRI findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV end-diastolic volume index (ml/m²)</td>
<td>121 ± 39</td>
<td>109 ± 32</td>
<td>0.33</td>
</tr>
<tr>
<td>RV end-systolic volume index (ml/m²)</td>
<td>80 ± 17</td>
<td>59 ± 16</td>
<td>0.0009</td>
</tr>
<tr>
<td>RV ejection fraction (%)</td>
<td>34 ± 7</td>
<td>45 ± 9</td>
<td>0.0006</td>
</tr>
<tr>
<td>RV mass index (g/m²)</td>
<td>91 ± 10</td>
<td>84 ± 7</td>
<td>0.02</td>
</tr>
<tr>
<td>RV wall stress index</td>
<td>87 ± 12</td>
<td>70 ± 9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>45 ± 10</td>
<td>48 ± 11</td>
<td>0.42</td>
</tr>
</tbody>
</table>

**Exercise test findings**

| Peak oxygen uptake (%)               | 47 ± 8       | 56 ± 7              | 0.001   |
| Peak oxygen pulse (%)                | 60 ± 11      | 69 ± 8              | 0.009   |
| Peak heart rate (%)                  | 88 ± 7       | 90 ± 10             | 0.52    |
| Oxygen respiratory quotient (%)      | 1.13 ± 0.3   | 1.14 ± 0.4          | 0.94    |
| Systolic blood pressure at rest (mm Hg)| 99 ± 13     | 102 ± 11            | 0.47    |

Data are expressed as mean ± SD.

**a** Data are reported and analyzed only for the 23 patients who underwent the Senning operation.

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Figure 2: Gadolinium-enhanced MRI short axis scan of the heart. The right ventricle is the interior ventricle in patients with atrial repair (left panel) and the posterior ventricle in patients with CCTGA (right panel). Three different patterns of LGE were observed: transmural LGE in (A), subendocardial in (B), and spotty LGE at the junction point between the right ventricle and the interventricular septum in (C).
RV LGE extent in Systemic RV

Figure 4. Correlation between extent of late enhancement (percentage of total RV myocardial mass) with age (a); RV end-systolic volume index (RVESVi) (b); RVEF (c); and QRS duration (QRSd) (d).

Babu-Narayan et al., Circulation 2005
Early insult or progressive change?

Multi-factorial

Pre-operative:
• cyanosis

Peri-operative surgical factors:
• Adequacy myocardial protection

Post-operative:
• chronic pressure overload
• ?excessive RVH
• demand supply ischaemia
Ventricular LGE in Fontan and NSVT

Rathod et al., JACC 2010
Repaired tetralogy of Fallot
LGE CMR patterns in TOF

N=92, mean age 32±11

• RV LGE ubiquitous in adults
• LV pathology is less common
• Evidence of fibrosis is:
  – in specific locations
  – to varying extent
  – sometimes in areas remote from surgical sites

Babu-Narayan et al., Circulation 2006
RV LGE and RWMA in Fallot

RVOT Aneurysm or akinesia are common

The RWMA relates to scarring

These also contribute to RVEDV and RVESV and hence RVEF

A major relative contributor to prolonged QRS duration and potential asynchrony

Davlouros et al., JACC 2002
Oosterhof et.al, Rad 2005, Babu-Narayan et al., Circ 2006, Wald et al., Circ 2009
Uebing et al., Circ 2008
RV LGE extent in TOF
RV LGE in rTOF

Babu-Narayan et al., Circulation 2006

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RV LGE extent correlated with sustained arrhythmia

Babu-Narayan et al., Circulation 2006

sonya@imperial.ac.uk
High negative predictive value for inducible VT

Figure 4. Sensitivity, specificity, and predictive values of scar and/or peak oxygen uptake <80% of maximum predicted value for inducibility of VA.

Tsai et al., AJC 2010
RVOT scar and VT

In collaboration with Sabine Ernst, RBH from Tetralogy of Fallot in Diagnosis and Management of ACHD, Gatzoulis, Daubeny and Webb, 2nd edition 2010
Site of VT at RV apex
3D LGE CMR
Left atrial scarring
Right atrial scarring

from Emerging Roles for Cardiovascular Magnetic Resonance in Adult Congenital Heart Disease Electrophysiology
Syed MA, Mohiaddin R, Magnetic Resonance Imaging of Congenital Heart Disease Springer-Verlag 2013 (in press)
Fontan fibrosis
Could LGE CMR be useful in risk stratification in ACHD?
Maybe!

So far studies are cross-sectional

Prospective studies are pending

Incremental value over conventional risk assessment unknown
Conclusions

• RV LGE imaging is feasible in ACHD

• Extent of LGE correlated with adverse ventricular mechanics and clinically significant arrhythmia in systemic RV, repaired TOF and Fontan patients

• Prospective data linking fibrosis to clinical outcomes are needed

• Longitudinal studies in ACHD patient groups are ongoing to investigate the predictive value of LGE imaging and its potential incremental value compared with conventional risk factors
Thank-you to patients and staff at Royal Brompton Hospital

Beatrice Bonello
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Yen Ho
Jenny Keegan
Philip Kilner
Wei Li
Raad Mohiaddin
Dudley Pennell
Mary Sheppard
Darryl Shore
Lorna Swan
Tom Wong
• SPARE SLIDES
METHODS
RV LGE considerations

• Partial volume effect
  – A single pixel in the thin RV wall may contain blood, contrast and fat
  – Chemical shift artefact related to differing values in the same pixel is more likely at low Ti in the RV

• Low spatial resolution leads to increased relative thickness

• Need good Ti choice, increased spatial resolution

• Systolic imaging useful

• Rapid acquisition with repeats and cross cuts
• 2D imaging

- Acquire data on alternate cardiac cycles
  - reduces sensitivity to heart rate variations and arrhythmias

- Adjusting the inversion time as the study progresses to maintain nulled normal myocardium

- Acquire each image over a 12 cardiac cycle breath-hold

- Spatial resolution limited to ~ 1.2mm x 1.8mm x 8mm

• 3D whole heart imaging

- Acquire data on each cardiac cycle
  - sensitive to heart rate variations and arrhythmias

- gadolinium washout as study progresses
  - Difficult to optimise inversion time and achieve nulled myocardium

- Imaging takes much longer therefore need free breathing
  - But if acquire during free-breathing with respiratory gating (not very efficient)

in collaboration with Jenny Keegan Senior CMR Physicist, RBH
RV LGE Methods – avoiding pitfalls

meticulous technique is essential when attempting to see RV pathology with LGE CMR

• Artefact reduction
  – Pre Saturation band over CSF
  – Meticulous TI adjustment
  – If 0.1 mmol/kg, >5 min
  – Most static part of cardiac cycle
  – Adjustment optimised for patient characteristics

• Proof of late gadolinium
  – Phase swap
  – Systolic and diastolic images

  • Careful comparison of LGE and corresponding cine images
  • Rapid, skilled acquisition for full coverage, including repeats as needed
RV LGE – phase swap, systole, artefact reduction

Red arrows point to superior and inferior RV insertion points and dark red arrow to full thickness RV anterior wall infarction / fibrosis.
<table>
<thead>
<tr>
<th>Region of RV</th>
<th>LGE score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Anterior wall of RVOT</td>
<td>(0-3)</td>
</tr>
<tr>
<td>2. Anterior wall of RV</td>
<td>(0-3)</td>
</tr>
<tr>
<td>3. Inferior wall of RV</td>
<td>(0-3)</td>
</tr>
<tr>
<td>4. RV surface of septum</td>
<td>(0-3)</td>
</tr>
<tr>
<td>5. VSD patch region</td>
<td>(0-3)</td>
</tr>
<tr>
<td>6. Trabecular bands</td>
<td>(0-3)</td>
</tr>
<tr>
<td>7. RV insertion points (each)</td>
<td>(0-1)</td>
</tr>
<tr>
<td><strong>Total RV score</strong></td>
<td><strong>(0-20)</strong></td>
</tr>
</tbody>
</table>

Figure 1.
Clinical Practice
The finding of very extensive LGE compared with other patients with other adults with that specific congenital heart disease may be a useful arbiter in otherwise borderline decisions.
• Secondary prophylaxis
  – Sustained symptomatic VT/VF/cardiac syncope
  – Including in addition to PVR?
• Primary prophylaxis
  – At least moderate LV dysfunction and QRSd 180ms
  – Mild LV dysfunction, QRS duration >180ms, impaired VO2 max and inducible VT with competent pulmonary valve where RV LGE is extensive
  – After successful VT ablation if very extensive scars
Guidelines
Recommendations for cardiovascular magnetic resonance in adults with congenital heart disease from the respective working groups of the European Society of Cardiology

Philip J. Kilner\textsuperscript{1*†}, Tal Geva\textsuperscript{2}, Harald Kaemmerer\textsuperscript{3‡}, Pedro T. Trindade\textsuperscript{4‡}, Juerg Schwitter\textsuperscript{5†}, and Gary D. Webb\textsuperscript{6‡}

\textsuperscript{1}CMR Unit, Royal Brompton Hospital, London SW3 6NP, UK; \textsuperscript{2}Division of Non-Invasive Imaging, Harvard Medical School, Children's Hospital Boston, Harvard Medical School, Boston, MA, USA; \textsuperscript{3}Department of Pediatric Cardiology and Congenital Heart Disease, Deutsches Herzzentrum, Munich, Germany; \textsuperscript{4}Cardiovascular Center, University Hospital, Zurich, Switzerland; \textsuperscript{5}University Hospital, Lausanne, Switzerland; and \textsuperscript{6}Cincinnati Children's Hospital, Cincinnati, OH, USA
8.3. Congenital Heart Disease

Recommendations

Class I

1. ICD implantation is indicated in patients with congenital heart disease who are survivors of cardiac arrest after evaluation to define the cause of the event and exclude any reversible causes. ICD implantation is indicated in patients who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*)

2. Patients with congenital heart disease and spontaneous sustained VT should undergo invasive hemodynamic and EP evaluation. Recommended therapy includes catheter ablation or surgical resection to eliminate VT. If that is not successful, ICD implantation is recommended. (*Level of Evidence: C*)

Class IIa

Invasive hemodynamic and EP evaluation is reasonable in patients with congenital heart disease and unexplained syncope and impaired ventricular function. In the absence of a defined and reversible cause, ICD implantation is reasonable in patients who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*)

Class IIb

EP testing may be considered for patients with congenital heart disease and ventricular couplets or NSVT to determine the risk of a sustained ventricular arrhythmia. (*Level of Evidence: C*)

Class III

Prophylactic antiarrhythmic therapy is not indicated for asymptomatic patients with congenital heart disease and isolated PVCs. (*Level of Evidence: C*)
ESC Guidelines for the management of grown-up congenital heart disease (new version 2010)

The Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC)

Endorsed by the Association for European Paediatric Cardiology (AEPC)

Authors/Task Force Members: Helmut Baumgartner (Chairperson) (Germany)*, Philipp Bonhoeffer (UK), Natasja M.S. De Groot (The Netherlands), Fokko de Haan (Germany), John Erik Deanfield (UK), Nazzareno Galie (Italy), Michael A. Gatzoulis (UK), Christa Gohlke-Baerwolf (Germany), Harald Kaemmerer (Germany), Philip Kilner (UK), Folkert Meijboom (The Netherlands), Barbara J.M. Mulder (The Netherlands), Erwin Oechslin (Canada), Jose M. Oliver (Spain), Alain Serraf (France), Andras Szatmari (Hungary), Erik Thaulow (Norway), Pascal R. Vouhe (France), Edmond Walma (The Netherlands).
RV/LV insertion points
RV LGE and RWMA
LV LGE in TOF

Babu-Narayan et al., Circulation 2006
RCA dissection in TOF
Restrictive RV physiology and extensive RV LGE

Restrictive Right Ventricular Physiology and Right Ventricular Fibrosis as Assessed by Cardiac Magnetic Resonance and Exercise Capacity After Biventricular Repair of Pulmonary Atresia and Intact Ventricular Septum

Xue-Cun Liang, MD; WWM Lam, MBBS; EWY Cheung, MMedSc; AKP Wu, MBBS; Sophia J. W Yiu-Fai Cheung, MD
Division of Pediatric Cardiology, Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong, China (Liang, E.W.Y. Cheung, Wong, Y.-F. Cheung); Department of Radiology, Queen Mary Hospital, Hong Kong, China (Lam, Wu)

Clin. Cardiol. 2010

N=27, mean age 16.5+-5.6, 22/27 restrictive